PROJECTIONS '73

1973 Annual Report
Pharmaceutical Manufacturers
Association Foundation, Inc.

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Projections '73

Complete assessment of the contribution of the PMA Foundation to the biomedical sciences since its founding in mid-1965 is yet to be made. But the constructive events which highlighted the Foundation's year in 1973, its activities and record of assistance to scientists and faculty members, encourage brightly optimistic projections of even greater heights of achievement during the rest of its first decade of service.

Around us, the hum of activity, as the nation prepares for the 1976 Bicentennial Celebration of its Independence, is a reminder of another anniversary that will fall in that same year. For in 1976, the PMA Foundation will be beginning its second decade of unique, trail-blazing service along the frontiers of biomedical sciences. Recognition of the years of effort and planning which have gone into the PMA Foundation will not occupy the center of the historical stage for the Bicentennial. But in a quiet way, the PMA Foundation's anniversary will be a milestone for earnest and symbolic meaning in the biomedical community.

During the past year, 56 more students, fellows, and faculty members were assisted by the Foundation. Each of these individuals is committed to or shows the potential for a productive career in a discipline which is vital to assure future progress in the science of therapeutics. Also, the ever necessary ingredient of funds, which enables the Foundation to offer its programs, reached an all time high in 1973, reflecting the continuing commitment of the pharmaceutical industry to the aspirations and purposes of this undertaking.

Other accomplishments, building on earlier Foundation efforts, demonstrate progress towards the longer range goals and add to the optimistic hopes for the years ahead. In the field of clinical pharmacology, three former holders of faculty awards are now directors of clinical pharmacology units, while another is scheduled to assume similar responsibilities in 1974. Many of the early pharmacology-morphology fellows are actively continuing this interdisciplinary interest in their academic settings, establishing themselves in ways which serve as models for those future doctoral level investigators who seek to make a unique contribution in this field. Also, reports are received frequently that former recipients of research starter grants have successfully secured larger and long term research support, thus building on the results of the work financed by the Foundation's starter grant—precisely the aim of the program.

The PMA Foundation expects that these gains will continue and accelerate with the passage of time, providing the basis for a thorough examination of the first decade of Foundation efforts. While 10 years is a relatively brief period in the life of a philanthropic organization, it does represent a bench mark for assessing programs and weighing their relevance in the current scientific world, as well as an opportunity to pause and look back and measure the progress that has been made since its inception.

In initiating its programs, the PMA Foundation sought ways to use the funds available as innovatively as possible. If the federal government or private groups with larger resources have been attracted to the areas pioneered by the Foundation, the job will be considered well done.

During the next two to three years, the Foundation's programs will reach scores of additional clinicians and scientists who will provide the future leadership in pharmacology and clinical pharmacology. The discernible impact these programs already have had will undoubtedly become even more meaningful.

The future financial growth upon which all of these efforts vitally depend is expected to continue. And, most importantly, the cohesive element which brings all of the components together—the counsel which the advisory committees provide the Board of Directors in deciding the scientific priorities for the PMA Foundation—will continue to be of the same high quality which has brought the Foundation to the level of success it currently enjoys.

These are the reasons for the optimistic forecast—the reasons for great expectations as the PMA Foundation looks towards the beginning of its second decade of service.

Information Update

For the fourth time since 1969, the recipients of awards under the PMA Foundation's postdoctoral educational programs and members of the Foundation's advisory committees spent an enlightening day and a half discussing developments in the fields of pharmacology-morphology and clinical pharmacology. This year, the awardees were joined by the recipients of awards from the newly offered faculty awards in pharmacology and fellows in clinical pharmacology programs. This meeting, held December 3-4, 1973, in New York City again provided the opportunity for those attending the Foundation sessions to meet with the members of the PMA Board of Directors.

