1983 Annual Report

Pharmaceutical Manufacturers Association Foundation, Inc.

A GOOD YEAR

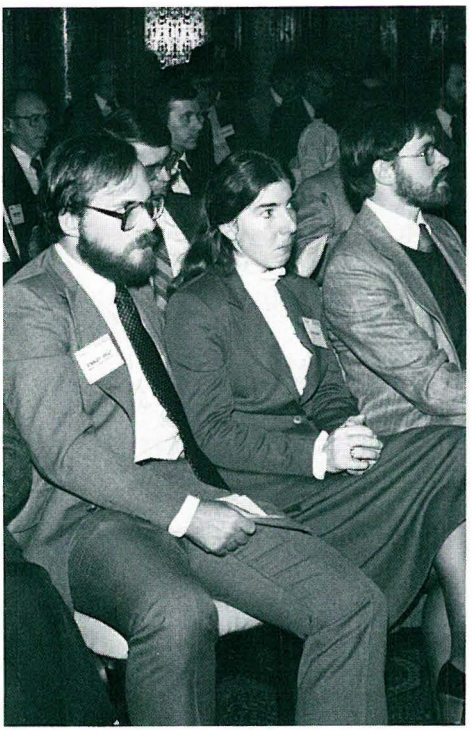
It is particularly gratifying that during a period of increased demand on the private sector for support of academic science that the needs of the PMA Foundation have not been overlooked by its contributors. In 1983, the rate of increase in contribution income was the highest ever enjoyed by the Foundation. This has allowed the Foundation to make additional awards under some of its programs. The hope of continuing increased levels of support allows the Foundation once again to look towards improvements in its program scope and levels of support. The Foundation is positioned better now to maintain its current programs in sound financial positions. Also, there are other scientific disciplines on which the pharmaceutical industry depends which the Foundation may be able to support as resources increase. New program development, even on the small scale of the Foundation's programs, takes a fair amount of increased funding.

On other fronts, the PMA Foundation has enjoyed a banner year as well. Reports from the awardees who are concluding their grants continue to relate very productive experiences. The number of former awardees who continue in academic science is exceptionally high, attesting to the careful review process by the Foundation's excellent advisory committees. One important measure of the vitality of the Foundation's programs is the degree of success enjoyed by those concluding Foundation support to find continuing sources of support. It is not unusual, for instance, for an individual who had a research starter grant to report that the preliminary data generated from the grant formed the basis for a funded National Institutes of Health or National Science Foundation grant. In addition, some of those who have had salary support from the Foundation have gone on to receive more senior awards such as the Burroughs-Wellcome Scholars Award, Research Career Development Awards from the federal government or investigator awards from national voluntary health agencies.

The Foundation awardees represent a sizeable accumulation of very talented scientists. For programs which in most cases offer two or three awards a year, the total number of awardees is impressive—over 600 individuals supported through the nine current programs. Only by offering finely-tuned programs aimed specifically at needs not otherwise being met by public or private funding agencies and an increasing base of financial support from the Foundation's contributors has the success enjoyed by the Foundation been possible. Support through the PMA Foundation is in addition to what individual companies continue to provide directly to academic science. It has been the task of the Foundation's Board of Directors and advisory committees to select wisely ways to use the funds entrusted to the Foundation.

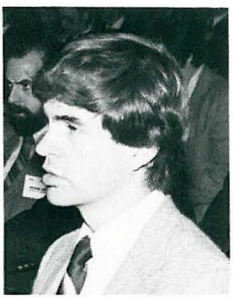
While there is a justifiable pride in what has been accomplished, there are many needs still to be addressed. The PMA Foundation has many choices open to it in terms of program development. Yearly reviews of the funding guidelines have not given any cause for major shifts in the program directions which currently guide the Foundation's efforts. Therefore, the ability to finance new program efforts will, in large measure, be dependent upon increased resources. The Foundation is hopeful that this will be possible.

INFORMATION UPDATE

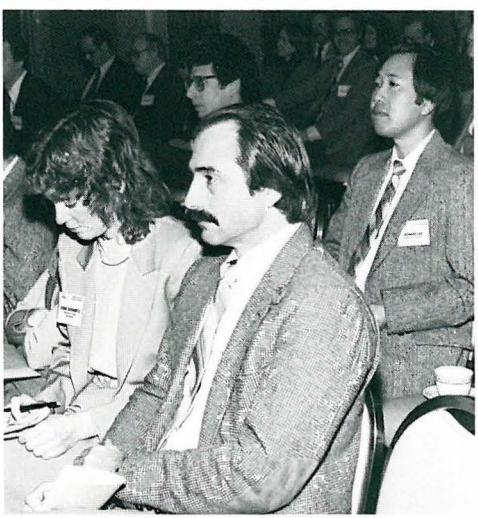


A meeting of the Foundation awardees was held in December. An excellent keynote address at the general session set the tone for the meeting. Dr. Eugene Braunwald, Hersey Professor of the Theory and Practice of Medicine, and Chairman of the Department of Medicine, Harvard Medical School, discussed "On the Trail of a New Orally Active Inotropic Agent: Will Digitalis Ever Be Replaced?". Dr. Albert Bowers, Vice Chairman of the PMA Foundation Board of Directors, welcomed the awardees and committee members and gave an update on 1984 awards which had been authorized the prior day. The general session concluded in mid-morning to enable three subgroups of awardees to convene in special sessions to hear papers from current and past awardees.

In the afternoon, the three groups again met separately. The clinical pharmacology subgroup heard Dr. John A. Oates, Professor of Medicine and Pharmacology, Vanderbilt University, speak on the "Application of Pharmacologic Principles to Early Studies on Drugs in Man: A Pathway to Discovery". The pharmacology-morphology subgroup devoted the afternoon to a presentation by Dr. Robert J. Van Ryzin, Director of Preclinical Safety Assessment Department, Sandoz, Inc. on the "Application of Transmission and Scanning Electron Microscopy in Pharmaceuti-



cal Research and Development", and a poster session. The basic pharmacology subgroup heard a presentation by Dr. A. J. Hopfinger, Director of Drug Design and Sweetner Research, G. D. Searle & Co., on the "Application of Computers and Computer Graphics in Molecular Design in the Drug Industry". Part of their afternoon was devoted also to presentations by selected awardees.



In August, 1983, a meeting was held with the research starter grantees and the advanced predoctoral fellows in pharmacology and toxicology during the Fall meeting of the American Society for Pharmacology and Experimental Therapeutics. The speaker was Dr. George Koelle, Distinguished Professor of Pharmacology, University of Pennsylvania, who spoke on "The Evaluation of Pharmacology and Its Implications for Teaching".

These meetings continue to provide opportunities for the advisory committee members to gain perspectives on how well the various progams are achieving their goals. For the awardees, the meetings provide unique opportunities for exchange of information in an informal atmosphere. Many of the awardees have indicated that this characteristic is a big 'plus' of the meeting. A common comment is that the meetings foster a real sense of camaraderie among the awardees.

ACTIVITIES

Since its formation in 1965, approximately $14.7 million has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects and educational programs. Of this amount, slightly more than $4.1 million has been used to support research and approximately $10.0 million has gone into educational awards. The remaining $500,000 has provided financial assistance for scientific meetings, along with a small portion for publications.

Virtually all of the 1983 grants and awards were made within programs sponsored by the Foundation. These include three faculty level programs of salary and fringe benefit support, four fellowship programs—two postdoctoral, one at the advanced predoctoral level and one at the medical student level—plus a program of research starter grants for beginning investigators wishing to move into areas of independent research. An award to assist in expediting the research efforts of new clinical pharmacology units or those with new directors is also available. The exceptions this year were the grants in the field of postmarketing monitoring of drugs.