Daniel C. Searle, Chairman of the PMA Foundation Board of Directors, welcomed the awardees to the meeting and recounted some of the achievements of the Foundation. At a session, moderated by Dr. I. C. Winter, member of the Scientific Advisory Committee, the subject of the scientific basis for carcinogenesis testing in drug development was discussed. The Foundation was fortunate in having two well known experts in the field leading the discussion. Harold M. Peck, M.D., Executive Director, Department of Safety Assessment, Merck Sharp & Dohme and Charles J. Kensler, Ph.D., Senior Vice President, Arthur D. Little, Inc. Dr. Peck discussed the design of experiments to detect carcinogenic effects of drugs. Dr. Kensler discussed general considerations surrounding the entire issue of the need for such testing and the relevance of the presence of carcinogenic activity at the animal level to the clinical situation.

The meeting then divided into two groups. The clinical pharmacologists spent part of the day discussing presentations of current research by four of the awardees. The rest of the day was devoted to discussion of approaches to teaching clinical pharmacology and the objectives of a training program in clinical pharmacology.

John A. Oates, M.D., Chairman of the Foundation's Clinical Pharmacology Advisory Committee and Professor of Medicine and Pharmacology, School of Medicine, Vanderbilt University moderated the session dealing with the research reports. Walter Modell, M.D., Emeritus Professor of Pharmacology, Cornell University Medical College moderated the session dealing with the teaching of clinical pharmacology.

He began the session by describing the **Cornell Conferences on Therapy,** a classic example of an approach to the teaching of this discipline.

The pharmacology-morphology fellows and advisory committee members spent their program time in a number of workshops on methodologies used in this interdisciplinary field. In past years, the format had called for a series of research reports from each fellow, followed by discussion by the group. This year, the methodological techniques used by the fellows were identified and the group divided along these lines. Three simultaneous workshops were developed – one on the use of electron microscope, another on teratology and teratogenecity and the last on histochemical techniques. Each fellow was allotted about 15 minutes to describe how he uses the particular method in his research, while also describing the design of the pharmacologic component in his research.

To enhance the value of each workshop, a number of senior investigators took part in the discussions. In the workshop on electron microscopy, discussions were guided by Don W. Fawcett, M.D., Harvard University; Walter F. Riker, Jr., M.D., Cornell University Medical College; Leonard L. Ross, Ph.D., Medical College of Pennsylvania; and Irwin C. Winter, M.D., Ph.D., G. D. Searle & Co.

In the workshop on teratology, the discussions were aided by Leon Z. Saunders, D.V.M., Ph.D., Smith Kline & French Laboratories; Joseph F. Borzelleca, Ph.D., Medical College of Virginia; and Hank P. K. Agersborg, Jr., Ph.D., Wyeth Laboratories

The workshop on histochemical techniques was moderated by David A. Wood, M.D., Cancer Research Institute, San Francisco; George B. Koelle, M.D., Ph.D., University of Pennsylvania; and Samuel W. Thompson, II, D.V.M., CIBA-GEIGY Corporation.

These yearly meetings provide the opportunity to assess the directions each program is taking. From the spirited discussions during the program, it appears that the goal of expanding academically based research and training is being accomplished very well through current programs.








Activities

Since its formation, more than $4.8 million has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects and educational programs. Of this amount $1.6 million has gone to support research and about $2.8 million to educational awards. The remaining $400,000 has been used to sponsor scientific meetings, including a small portion for publications.

Workshops and Conferences

Assistance for the first workshop in drug metabolism was authorized by the Foundation in late 1965, and since then particularly pertinent meetings have continued to receive financial aid. However, with expansion of the Foundation's educational and training programs, support of meetings has necessarily decreased.

Clinical Pharmacology. An award of $13,250 was made to the Drug Research Board, National Academy of Sciences – National Research Council for support of a workshop on biochemical approaches to clinical pharmacology. This was the second such workshop supported by the Foundation. The meeting was held at the University of California, San Francisco, July 16-20, 1973. Dr. Kenneth L. Melmon, Chief, Division of Clinical Pharmacology, was Chairman. As with past workshops with laboratory sessions, the attendence was limited to 40 participants. An Admissions Committee of the Drug Research Board selected the participants from among the applicants.

Carcinogenesis. An award of $8,000 was made to the Drug Research Board, National Academy of Sciences – National Research Council, for support of a Conference on Carcinogenesis Testing in the Development of New Drugs, held at the Academy May 23-25, 1973. The Conference reviewed the question of the clinical relevance of carcinogenesis testing and reviewed the present status of the methodology available. The meeting was under the chairmanship of Dr. Leon Golberg, Scientific Director, Institute of Experimental Pathology and Toxicology, Albany Medical College.