Through these programs in 1983, the Foundation assisted an additional 51 individuals. All of these individuals were helped at a crucial time in their professional development. The Foundation has, in its slightly more than eighteen years of existence, helped about 800 individuals through its research and educational support programs.

EDUCATION AND TRAINING PROGRAMS

To further its objectives in the field of education, the PMA Foundation sponsors four programs in clinical pharmacology, one in the combined field of pharmacology-morphology, one in pharmacology or toxicology, one in basic pharmacology and one in toxicologic pathology.

CLINICAL PHARMACOLOGY
Faculty Awards in Clinical Pharmacology

The four clinical pharmacology programs provide opportunities at the student, fellow and faculty levels. Through the Faculty Development Awards in Clinical Pharmacology program, the Foundation makes two-year awards to medical schools for salary and fringe benefits support of full-time junior faculty members. The Foundation has set a ceiling of $30,000 on the amount of its participation in total yearly salary and fringe benefits for any candidate.

With the awards scheduled to begin July 1, 1984, 67 individuals have been supported under this program since 1967.

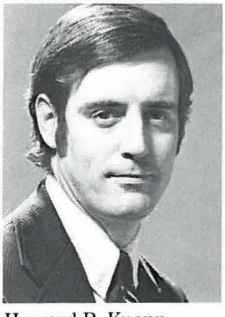
Recipients of the four awards to begin July 1, 1984 are:

Marc S. Ernstoff, M.D.

• Marc S. Ernstoff, M.D., Assistant Professor of Medicine, Department of Internal Medicine/Medical Oncology, Yale University School of Medicine. Dr. Ernstoff's research is concerned with biological response modifiers. Interferon, the most potent of the biologic response modifiers, has shown limited activity in a wide range of cancers during early phase I studies. The actual mechanism of its antitumor effect is still not known, with evidence both for direct effect on the tumor cell as well as an immunostimulant. Dr. Ernstoff has propossed to investigate the possible mechanisms of action of interferon both *in vitro* and *in vivo*. The pleiotropic effects of the interferons range from antiviral effects and growth inhibition in a range of normal and neoplastic tissue to potent immunomodulatory effects. Dr. Ernstoff will be evaluating: (1) the immunomodulatory effects by studying (a) delayed type hypersensitivity of known and *de novo* antigens, (b) natural killer function, (c) T cell subsets, (d) macrophage Fc dependent phagocytosis; (2) the induction of oligo 2′5′ adenylate synthetase which is the first of many interferon inducible enzymes; and (3) direct cytotoxic effects on tumor cells. The rationale for the design of clinical trials will be based on this data and conducted at the Yale Comprehensive Cancer Center. During these trials which are ongoing at Yale, Dr. Ernstoff will assess the pharmacokinetics of the interferons as well as defining the range of toxicity.

Marilynn C. Frederiksen, M.D.

• Marilynn C. Frederiksen, M.D., Assistant Professor, Department of Obstetrics and Gynecology, Northwestern University Medical School. Dr. Frederiksen's research is directed to issues of drug therapy in the pregnant patient. She will direct her attention to specific pharmacokinetic studies in pregnant patients towards the end of securing the information needed to develop therapeutic guidelines for many of the drugs that are used during pregnancy. Dr. Frederiksen's work will focus on two populations of pregnant women who must receive drug therapy during pregnancy. In the first project, theophylline pharmacokinetics will be defined in asthmatic patients for whom theophylline therapy is required. In the second project the kinetics of anticonvulsant drugs will be studied in pregnant epileptic patients, beginning with phenytoin.



Howard R. Knapp, Ph.D., M.D.

• Howard R. Knapp, Ph.D., M.D., Assistant Professor, Department of Pharmacology and Medicine, Vanderbilt University School of Medicine. Dr. Knapp's research will focus on the clinical pharmacology of eicosapentaenoic acid (EPA). Epidemiologic data suggests that populations which consume large amounts of EPA (e.g. Eskimos and coastal Japanese) have a low incidence of atherosclerosis and numerous clinical studies are being carried out to see whether enrichment of the Western diet with this prostaglandin precursor fatty acid might prevent atherosclerosis and its complications. No studies on the effects of feeding EPA on the many pathways of arachidonic acid metab-

olism in man have been performed, however, so the net *in vivo* result of such dietary manipulation on the production of prostanoids with antagonistic functions (e.g. pre-aggregatory thromboxame vs anti-aggregatory prostacyclin) is unknown. Dr. Knapp will study the change in both lipoxygenase and cyclooxygenase metabolites *in vivo* during dietary supplementation with EPA in volunteers. These studies will help to determine whether altering the prostaglandin precursor pool in man by increasing EPA intake would be a useful pharmacologic approach in the treatment of a number of disease states, such as hypertension and asthma.

Charles E. Riggs, Jr., M.D.

- Charles E. Riggs, Jr., M.D., Assistant Professor, Department of Internal Medicine, University of Iowa College of Medicine. Dr. Riggs' research is focussed on basic and clinical research in the pharmacology of antineoplastic agents, primarily anthracycline antibiotics. His current interests during the award include studies on interactions of anthracyclines with other drugs, cellular pharmacology of daunorubicin and Adriamycin, clinical pharmacokinetics of daunorubicin in patients with acute leukemia and infections, and clinical pharmacokinetics of Adriamycin in combination with biological modifier compounds. Drug interaction studies are being carried out by utilizing an *in vitro* enzyme system incorporating cytochrome P450 reductase, which is capable of metabolizing anthracyclines to aglycones. Agents which modify cytochrome P450 reductase activity are being investigated for their abilities to alter anthracycline metabolism. These results will be correlated to pharmacokinetic and toxicological studies on anthracyclines in man.

  Biological modifier compounds, including 13-cis-retinoic acid, dimethyl sulfoxide, vitamin E, amphotericin B, and others, are being tested for their abilities to alter anthracycline metabolism, to alter anthracycline uptake and metabolism by neoplastic cells *in vitro*, and to augment the cytotoxicity of anthracyclines. Dr. Riggs has a special interest in defining pharmacological aberrations in daunorubicin disposition in patients with acute leukemia and infections in efforts to increase their response rate to chemotherapy. The goal of these trials is to define beneficial combinations and intereactions which may result in improved therapeutic indices and broader spectra of activity of anthracyclines.

Those individuals whose awards began July 1, 1983 are:

- Frank L. Douglas, M.D., Ph.D., Assistant Professor, Department of Medicine, Committee on Clinical Pharmacology, University of Chicago.

- Garret A. FitzGerald, M.Sc., M.D., Assistant Professor, Departments of Medicine and Pharmacology, Vanderbilt University School of Medicine.

- David W. Nierenberg, M.D., Assistant Professor, Departments of Medicine and Pharmacology & Toxicology, Dartmouth Medical School.

- John W. Turk, M.D., Ph.D., Assistant Professor, Departments of Medicine and Pharmacology, Washington University School of Medicine.

Those individuals who entered their second year of awards in July, 1983 are:

- Brian B. Hoffman, M.D., Assistant Professor, Departments of Medicine and Pharmacology, & Toxicology, Dartmouth Medical School.
- Janice B. Schwartz, M.D., Instructor, Section of Cardiology and Section of Hypertension and Clinical Pharmacology, Baylor College of Medicine.
- Jack P. Uetrecht, M.D., Ph.D., Assistant Professor, Departments of Pharmacology and Medicine, Vanderbilt University School of Medicine.

Those individuals who concluded their awards in 1983 are:

- Ka Kit Hui, M.D., Assistant Professor, Department of Medicine, University of California, Los Angeles, School of Medicine.
- Brian Leyland-Jones, M.B., M.S., Assistant Professor, Department of Pharmacology and Medicine, Cornell University Medical College: now at National Cancer Institute, NIH.
- John R. Luderer, M.D., Assistant Professor, Departments of Medicine and Pharmacology, Pennsylvania State University College of Medicine.
- Richard D. Mamelok, M.D., Assistant Professor of Medicine and Pharmacology, Department of Medicine, Stanford University School of Medicine.
- James A. Nathanson, M.D., Ph.D., Associate Professor, Department of Neurology, Harvard Medical School.
- Juerg Reichen, M.D., Assistant Professor, Department of Medicine, University of Colorado School of Medicine.
- Branimir Sikic, M.D., Assistant Professor of Medicine, Division of Oncology, Stanford University School of Medicine.
- Alastair J. J. Wood, M.D., Ch.B., M.R.C.P., Associate Professor, Departments of Medicine and Pharmacology, Vanderbilt University School of Medicine.

Geographical distribution of Foundation awards under the "Faculty Development Awards in Clinical Pharmacology" program, 1967-1984.

● One
○ More than One

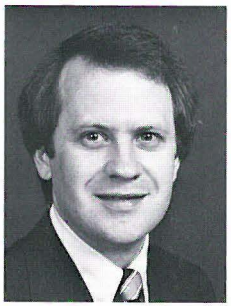
Fellowships for Careers in Clinical Pharmacology

The second program 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 the basic pharmacologic sciences needed to complement his clinical skills.

The program was amended in 1982 to allow 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 1984 may elect to ask that the fellowship be for July 1985 or July 1986.

The first awards under this program were made in 1973. Since that time, 32 fellowships have been awarded.

Nancy Jo Braden, M.D.



Gregory G. Gaar, M.D.

Celine M. Stahl, M.D.

Recipients of the three fellowships beginning July 1, 1984 are:

- Nancy Jo Braden, M.D., Fellow, Department of Pediatrics, The Ohio State University, College of Medicine. Dr. Braden's research project explores the mechanism of bronchodilation by xanthine derivatives, using a tissue bath preparation of guinea pig and human tracheal rings. She will also have some clinical teaching responsibilities during the fellowship.

- Gregory G. Gaar, M.D., Fellow, Departments of Pediatrics and Pharmacology, University of Arizona College of Medicine. Dr. Gaar's research efforts will center on adrenergic receptor mechanisms. Evidence is accumulating that theophylline, a methylxanthine, raises the concentrations of serum catecholamines, even in therapeutic concentrations. If so, it should affect vascular alpha- and beta-adrenergic receptors when administered on a chronic basis. Dr. Gaar plans to study these effects with both receptor radioligand binding assays and concomitant muscle function studies to allow correlation of adrenergic receptor changes and vascular smooth muscle function after long-term theophylline administration.

- Celine M. Stahl, M.D., Fellow, Department of Pharmacology and Medicine, Cornell University Medical College. Dr. Stahl's research will be in the area of clinical pharmacology of antiviral drugs. She will study the use of antiviral agents as selective substrates for viral specific enzymes and the selective accumulation of antiviral drugs into cells infected with herpesviruses. Dr. Stahl will exploit this selectivity of antiviral drugs as a possible tool for rapid viral diagnosis and as a means to study herpesvirus infections. She will also study the pharmacology and efficacy of antiviral drugs in man.

Those individuals whose fellowships began July 1, 1983 are:

- Bonnie S. Glisson, M.D., Fellow, Division of Medical Oncology, Department of Medicine, University of Florida College of Medicine.

- Andrew Guterman, M.D., Ph.D., Fellow, Department of Neurology, University of Miami School of Medicine.

- Jonathan R. Wispe, M.D., Fellow, Departments of Pediatrics and Pharmacology, University of Iowa College of Medicine.

Those individuals whose fellowships entered the second year of the award on July 1, 1983 are:

- Howard R. Lee, M.D., Fellow, Department of Pharmacology, University of Arizona College of Medicine.

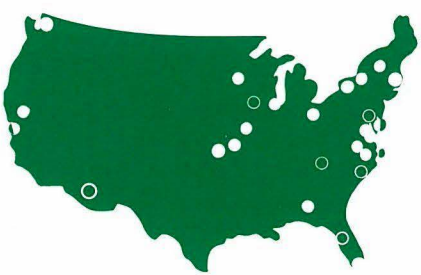
- Mark S. Smith, M.D., Fellow, Clinical Pharmacology Division, Duke University School of Medicine.

Those individuals whose awards concluded in 1983 are:

- Eric P. Brass, M.D., Fellow, Division of Clinical Pharmacology, University of Washington School of Medicine. Dr. Brass resigned his fellowshop a year early to assume a position as Assistant Professor in the Division of Clinical Pharmacology at the University of Colorado.

- Richard P. Day, M.D., Fellow, Department of Medicine, University of Washington School of Medicine.

- Thomas A. Kent, M.D., Fellow, Department of Psychiatry, University of Kansas College of Health Sciences and Hospital. Dr. Kent resigned his fellowship six months early to assume a position in the Department of Neurology at the University of Texas Medical Branch at Galveston.



Geographical distribution of Foundation awards under the "Fellowships for Careers in Clinical Pharmacology" program, 1973-1984.

● One
o More than One

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, provides students an opportunity to spend up to one year full-time conducting an investigative project in pharmacology-clinical pharmacology. The minimum period of the award is three months. It is hoped that by having students become involved in investigative projects at a point when career choices are still relatively flexible, they will opt for research careers in clinical pharmacology. Fifty-three awards have been made since 1974.

The four students whose fellowships began July 1, 1983 are:

- Harley I. Kornblum, University of California School of Medicine at Irvine, has a twelve month fellowship. His principal advisor is Dr. Frances M. Leslie, Assistant Professor, Department of Pharmacology. Mr. Kornblum's research is directed towards an examination of the role of endogenous compounds and their receptors in the ontogeny of the mammalian nervous system. The opioid system appears early in the developing brain and changes dramatically throughout the developmental period. Opioid peptide and receptor systems which predominate in the fetal nervous system become minor components in the adult.

  Several theories have been proposed in order to explain this phenomenon. These include: (1) that endogenous opioids and their receptors play a role in neuronal guidance and organization; (2) that certain opiate systems serve as developmental precursors to others; and (3) that the early appearance of opioids and their receptors are merely the result of random genetic expression. Mr. Kornblum will attempt to distinguish among these theories by applying autoradiographic, immunocytochemical and developmental techniques to:
  (1) determine the developmental changes in the localization of beta-endorphin, enkephalin and their associated receptors in rat striatum.
  (2) the disruption of the endogenous opioid system in fetal and early postnatal development and assessment of biochemical morphologic and functional changes in rat striatum.