Education and Training Programs

To further its objectives in the field of education, the PMA Foundation sponsors three programs in clinical pharmacology, one in the combined field of pharmacology-morphology and one in basic pharmacology.

Clinical Pharmacology. The three clinical pharmacology programs provide educational 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 benefit support of fulltime junior faculty members. The level of support is variable and is in keeping with the existing salary structure of the applicant university.

With the awards scheduled to begin July 1, 1974 a total of 31 individuals have been supported under this program since its inception in 1967. While the award is for a two-year period, a third year of support is available to those awardees who, at the end of their first year, show sufficient progress and need to warrant support for the third year.

Recipients of new awards, which begin July 1, 1974 are:

- Terrence F. Blaschke, M.D., will be appointed Assistant Professor of Medicine, Stanford University School of Medicine as a result of the award. He will examine possible mechanisms underlying clinically significant drug-drug interactions by searching for changes in drug kinetics or protein binding of drugs during such interactions. A second area of research is in the area of drug-disease interactions. The influence of altered hepatic function and variations in hepatic blood flow on the disposition of highly metabolised drugs will be investigated by pharmacokinetic techniques.

Terrence F. Blaschke, M.D.

- Dr. Blaschke will also assist in the consultative and teaching services of the Division of Clinical Pharmacology and in the development of a clinical facility to provide plasma or blood drug concentrations.
- Robert L. Capizzi, M.D., Assistant Professor of Internal Medicine and Pharmacology, Yale University School of Medicine. Studies will be carried out in the area of interactions between antineoplastic drugs on normal and tumor cells. These studies will be conducted in experimental tumor models in cell culture and in leukemic mice and with human leukemia cells.

Robert L. Capizzi, M.D.

A second major area of research is the development of a screening system which will identify mutagenic chemicals in the environment. Since the carcinogenic process may involve mutations, the identification of mutagenic chemicals is important.

Teaching responsibilities include the instructing of physicians, medical students and other personnel in the laboratory and clinical pharmacological aspects of antineoplastic drugs. He will also use part of the period of the award to engage in formal study in biochemical genetics.

- Elsa-Grace V. Giardina, M.D., Associate in Medicine, College of Physicians and Surgeons, Columbia University. Dr. Giardina's interests are in the area of pharmacokinetic behavior of anti-arrhythmic drugs and their metabolites to establish safe and

Elsa-Grace V. Giardina, M.D.

effective ways of administering these agents; and in the area of elucidating the mechanism of action of antiarrhythmic drugs.

She has teaching responsibilities with house officers and medical students. Her work with students involves supervision during their elective work in clinical pharmacology.

Ralph E. Kauffman, M.D.

• Ralph E. Kauffman, M.D., Assistant Professor of Pediatrics and Pharmacology, Clinical Pharmacology-Toxicology Center, The University of Kansas Medical Center. Dr. Kauffman's major research interests involve the investigation of the pharmacokinetics of anticonvulsant drugs in children being treated for seizure disorders, while other studies involve the kinetics of placental transfer of drugs in an in vivo model in goats and also in women receiving drugs during pregnancy.

He will also participate in the teaching of medical students, graduate students, and postdoctoral trainees in pediatrics and clinical pharmacology.

Recipients of the awards which began July 1, 1967 are:

• Faruk S. Abuzzahab, Sr., M.D., Ph.D., Clinical Associate Professor, Psychiatry and Pharmacology, University of Minnesota. Present research involves the study of the neurochemical mechanism of neuroleptic-induced extrapyramidal side effects both in animals and man. In addition, a number of investigations in the field of clinical psychopharmacology are underway involving antidepressant and antipsychotic compounds. Two new areas in clinical psychopharmacology are being explored: enhancement of memory in geriatric patients and improving male sexual impotence.