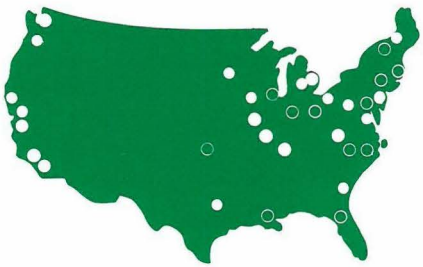
- Howard L. Lippton, Tulane University School of Medicine, has an eight month fellowship. His principal advisor is Dr. Phillip J. Kadowitz, Professor, Department of Pharmacology. Mr. Lippton's research is aimed at improving the understanding of the influence of the parasympathetic nervous system on the pulmonary

vascular bed. It is known that the pulmonary vascular bed is innervated by both divisions of the autonomic nervous system and that stimulation of the sympathetic system increases vascular resistance and decreases vascular compliance. Little is known about responses to parasympathetic stimulation. In addition to the presence of the adrenergic and cholinergic transmitters, it is now known that autonomic nerves store and release small peptide hormones. Vasoactive intestinal peptide (VIP) is a small peptide that could be released along with acetylcholine as a co-transmitter. It is, therefore, possible that acetylcholine and/or VIP could act directly on vascular smooth muscle in the lung or on adrenergic terminals to modulate the release of the adrenergic transmitter. Therefore, responses to vagal stimulation and the effects of VIP will be investigated using newly modified techniques to maintain pulmonary blood flow, systemic hemodynamics and left atrial pressure constant. Mr. Lippton anticipates that these studies will improve the understanding of the roles of the adrenergic, the cholinergic and the peptidergic system in the regulation of the pulmonary vascular bed and this understanding may lead to new forms of therapy for pulmonary hypertensive disorders.

• Jaroslav G. Vostal, Wayne State University School of Medicine has a twelve month fellowship. His principal advisor is Dr. Roy B. McCauley, Associate Professor of Pharmacology. Mr. Vostal's research is directed at determining the steps involved in the degradation of the blood clotting factor prothrombin. Prothrombin is a serum glycoprotein which contains sialic acid and glactose as the terminal and penultimate residues of the carbohydrate substituent. Other serum proteins containing this carbohydrate configuration have been shown to be desialated, then recognized by asialoglycoprotein receptors in the parenchymal cells of the liver and finally degraded to amino acids and small peptides within the hepatocyte. Mr. Vostal would like to determine whether prothrombin undergoes similar processing by comparing the *in vivo* half-lives and distributions of ^{125}I derivatives of the native and asialoprotein in experimental animals. If as he suspects, prothrombin is considerably more stable than asialoprothrombin, he will study the interaction of the asialo-derivative with isolated hepatocytes and, if indicated, Kupffer cells. Those *in vitro* studies will entail experiments describing the recognition, accumulation and preliminary studies concerning the degradation of asialoprothrombin.

• Aeron D. Wickes, University of California, School of Medicine, San Diego, has a three month fellowship. His principal advisor is Dr. Stephen B. Howell, Associate Professor of Medicine. Mr. Wickes' research is aimed at studying the pharmacokinetics of intraperitoneal administrations of hexamethylmelamine in oil emulsion vehicles. Hexamethylmelamine is a drug with estab-

lished activity against ovarian carcinomas, which tend to remain localized in the peritoneum. Oil emulsion vehicles provide a depot to concentrate the drug in the peritoneum yet limit clearance from that compartment and so limit systemic drug levels and toxicity. Drug concentrations will be assayed by high pressure liquid chromatography. Solubility and stability of the drug in saline and in the oil emulsion vehicles emulphor and intralipid will be determined. Using these vehicles, the drugs will be administered to mice via the intraperitoneal route and the peritoneal and systemic concentrations and relative clearance rates followed. The activity of the drug against ovarian tumor lines in soft agar colony forming assay will also be investigated.



Geographical distribution of Foundation awards under the "Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology" program, 1974-1983.

● One
○ More than One

Clinical Pharmacology Unit Support

This program is designed to assist directors of clinical pharmacology units established within the prior two years of the award and for units with a change in directorship during that period. The grant provides a total of $50,000 which may be used at any time during a three year period. The program is aimed at providing some initial funds to enable the unit's research efforts to be maintained until other research grants are obtained. The first grants were made in 1978. The total number of awards made to date is nine.

The award beginning July 1, 1983 was made to:

● Section of Clinical Pharmacology, Department of Pharmacology, Tulane University School of Medicine. Juan J. L. Lertora, M.D., Ph.D., Associate Professor of Medicine and Pharmacology, was appointed Head of the Section as of January 1, 1981. The research interests of the unit emphasize cardiovascular clinical pharmacology. Studies underway include: inotropic actions of some common antiarrhythmic drugs; the effects of intravenous N-acetylprocainamide on blood pressure and myocardial performance in human subjects; clinical studies to characterize the pharmacodynamics and pharmacokinetics of new beta blockers in human subjects; and basic computer-assisted techniques for pharmacokinetic analysis.

Geographical distribution of Foundation awards under the "Developmental Grant for Clinical Pharmacology Units" program, 1978-1983.

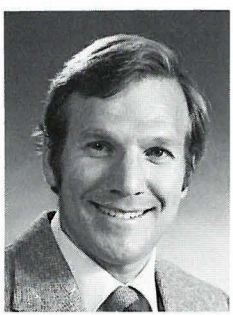
● One
○ More than One

BASIC PHARMACOLOGY
Faculty Development Awards in Basic Pharmacology

The purpose of these Faculty Development Awards is to strengthen basic pharmacology by helping maintain existing academic capability and, ultimately, to expand it by enlarging the faculty base. To accomplish these goals, support is provided to full-time junior faculty members committed to careers in pharmacology who give promise of outstanding accomplishments.

The first awards, which are for a two-year period, were made in 1973. The program provides salary and fringe benefits. The Foundation has set a ceiling of $25,000 on the amount of its participation in the total yearly salary and fringe benefits for any candidate beginning with the 1980 awards. The total number of awards made to date is 34.

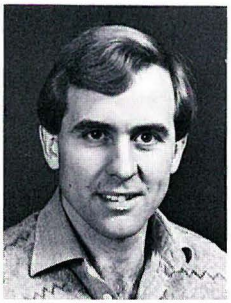
Those who received awards beginning July 1, 1984 are:



James R. Halpert, Ph.D.

● James R. Halpert, Ph.D., Assistant Professor, Department of Pharmacology & Toxicology, University of Arizona College of Pharmacy. Dr. Halpert's research involves the biochemical toxicology of chloramphenicol and congeners. This proposal will focus on: 1) the precise mechanism of and the pharmacological and toxicological consequences of the suicide inactivation of specific isozymes of rat and rabbit cytochrome P-450 by chloramphenicol; and 2) the enzymatic pathways by which metabolites of chloramphenicol capable of causing bone marrow toxicity are formed. The enzyme inactivation studies will provide information about the relationship between the structure and function of cytochrome as well as serve as the basis for the design of inhibitors of specific isozymes of the cytochrome. Specific inhibitors could be used diagnostically to assess the role of various isozymes of cytochrome P-450 in mediating chemical toxicity and therapeutically to protect against toxicity. Identification of the enzyme systems responsible for the formation of myelotoxic nitroreduction products of chloramphenicol is important for two

reasons. First, it suggests a means of protecting against the toxic response by modifying the activity of the enzymes in question. Second, it may allow the identification of individuals in the human population who run an excess risk of suffering adverse effects when exposed to nitro-aromatic compounds. Since such chemicals are found not only in drugs but as environmental contaminants and industrial chemicals, understanding of the mechanism by which chloramphenicol causes bone marrow toxicity may be of great relevance for the toxicology of a number of other compounds as well.


Kevin M. Mullane, Ph.D.

• Kevin M. Mullane, Ph.D., Assistant Professor, Department of Pharmacology, New York Medical College. Dr. Mullane's research is focussed on myocardial ischemia. Myocardial ischemia initiates an inflammatory response in which the invading neutrophils exacerbate the myocardial damage. Neutrophils elaborate and release a variety of potentially proinflammatory mediators including lipoxygenase products of arachidonic acid, platelet-activating factor, oxygen metabolites (free radicals) and proteolytic enzymes, which can induce lipid peroxidation, endothelial cell damage, lysosomal enzyme release and myocellular injury. Interactions between the leukocytes and platelets, with increased generation of some mediators, may enhance the myocardial damage. Specifically, he will be examining how selective inhibition or modulation of these different facets of the inflammatory process may provide a therapeutic basis for limiting ischemia-induced myocardial injury, without compromising the healing process, which is the main function of the inflammatory response.


Nancy Zahniser, Ph.D.

• Nancy Zahniser, Ph.D., Assistant Professor, Department of Pharmacology, University of Colorado School of Medicine. Dr. Zahniser's research will focus on characterization, localization and regulation of dopamine receptors and their associated physiological functions in rat brain. Functions which appear to be modulated or regulated by dopamine receptors in the striatum and which will be investigated include stimulation-evoked release of neurotransmitters and stimulation or inhibition of adenylate cyclase activity. These studies should allow correlation of functional measurements with receptor binding and, thus, help to identify particular dopamine receptor subtypes. Additionally, the relationship between the binding of [3] H-nomifensine to putative recognition sites for the dopamine uptake pump and the high affinity uptake of [3]H-dopamine will be examined. The receptors will be localized using lesioning techniques and quantitative autoradiography. Once particular dopamine receptors have been identified, the regulation of these receptors and the functional consequences of such regulation by administration of dopamine receptor agonists and antagonists (neuroleptics) will be examined. A long-term goal of these studies is to compare the consequences of perturbation of central nigrostriatal, mesolimibic and mesocortical dopaminergic systems by neuronal degeneration and drug therapy.

Those who began their awards July 1, 1983 are:

- Keith T. Demarest, Ph.D., Assistant Professor, Department of Pharmacology & Toxicology, Michigan State University.
- Edward Hawrot, Ph.D., Assistant Professor, Department of Pharmacology, Yale University School of Medicine.
- G. Allen Nickols, Ph.D., Assistant Professor, Department of Pharmacology, Southern Illinois University School of Medicine.

Those who entered the second year of their awards on July 1, 1983 are:

- Walter R. Dixon, Ph.D., Assistant Professor, University of Kansas School of Pharmacy.
- Jerry A. Farley, Ph.D., Assistant Professor, Department of Pharmacology and Toxicology, University of Mississippi Medical Center.
- Gregory A. Weiland, Ph.D., Assistant Professor, Department of Pharmacology, New York State College of Veterinary Medicine.

Those whose awards concluded in 1983 are:

- Allyn C. Howlett, Ph.D., Assistant Professor, Department of Pharmacology, St. Louis University School of Medicine.
- Edwin K. Jackson, Ph.D., Associate Professor, Department of Pharmacology, Vanderbilt University School of Medicine.
- Kenneth P. Minneman, Ph.D., Assistant Professor, Department of Pharmacology, Emory University School of Medicine.

Geographical distribution of Foundation awards under the "Faculty Development Awards in Pharmacology" program, 1978-1984.

● One
○ More than One

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

The program, offered initially in 1977, is designed to assist those candidates who have one or two years remaining in their predoctoral training, the time during which they are engaged in their thesis research.

The fellowship program provides a stipend of $5,040 a year, payment of tuition and $500 a year for incidentals directly associated with the thesis research preparation. The program has been funded to provide eight fellowships each year. However, one extra fellowship was authorized for 1984. A total of 72 fellowships has been made since 1977.

Those who received fellowships which begin between January and August 1984 are:

- Margaret Jean Chandler, Department of Pharmacology, University of Oklahoma Health Science Center. Her advisor is Dr. John M. Carney, Associate Professor. Ms. Chandler's research is a study of the pharmacological and structural changes following stroke in the gerbil.

- Nancy J. Duda, Department of Pharmacology/Toxicology, Michigan State University, College of Human Medicine. Her advisor is Dr. Kenneth E. Moore, Professor. Ms. Duda's research is focussed on regulation of hypothalamic 5-hydroxytryptaminergic neuronal activity.

- Brent Finley, Department of Pharmacology/Toxicology, Washington State University College of Pharmacy. His advisor is Dr. Garold S. Yost, Assistant Professor of Pharmaceutical Chemistry. Mr. Finley's research is aimed at studying the isolation and characterization of ethanol induced UDP-glucuronyl transferase.

- Lynn E. Heasley, Department of Medicine, University of California, San Diego, School of Medicine. His advisor is Dr. Laurence L. Brunton, Assistant Professor. Mr. Heasley's research examines the characterization of PGS sensitive cyclic AMP extrusion from pigeon erytarocytes.

- John M. May, Department of Pharmacology, Emory University School of Medicine. His advisor is Dr. Kenneth P. Minneman, Assistant Professor. Mr. May's research focuses on the characterization of β-adrenergic receptor occupancy and response in rat vas deferens.

- Donna A. Robertson, Department of Pharmacology, Cornell University Medical College. Her advisor is Dr. Roberto Levi, Professor. Ms. Robertson's research is aimed at endogenous mediators of human cardiac dysfunction.

- Thomas E. Smithgall, Department of Pharmacology, University of Pennsylvania School of Medicine. His advisor is Dr. Trevor M. Penning, Assistant Professor. Mr. Smithgall's research involves the studies of indomethacin-sensitive 3 -hydroxysteriod dehydrogenases, a major class of drug metabolizing enzymes.

• Ethan Will Taylor, Department of Pharmacology/Toxicology, University of Arizona College of Pharmacy. His advisor is Dr. David L. Nelson, Assistant Professor. Mr. Taylor's research deals with the development and characterization of new agents selective for subtypes of serotonin (5-HT).

• Marina E. Wolf, Department of Pharmacology, Yale University School of Medicine. Her advisor is Dr. Robert H. Roth, Professor of Pharmacology and Psychiatry. Ms. Wolf's research is aimed at the role of protein carboxyl methylation in dopamine autoreceptor-mediated modulation of dopamine synthesis and release.

Geographical distribution of Foundation awards under the "Fellowships for Advanced Predoctoral Training in Pharmacology/Toxicology" program, 1978-1984.

• One
○ More than One

Fellowship Awards in Pharmacology-Morphology

The aim of this program is to advance understanding of drug action through the discovery of specifically related cellular and tissue changes; and, concurrently, to uncover associations between normal and abnormal function in particular tissue and cellular structure.

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. Since 1968 when the first fellowships were offered, fifty-five awards have been made.

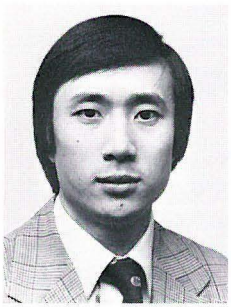
The program requires that the candidate be qualified primarily either in a morphologic specialty or in pharmacology. However, training to be achieved under the fellowship in the complementary discipline need not be formal. The candidate's program should result in a familarity with a new discipline approach by using his primary discipline as a medium for acquiring the second.

Theresa Branchek, Ph.D.