• John S. Holcenberg, M.D., Associate Professor of Medicine and Pharmacology, University of Washington, Seattle. Efforts are currently directed toward finding unusual amino acid requirements in cancer and leukemias. Various animal and human tumors are being screened for their requirements for amino acids which are not needed by the host. Enzymes are being developed which can degrade these amino acids. The eventual aim is to produce tumor remission by treating the animal or patient with a specific amino acid degrading enzyme. Insoluble and chemically modified enzymes are under study in an attempt to decrease the immune response and prolong the anti-tumor effects of these enzymes.

• John L. McNay, Jr., M.D., Professor of Pharmacology and Medicine, Emory University School of Medicine. Dr. McNay is conducting research mainly centered on hypertension autonomic and renal circulatory pharmacology.

Recipients of awards which began July 1, 1968, and which were extended until June 30, 1971 are:

• William Y. W. Au, M.D., Associate Professor of Pharmacology and Medicine, University of Rochester, School of Medicine and

Dentistry, is engaged in studies on agents which affect parathyroid and bone metabolism, including such agents as thiazide diuretics, calcitonin, and fluoride. Organ culture methods are used to assess the direct effects of these agents. The clinical pharmacology of agents are being assessed in certain metabolic bone diseases; calcitonin in Pagent's disease and in hypercalcemia and controlled trial of fluoride in osteoporosis are being carried out.

- Arthur H. Hayes, Jr., M.D., Chief, Division of Clinical Pharmacology, Milton S. Hershey Medical Center has various studies of antihypertensive agents and regimens underway in patients with essential hypertension. The relative efficacy and safety of several oral, intramuscular and intravenous antiarrhythmics are being evaluated clinically and correlated with drug blood levels in patients who have suffered a myocardial infarction. Alterations in cardiac function produced by cardiac glycosides and beta adrenergic blocking drugs are being monitored physiologically with concurrent drug-blood concentration determinations. Pharmacologic investigation of the cardiac slowing properties of atropinic compounds is being conducted to define their mechanism of action and determine their optimal use as diagnostic and therapeutic agents.

- Donald S. Robinson, M.D., Associate Professor of Medicine and Pharmacology and Director, Clinical Pharmacology Unit, University of Vermont, College of Medicine, is involved in a number of studies of clinical and biochemical changes in aging and mental illness, the drug treatment of psychiatric disorders, and hypertension and antihypertensive therapy.

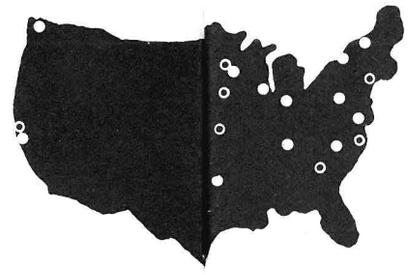
He is also involved in investigations of drug interactions. A further field of interest is in the development of sustained action narcotic antagonists.

Recipients of awards which began July 1, 1969 are:

- Vincent S. Aoki, M.D., an Assistant Professor, University of Iowa, when the award was made, was involved in studies of the effects of drugs on the pulmonary vascular bed. He resigned a third year of support in December, 1971 to enter the private practice of medicine in Hawaii.

- Lester F. Soyka, M.D., Professor of Pharmacology and Pediatrics, University of Vermont, College of Medicine, is involved in research directed toward an understanding of changes in drug effects during ontogeny in biochemical and mechanistic terms. The approach is two fold. Basic studies are in progress to define certain relationships between liver and brain mixed-function oxidase enzymes and progestational steroids. Studies of the pharmacokinetics of digoxin are being carried out in infants and children.

- Pate D. Thompson, M.D., an Instructor, University of California, San Francisco Medical Center, when the award was made, resigned the second year of the award to take a position of Chief of Cardiology at Alta Bates Hospital, California.



Geographical distribution of Foundation awards under its "Faculty Development Awards in Clinical Pharmacology" program, 1967-1973
● One
○ More than one

- Stanley C. Ushinski, M.D., an Assistant Professor of Pediatrics and Pharmacology, University of Pittsburgh, when the award was made, resigned the second year of the award to enter private practice.

Recipients of awards which began July 1, 1970 are:

- Arthur J. Atkinson, Jr., M.D., Associate Professor of Medicine and Pharmacology, and Director, Clinical Pharmacology Unit, Northwestern University Medical School, is conducting research into both antiarrhythmic and anticonvulsant drugs.