The recipients of the fellowships which began July, 1983 are:

• Theresa Branchek, Ph.D., Postdoctoral Fellow, Department of Anatomy and Cell Biology, College of Physicians and Surgeons of Columbia University. Dr. Branchek's research concentrates on analyzing neural receptors for serotonin. She has already charac-

terized a binding site on enteric neurons that has receptor-like properties and now would like to determine if the ^{3}H-serotonin binding activity that she has studied by radioligand-filtration and radioautographic assay is actually a neural serotonin receptor. This will be done by quantitatively evaluating the actions of serotonin and its structural analogues on electrophysiologically identified neurons in the guinea pig's myenteric plexus. Neurons will be recorded with intracellular microelectrodes; potential agonist drugs will be applied to the neural surface by pressure or iontophoresis while anagonists will be added to the bath. Antagonists will be evaluated against applied serotonin or the evoked serotonergic slow epsp. Physiological results will be correlated with the ability of agents to displace ^{3}H-serotonin in radioligand binding assays. After recording from them, neurons will be injected with horseradish peroxidase (HRP) and the preparations will be perfused with ^{3}H-serotonin. The HRP will identify the cell that had been recorded from and the ^{3}H-serotonin with EM radioautography to reveal serotonergic synapses. This will help establish the physiological significance of the data by assuring that serotonin receptor characterization will be done only on cells that are anatomically as well as physiologically identified, and that actually receive a serotonergic input.



Christopher Lau, Ph.D.

• Christopher Lau, Ph.D., Postdoctoral Fellow, Department of Anatomy, Medical College of Pennsylvania. Dr. Lau's efforts are devoted to developing ultrastructural correlates of drug and hormone actions. His research program calls for the use of pharmacologic agents to determine the central and peripheral influences regulating the development of the sympatho-adrenomedullary system. Various pharmacologic manipulations will be accompanied by a broad spectrum of morphological analyses, including histochemistry, immunocytochemistry, electron microscopy and computer-aided stereology. The events which occur during the functional and structural maturation of the sympatho-adrenomedullary system are complex and involve virtually every system in the body. Dr. Lau's multi-disciplinary approach to this program represents the most effective way to dissect out these events.

Dorie W. Schwertz, Ph.D.

• Dorie W. Schwertz, Ph.D., Research Fellow, Department of Pathology and Department of Medicine, University of Texas Health Science Center, San Antonio. Dr. Schwertz is examining the hypothesis that the critical event in aminoglycoside-induced renal damage may be altered phosphatidylinositol metabolism and associated structural changes in the proximal tubule brush border membrane (BBM). This hypothesis is based on facts that aminoglycosides: (1) bind intensely to phosphatidylinositol and polyphosphoinositides in the BBM; (2) have the potential to in-

hibit phospholipase C activity; and (3) are associated with renal myeloid body formation, phosphatidylinositol phospholipidosis and BBM phospholipiduria. Aminoglycoside-induced alterations in proximal tubule BBM would interfere with vital membrane transport, barrier and homeostatic functions. She will study the influence of *in vitro* aminoglycoside exposure on a BBM-associated phosphatidylinositol specific phospholipase C, previously characterized in the laboratory in which she is doing her research. Aminoglycoside-induced alterations in BBM and cell morphology will be correlated with changes in phosphatidylinositol and other glycerolipid metabolism in three model systems including suspensions of isolated proximal tubules, cultured pig kidney proximal tubule cells, and the rat *in vivo*.

Those who entered the second year of their fellowships in 1983 are:

- Mark G. Currie, Ph.D., Postdoctoral Fellow, Department of Pharmacology, Washington University School of Medicine.
- Linda M. Marshall-Carlson, Ph.D., Postdoctoral Fellow, Department of Biochemistry, University of Texas Health Science Center, San Antonio.

Those individuals whose fellowships concluded in 1983 are:

- Barbara J. Crain, Ph.D., M.D., Assistant Professor, Department of Pathology, Duke University Medical Center. Dr. Crain resigned her fellowship early in order to accept her current position.
- Stanley R. Jolly, Ph.D., Postdoctoral Fellow, Department of Pharmacology, University of Michigan Medical School. Dr. Jolly has since accepted a position in the Department of Pharmacology at the Medical College of Georgia.
- Iris Nemhauser, Ph.D., Postdoctoral Fellow, Department of Pharmacology, College of Physicians and Surgeons of Columbia University.
- Howard, Ratech, M.D., in the Departments of Pathology and Medicine, New York University Medical Center during his fellowship. Dr. Ratech is now affiliated with the City of Hope, Department of Anatomic Pathology, Duarte, California.

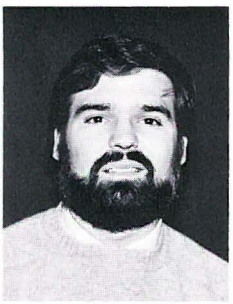
Geographical distribution of Foundation awards under the "Fellowship Awards in Pharmacology-Morphology" program, 1968-1983.

● One
○ More than One

Faculty Awards in Toxicologic Pathology

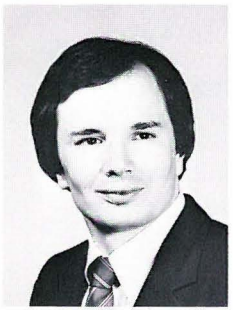
This is a new program to attract scientists interested in analyzing, reviewing and questioning where appropriate, the present state of the art in the field of toxicology. To examine the degree of interest the academic community may have, a junior faculty program was authorized for a three year period. The goal of the program is to attract veterinary and comparative pathologists who are interested in spending two years in drug toxicology research. During the pilot period, a total of four awards were made.

Those individuals whose awards begin July 1, 1984 are:



R. Gayman Helman, D.V.M., Ph.D.

- R. Gayman Helman, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Pathobiology, University of Tennessee College of Veterinary Medicine. Dr. Helman's research is directed towards the development of a more mechanistic approach to evaluate acute dermatotoxicity. Rabbit, guinea pig, and rat skins will be used in whole organ skin culture to evaluate acute toxicity produced by a number of chemicals of varying irritancies. Currently, he is using cellular enzyme leakage as well as histopathology and alterations in DNA, protein, and glucose metabolism as cytotoxicity endpoints in the culture system. Additionally, specific studies are planned to define the contributions of the various adnexal structures to the pathogenesis of cutaneous toxicity.



Richard K. Jensen, D.V.M., Ph.D.

- Richard K. Jensen, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Michigan State University, College of Veterinary Medicine. Dr. Jensen's research involves studying the toxicity and carcinogenicity of lipophilic xenobiotics. He is using purified polybrominated biphenyl congeners as models for studying the promoting and inhibitory effects of polyhalogenated hydrocarbons in chemical carcinogenesis. Dr. Jensen is also investigating how lipophilic xenobiotics such as polybrominated biphenyls alter the homeostatis and metabolism of essential nutrients such as vitamin A. The overall goal of the research is to understand the long term carcinogenic and toxic effects of lipophilic environmental contaminants.

Those who received awards beginning July 1, 1983 are:

- Gerald G. Long, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Microbiology, Pathology and Public Health, Purdue University School of Veterinary Medicine.

- Glen K. Miller, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Colorado State University College of Medicine and Biomedical Sciences.

Geographical distribution of Foundation awards under the "Faculty Awards in Toxicologic Pathology" program, 1982-1984.

- ● One
- ○ More than One

RESEARCH GRANTS

An important aspect of the PMA Foundation effort has been the support of fundamental research in drug toxicology. Between 1966 and 1971, 26 research grants of relatively large amounts for two to five years were awarded, principally to established investigators to either extend existing research or to provide "seed" monies to follow a promising lead. In 1971, a change in emphasis within the Foundation's programs shifted the bulk of the funds into educational support programs and, therefore, less into research. The Foundation does, however, continue to accept requests for 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.

Geographical distribution of Foundation general research grants, 1966-1983.

- ● One
- ○ More than One
- ★ Outside U.S.

Research Starter Grants

As part of the change of emphasis in 1971 which sought to direct monies more toward the development of the individual, a program of Research Starter Grants was initiated. These grants are intended to provide financial support for beginning investigators. The program allows for approximately 20 research starter grants each year. The first awards were made in 1972. A total of 311 research starter grants have been made, including the 21 awards beginning January 1, 1984.

The recipients of the grants beginning January 1, 1984 are:

JOHN R. BABSON, Ph.D.
University of Minnesota
Medical School

BRUCE P. BEAN, Ph.D.
University of Iowa
School of Medicine

JAMES P. BENNETT, JR., M.D., Ph.D.
University of Virginia
College of Medicine

STEPHEN M. BEVERLEY, Ph.D.
Harvard University
School of Medicine

MARC C. BROWNING, M.D.
Wake Forest University
Bowman Gray School of Medicine

DUNCAN C. FERGUSON, V.M.D., Ph.D.
Cornell University, New York State
College of Veterinary Medicine

WILLIAM T. GERTHOFFER, Ph.D.
University of Nevada
School of Medicine

JAMES R. HALPERT, Ph.D.
University of Arizona
School of Pharmacy

PETER C. ISAKSON, Ph.D.
University of Virginia
Medical School

GARY S. JOHNSON, D.V.M., Ph.D.
University of Missouri
College of Veterinary Medicine

ROBERT E. KRAMER, Ph.D.
University of Tennessee
College of Medicine

OSCAR L. LASKIN, M. D.
Cornell University
Medical College

JONATHAN MAYBAUM, Ph.D.
University of Michigan
College of Medicine

DAVID C. PERRY, Ph.D.
George Washington University
School of Medicine

ROBIN W. ROCKHOLD, Ph.D.
University of Mississippi
School of Medicine

DANIEL D. SAVAGE, II, Ph.D.
University of New Mexico
School of Medicine

JOHN A. SCHRIEFER, JR., Ph.D.
Ponce School of Medicine
Puerto Rico

BRUCE A. STANTON, Ph.D.
Yale University
School of Medicine

JEANNINE S. STROBL, Ph.D.
West Virginia University
School of Medicine

JOHN B. WATKINS, III, Ph.D.
Indiana University
School of Medicine

STANLEY K. WONG, Ph.D.
College of Osteopathic Medicine
of the Pacific

Review of the need of the 23 research starter grantees whose awards began January 1, 1983 for a second year of the awards resulted in 11 of them having their awards continued. These are:

JOSEPH COHEN, Ph.D.
Howard University
Graduate School of Arts & Sciences

KEITH T. DEMAREST, Ph.D.
Michigan State University
College of Osteopathic Medicine

WILLIAM C. ELLIOTT, M.D.
State University of New York,
Syracuse, College of Medicine

FRANK J. GORDON, Ph.D.
Emory University
School of Medicine

TREVOR M. PENNING, Ph.D.
University of Pennsylvania
School of Medicine

STEVEN L. PETERSON, Ph.D.
Texas A. & M University
College of Medicine

YASUKO RIKIHISA, Ph.D.
Virginia Polytechnic Institute
School of Veterinary Medicine

ROBERT E. SHERIDAN, JR., Ph.D.
Georgetown University
School of Medicine/Dentistry

ROBERT E. HRUSKA, Ph.D.
State University of New York,
Buffalo, School of Pharmacy

RICHARD S. JOPE, Ph.D.
University of Alabama,
Birmingham,
School of Medicine/Dentistry

JOHN W. TURK, M.D., Ph.D.
Washington University
School of Medicine

Geographical distribution of Foundation awards under the "Research Starter Grants" program, 1972-1984.

- One
- More than One
- ★ Puerto Rico

OTHER SUPPORT

A special fund was made available to the PMA Foundation to provide support for projects in postmarketing drug monitoring. The Foundation decided to focus on providing a methological grant. The intent of the grant is to fund studies aimed at extending or developing imaginative, feasible methodologies to systematically generate information about prescription medications as they are customarily used in the non-hospitalized population, with particular application to the study of adverse reactions.

Considerable interest was shown in the program and selection was most difficult.

Those who were chosen for one-time grant are:

- Ann Karen Henry, Pharm.D., Assistant Professor, Department of Pharmacy Practice, College of Pharmacy, and Adjunct Assistant Professor, Department of Family Community Medicine, College of Medicine, University of Arizona, as principal investigator. Other staff on the project are Janet H. Senf, Ph.D., Research Associate, and Ronald S. Fischler, M.D., Assistant Professor, both of the Family and Community Medicine Department of the College of Medicine, and J. Lyle Bootman, Ph.D., Associate Professor, Department of Pharmacy Practice, College of Pharmacy. The project will run for twelve months beginning May 1, 1984, supported by a grant of $66,372.

The goals of the project are to evaluate direct-patient-to-data-center reporting of information and to develop the methodology for collecting the data. The patients involved in the study will be

drawn from the patient load of the University of Arizona Family Practice Office, which is a teaching clinic for a family medicine residency program. The patients come to the Family Practice Office from outside referral, as enrollees in prepaid health care programs, one of which is the Arizona Health Care Cost Containment System (AHCCCS). Patients enrolled in AHCCCS must use the services of the same provider group for one year or assume the financial responsibility for their own care. Consequently, patients in this system are rarely lost to follow-up and all care provided is recorded in the program records. The study group anticipates about 1,250 to 1,500 patient contacts for evaluation, follow-up and analysis.

A special prescription blank will be designed for the study, using a three copy NCR pad. Those patients agreeing to participate will receive one copy of the prescription blank on which the patients will record symptoms they develop while on the drug, the onset and duration of the symptoms and other medical information which the physician will provide to the patient. The form will be sent by the patients at the appropriate time to the data collection center.

The following questions will be examined:

(1) Will patients consistently report adverse drug reactions?
(2) Can patients report accurately their health status as reflected in diagnosis, laboratory findings and physical findings?
(3) Does patient reporting of adverse reactions produce more complete information than that obtained from physician reporting? Adverse drug effects documented by physicians in the medical records will be compared with those reported directly by the patient to the data collection center.

• Holly L. Mason, Ph.D., Assistant Professor of Pharmacy Administration, principal investigator, and Robert K. Chalmers, Ph.D., Professor of Pharmacy Practice, co-investigator, Purdue University School of Pharmacy and Pharmacal Sciences. Other staff on the project from the Indiana University School of Medicine include B. L. Martz, M.D., Professor of Medicine, and Jeffrey C. Darnell, M.D., Associate Professor of Medicine. The grant is for $151,186 for a two year period beginning May 1, 1984.

The methodology is designed to examine the possible role of community pharmacists in gathering information on prescription drugs from patients. Pharmacists in Indiana will be trained to employ a broadly applicable drug therapy monitoring process for participating patients receiving prescriptions for selected study medications. The monitoring process will include an initial patient medication history, a minimum of three follow-up drug experience screening interviews with the patient and follow-up contacts with the patient's physician.

A Project Coordinating Committee composed of pharmacist and physician experts in the area of drug therapy monitoring and research methodology will guide each of the processes. It is expected that the project will generate information on the reliability of pharmacist data-recording procedures and the level of acceptance by patients and physicians of such an approach.

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 support of fundamental research on drugs and programs for training personnel in basic and clinical pharmacology and toxicology.

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. 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.