- Samuel A. Cucinell, M.D., an Assistant Professor of Medicine, Emory University School of Medicine, when the award was made, is now Chief, Clinical Research Branch, U. S. Army Edgewood Arsenal. His responsibilities include studies which deal with the reevaluation of the treatment of poisoning to cyanide, phosgene, organophosphorous compounds and atropine; the metabolism of antimalarials; and drug metabolism in environmental stress.

- Aryeh Hurwitz, M.D., Associate Professor of Medicine and Pharmacology, Clinical Pharmacology-Toxicology Center, University of Kansas Medical Center, is conducting studies of gastrointestinal drug interactions. These studies include an examination of the effects of drugs which alter gastrointestinal function on the absorption of other drugs, and the mechanisms and clinical significance of these interactions. He is also involved in studies of hepatotoxicity.

Recipients of the awards which began July 1, 1971 are:

- I. David Goldman, M.D., Associate Professor of Medicine and Pharmacology, University of North Carolina, School of Medicine. Dr. Goldman is involved in the study of cellular pharmacokinetics of antitumor agents. Biophysical techniques are employed to quantitate the basic mechanisms and kinetics of drug transport as distinguished from the subsequent drug-target interaction within the cell. This approach complements studies on the kinetics of drug-target interaction in cell-free systems and considers the problems of cytotoxicity, selectivity, and resistance in terms of the drug interaction with the intact cell. The intact cell is a model which may be most relevant to the way anti-cancer agents interact with cells *in vivo* in the treatment of experimental animal tumors and human malignancies.

- Urs A. Meyer, M.D., Assistant Professor of Medicine and Pharmacology, University of California, San Francisco Medical Center. Dr. Meyer's primary research interest is in the area of drug metabolism, with the goal of developing an *in vitro* model of drug-induced increase in synthesis of P-450 enzymes using cell culture techniques. A third year of support was granted, extending the award until June 30, 1974.

- Alan S. Nies, M.D., Associate Professor of Medicine and Pharmacology, Vanderbilt University, School of Medicine. Dr. Nies

is studying the effects of alterations of regional blood flow by disease or drugs. Studies are being done in the experimental animal and man. A third year of support was awarded, extending the award until June 30, 1974.

• Harold C. Strauss, M.D., Assistant Professor of Medicine, Duke University Medical Center and Associate Editor, Circulation. Dr. Strauss is engaged in studies using the technique of premature depolarizations to determine refractoriness to characterize the electrophysiological properties of antiarrhythmic drugs on atrial arrhythmias and sinus node function in man. Studies are planned to determine the relationship between plasma drug concentration and antiarrhythmic action, and manifestations of toxicity. The effects of the same antiarrhythmic agents on the electrophysiology of the varius atrial fiber types using standard microelectrode techniques and isolated preparations of cardiac tissue are to be examined.

• Wilmer Leigh Thompson, Jr., Ph.D., M.D., Assistant Professor of Medicine and Assistant Professor of Pharmacology and Experimental Therapeutics, Johns Hopkins University, School of Medicine. He is engaged in studies on drug therapy in critically-ill patients. Studies are underway of three modalities of the therapy of shock: plasma substitutes, inotropic agents, and glucocorticoids.

He is also involved in studies of drug kinetics in man, optimization of dosage regimens and human drug interaction.

• Thomas L. Whitsett, M.D., Associate Professor of Medicine and Assistant Professor of Pharmacology, University of Oklahoma, School of Medicine. Dr. Whitsett's research is involved in cardiovascular and renal effects of autonomic and antihypertensive agents. A third year of support was granted extending the award until June 30, 1974.

Recipients of awards which began July 1, 1972 are:

• David S. Alberts, M.D., Instructor, Cancer Research Institute, University of California, San Francisco, is investigating in humans the correlation of drug concentration, distribution, route and method of administration of cancer chemotherapeutic agents with their effectiveness in tumor cell kill.

He is also involved in developing a mouse spleen colony assay to evaluate interacting effects of cancer and non-cancer drugs on bone marrow and leukemic spleen colony forming potential. The investigator is developing a protocol to employ autologous bone marrow transplants in the mitigation of bone marrow toxicity from certain anti-cancer drugs.