(4) Funds to cover entertainment costs.

In 1971, the Board of Directors authorized a major shift in program emphasis. While Foundation support of research continues, such support is to be primarily available in a redirected fashion such as the Research Starter Grants program discussed on page 21.

In line with this change of emphasis, the Foundation is expanding support within its current educational programs as outlined in the Education and Training Programs Section on page 4.

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

FOUNDATION FINANCES

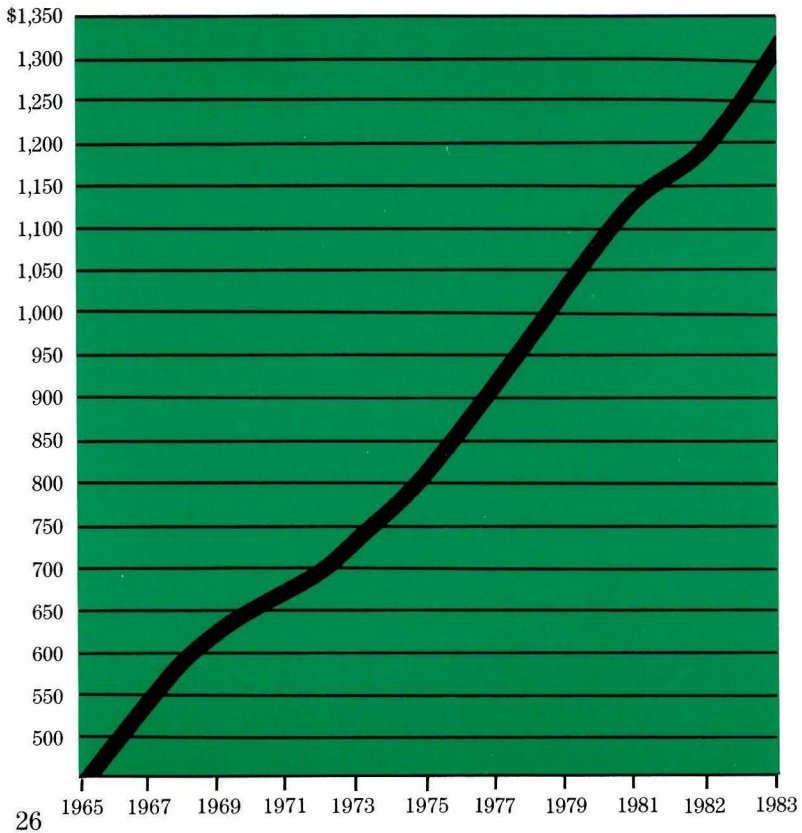
The total income of the Foundation in 1983 was $1,583,135. Of this amount, $1,335,970 came from contributions. The balance of $247,165 came from investments, gain on sale of stock, and refunds of unexpended balances from grants.

Contributions were received from approximately four out of every five PMA Member Firms. Contributions were also received during 1983 from individuals and other groups in the health field.

Grants, Foundation-sponsored programs, special meetings and other expenses for 1983 amounted to $1,421,070. Of this total, $1,116,021 represent expenditures for grants. There was a fund balance of $1,833,816 as of December 31, 1983. 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, 1983, the contingency liability for 1984 was approximately $1,143,292.

The Foundation's financial position as of December 31, 1983 has been audited by the Washington, D.C. accounting firm of Buchanan & Company.

PMA Foundation
Contribution Income
1965-1983 (Thousands)



Statement of Income and Expenditures For the Year Ended December 31, 1983

Income

Contributions—Note A	$1,335,970
Income From Investments	142,930
Gain on Sale of Stock	96,855
Miscellaneous Income	7,380
TOTAL INCOME	$1,583,135

Expenditures

Grants—Note B	
Clinical Pharmacology Faculty Awards	$ 263,357
Clinical Pharmacology Fellowships	105,358
Clinical Pharmacology Unit Support	70,735
Basic Pharmacology Faculty Awards	149,632
Medical Student Research Fellowships	17,500
Pharmacology-Morphology Fellowships	81,383
Research Starter Grants	260,000
Advanced Predoctoral Fellowships	133,056
Toxicologic Pathology Faculty Awards	25,000
Second International Clinical Pharmacology Conference	10,000
	$1,116,021
Administrative, December Awardee Meeting and Special Toxicology Workshop Expenses	305,049
TOTAL EXPENDITURES	$1,421,070
Excess of income over expenditures	$ 162,065
General fund balance at January 1, 1983	$1,671,751
General fund balance at December 31, 1983	$1,833,816

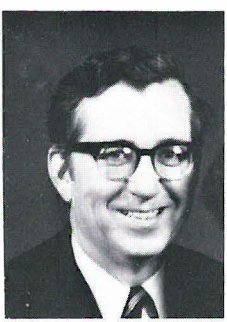
Note A—The Foundation received contributions of $72,300 prior to December 31, 1983 which the Foundation considered applicable to 1984 and, therefore, not recorded as income in 1983.

Note B—In addition to the amounts shown, the Foundation has committed itself, subject to annual review, to make certain grants. At December 31, 1983, the amounts still to be disbursed with respect to these grants amounted to approximately $2,082,979, with approximately $1,143,292 of this to be disbursed during 1984.

ORGANIZATION AND ADMINISTRATION

The PMA Foundation operates through its officers and four advisory committees. In April, 1983, Irwin Lerner, President and Chief Executive Officer, Hoffmann-La Roche Inc., was re-elected Chairman of the Board. Albert J. Frey, Ph.D., Chairman, Sandoz, Inc., was re-elected Vice Chairman, and Dale E. Wolf, Ph.D., Vice President, Biochemicals, E.I. du Pont de Nemours & Company was elected Secretary-Treasurer. In September, 1983, Dr. Dale E. Wolf resigned from the Board of Directors and in August, 1983, Dr. Albert J. Frey died. Named to replace these individuals as officers were Albert Bowers, Ph.D., Chairman, President and Chief Executive Officer, Syntex Corporation, as Vice Chairman, and William R. Miller, President, Pharmaceutical and Nutritional Group, Bristol-Myers Company, as Secretary, Treasurer. Thomas E. Hanrahan is President and Irwin C. Winter, M.D., Ph.D., serves as staff consultant.

Irwin Lerner



Thomas E. Hanrahan

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Albert Bowers, Ph.D., Vice Chairman
William R. Miller, Secretary, Treasurer
Thomas E. Hanrahan, President

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Syntex Corporation
Palo Alto, California

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Pharmaceutical Manufacturers Association
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Executive Committee Member and Member of the Board of Directors
Johnson & Johnson
New Brunswick, New Jersey

DALE E. WOLF, Ph.D.[5]
Vice President, Biochemicals
E. I. du Pont de Nemours & Company
Wilmington, Delaware

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[1]Died August, 1983
[2]Named to the Board of Directors October, 1983
[3]Term Expired April, 1983.
[4]Named to the Board of Directors April, 1983.
[5]Resigned September, 1983.

Albert J. Frey, Ph.D.

In Memoriam

Dr. Albert Frey served on the PMA Foundation Board of Directors with distinction from May, 1976 until his death on August 8, 1983. His insight into the issues which came before the Foundation added immensely to their resolution. It is with a deep sense of loss that we note his death.

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[6]Term Expired April, 1983
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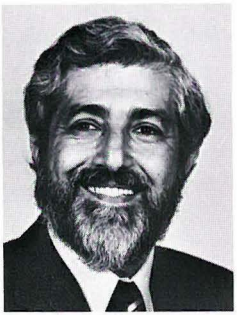

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