• Carlos A. Dujovne, M.D., Assistant Professor of Medicine and Pharmacology, University of Kansas Medical Center, is involved with the investigation of the mechanism of drug-induced intrahepatic cholestasis in man and experimental studies on the effects

of therapeutic agents on tissue culture systems and its possible value, as a tool for toxicologic screening of drugs. Also engaged in clinical therapeutic trials with new hypolipidemic drugs and special studies of effects of hypolipidemic drugs on liver functions and structure.

• John S. Kaufmann, M.D., Ph.D., Assistant Professor of Medicine and Pharmacology, The Bowman Gray School of Medicine, Wake Forest, is involved in investigations related to the distribution, metabolism, and excretion of antihypertensive agents (e.g. guanidinium compounds); interaction of tricyclic antidepressants and similar compounds with antihypertensive agents in man; alterations in platelet aggregation due to selected anti-inflammatory and anti neoplastic drugs; mechanisms of amine transport in human platelets and their relationship to platelet aggregation; possible effects of ultrasonic irradiation on the uptake and antineoplastic effects of known oncolytic agents.

• Robert A. Mueller, M.D., Ph.D., Associate Professor of Anesthesiology and Assistant Professor of Pharmacology, University of North Carolina, School of Medicine, is investigating cardiovascular and respiratory effects of Δ –9 tetrahydrocannabinol, a marijuana component. He is also examining both sympathetic nervous system activity and the administration of anesthetics to hypertensive patients.

He is further involved in an investigation of the mechanism of action of alpha methyl-DOPA as an antihypertensive agent in experimental hypertensive rats. Another major investigative effort is an investigation of the effects of several different drugs and experimental pathologic conditions to alter the ability of stress, both pharmacologic and environmental, on inducing the biosynthetic enzymes of catecholamine biosynthesis.

• August M. Watanabe, M.D., Assistant Professor of Medicine and Pharmacology, Indiana University School of Medicine, is conducting research on the effects of certain drugs on myocardia metabolism. A third year of support was awarded, extending the award until June 30, 1975.

Recipients of awards which began July 1, 1973 are:

• Robert J. Roberts, Ph.D., M.D., Associate Professor, Pharmacology and Pediatrics, University of Iowa College of Medicine. Dr. Roberts is investigating the mechanisms responsible for drug and chemical-induced hepatotoxicity and exploring various aspects of carbon monoxide toxicity.

He is also involved in several clinical research projects in pediatric patients. Included are studies of the maturation of the enterohepatic circulation of drugs, interaction of prednisone and salicylates and the treatment of hepatic dysfunction in cystic fibrosis.

• Thomas F. Rolewicz, M.D., Ph.D., Assistant Professor, Pharmacology and Pediatrics, University of Minnesota Medical

School, is presently working to develop microanalytical methods of analysis of antibiotics utilizing high speed liquid chromatography. The aim is to refine various techniques to enable the rapid and accurate analysis of antibiotic levels in the blood and other body fluids. Data relevant to antibiotic disposition is minimal in the pediatric age group. Studies in the pediatric age group are handicapped by a lack of appropriate technology for the rapid, quantitative analysis of antibiotics utilizing minute volumes of body fluids. The data obtained from these studies will be applied clinically in the management of pediatric patients receiving antibiotics alone, or in combination with other drugs that may influence the disposition of antibiotics.

• Richard M. Weinshilboum, M.D., Assistant Professor, Pharmacology and Internal Medicine, Mayo Medical School, is investigating the use of biochemical techniques to measure the function of the sympathetic nervous system in man. He has studied the circulating levels of the enzyme dopamine-B-hydroxylase, a catecholamine biosynthetic enzyme which is released from sympathetic nerves with norepinephrine, in blood samples from large control populations. The results of these studies have demonstrated that genetic factors are important in the regulation of these enzyme levels in man. Investigations are now being widened in order to use this adrenergic enzyme marker to study the possible role of the sympathetic nervous system in diseases such as hypertension.

He is continuing studies of the mechanism by which sympathetic nerves release norepinephrine, using a combined biochemical and morphological approach to isolated catecholamine-containing vesicles from sympathetic nerves which have been obtained from experimental animals.

The program of **Fellowships for Careers in Clinical Pharmacology** provides clinicians with 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 a career in clinical pharmacology. With the year or two of support offered by this fellowship program, depending on the particulars of his undertaking, the individual can pursue full-time the basic pharmacologic science needed to complement his clinical skills.

The first awards under this program were made in February and began July 1, 1973. The second set of awards for the year beginning July 1, 1974 were made in December, 1973.

Recipients of awards which begin July 1, 1974 are:

• David M. Kornhauser, M.D., Research Associate, Department of Pharmacology, Vanderbilt University, School of Medicine. During the tenure of the two year fellowship, emphasis will be given both to training and experience in applying the principles of pharmacology to

David M. Kornhauser, M.D.

James J. Lipsky, M.D.

problems in clinical pharmacology. He will participate in the seminar activities of the Department of Pharmacology as well as the Clinical Research Rounds. During each year, he will spend from six to eight weeks as a primary clinical consultant for the Clinical Pharmacology Division working directly with the attending staff on problems regarding drug therapy. Also during the fellowship, he will become acquainted with the analytical methods employed in the Drug Analysis Laboratory.

• James J. Lipsky, M.D., Fellow in Clinical Pharmacology, Departments of Internal Medicine and Pharmacology, The Johns Hopkins University, School of Medicine. His research interests are in the field of antibiotics and antibacterial chemotherapeutic agents in relation to suppression of immune response. An examination of these agents may develop into clinically useful and relatively non-toxic approaches to immuno-suppression. Furthermore, each of these types of drugs exerts its selective toxicity on bacterial cells as opposed to mammalian cells. It therefore, is important to understand the biochemical basis for this immunosuppression. An understanding of the biochemical mechanism could lead to the selection of other agents with immunosuppression action and possibly to the design of new agents or the modification of existing agents to selectively provide immunosuppression. Both **in vitro** and **in vivo** models will be used to evaluate the biologic and biochemical nature of immunosuppression by antibiotics and chemotherapeutic agents.

He will have a teaching role in the weekly clinical pharmacology course for junior and senior medical students.

Thom J. Zimmerman, M.D.

• Thom J. Zimmerman, M.D., a resident in Ophthalmology, University of Florida, College of Medicine. He will pursue a program of research and course work during the two years of the fellowship. Investigations of aqueous humor dynamics and ophthalmic autonomic function are his primary research interests. Advanced courses in physiology, chemical and theoretical pharmacology, research methodology and the pharmacology of excitable membranes are scheduled during the fellowship.

Recipients of awards which began July 1, 1973 are:

Michael J. Scollins, M.D.

• Michael J. Scollins, M.D., Instructor in Medicine and Senior Fellow in Clinical Pharmacology, The University of Vermont, College of Medicine. His basic interest lies in the field of auditing or monitoring drug prescribing and utilization in the hospital setting. In one aspect of his training, he is working with Dr. Lawrence Weed in the preparation of computerized drug information. He serves as an instructor in principles and practices of clinical pharmacology in both formal and informal case-related ward conferences. During the one year fellowship he is enrolled in a formal course in medical pharmacology.

• Anthony P. Zavadil, M.D., Fellow, Clinical Pharmacology Unit, Georgetown University, School of Medicine and Dentistry. His program of research during the two years of the fellowship includes clinical and basic neuropharmacological investigations. The clinical studies are concerned with two barbiturate derivatives, primidone and dimethoxymethyl-phenobarbital (DMMP). These studies will be conducted with patients with epilepsy.

The basic neuropharmacological studies involve the acquisition of appropriate laboratory techniques including gas-liquid chromatography, thin-layer chromatography, liquid scintillation counting, spectroscopy, etc., which are required for the quantitative analysis of the two drugs and their metabolites.

He has a teaching role in the clinical pharmacology sequence given to junior and senior medical students.

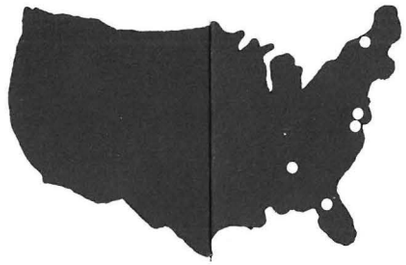
The **Medical Student Traineeships in Clinical Pharmacology** program provides opportunities to students to learn the basic techniques used in the field of clinical pharmacology. The program provides a stipend of $1,000 to each student for a three month period. Since the first awards in 1967, 133 awards have been made to medical schools across the United States.

The aim of all of the Foundation's programs is to identify those individuals who demonstrate a high degree of commitment to careers in the fields of interest to the Foundation. While this program has been successful in that a number of students have continued careers in clinical pharmacology, the awards in 1973 are the last under this present approach to medical student support.

The Foundation will continue its support of medical students, but through a new program. The new program offers support for an entire year to enable a student to spend full time in an investigative project in pharmacology-clinical pharmacology. The details of this program were announced in the fall, 1973. The first awards are scheduled for July 1, 1974.

The last 20 traineeships were awarded to:

The University of Arizona –
Anthony F. O'Malley
University of California, Los Angeles – Steven M. Grunberg
University of California, San Francisco – Steven Berkov
Case Western Reserve University –
Rebecca L. Saltonstall
Hahnemann Medical College –
Paul Roda
Howard University –
Ayodeji Adelaja O. Coker
Edith A. Higginbotham
Indiana University –
Dianne Minneman
Jefferson Medical College –
Ira Schwartz
The Johns Hopkins University –
Scott Young
University of Minnesota –
David L. Bransford
State University of N.Y. (Buffalo) –
John L. Lovecchio
University of Oklahoma –
James M. Richard
Temple University –
Ellen Boudlock
University of Texas –
Steven N. Brooks
Anthony C. Jung
University of Utah –
Patrick H. English
Medical College of Wisconsin –
Michael P. Miller
Yale University –
Irl Extein
University of Kentucky –
Steven T. Deak



Geographical distribution of Foundation "Fellowships for Careers in Clinical Pharmacology" program, 1973 1974
● One

Anthony P. Zavadil, M.D.

Ing Kang Ho, Ph.D.

Michael G. Mawhinney Ph.D.

Samuel J. Strada, Ph.D.

Pharmacology. The purpose of the **Faculty Development Awards in Pharmacology** is to strengthen basic pharmacology by helping maintain the present academic capability and, ultimately, to expand this capability by enlarging the faculty base. To accomplish these goals, support is provided to junior faculty members committed to careers in pharmacology who give promise of outstanding accomplishments. Implicit in the decision to offer this faculty program is the recognition that the future development of clinical pharmacology depends on the impetus and scientific principles provided by the basic discipline.

The first awards, which are for a two-year period, were made beginning July 1, 1973. The awards provide salary and fringe benefits, at levels which are expected to be in accord with the existing amounts within the applicant university. The second set of awards to begin July 1, 1974 were made in December, 1973.

Recipients of these 1974 awards are:

• Ing Kang Ho, Ph.D., Adjunct Assistant Professor, Department of Pharmacology, University of California, School of Medicine, San Francisco. His primary research interests deal with the biochemical mechanisms involved in the development of tolerance to and physical dependence on morphine and barbiturates. The possible role of neurohormone and neurotransmitters involved in the development of morphine tolerance and physical dependence will be investigated. Following this, differentiation between physiological disposition tolerance and central nervous system tolerance to barbiturates and the contributory role of the putative neurotransmitters in barbiturate tolerance and dependence mechanism will be studied.

• Michael G. Mawhinney, Ph.D., Assistant Professor of Pharmacology and Urology, West Virginia University, School of Medicine. His research is in hormonal control of normal and abnormal prostatic growth with particular emphasis on aging. An important corollary of his laboratory activity will be the research training of pharmacology graduate students and urology fellows and residents. This will allow him to bring his basic knowledge of pharmacology and endocrinology into the clinical setting. Conversely, his participation in clinical conferences will greatly enhance his contribution to the basic pharmacology course for medical students.

• Samuel J. Strada, Ph.D., Assistant Professor of Pharmacology, University of Texas, Medical School, Houston. His primary research interest is concerned with isozymes of cyclic nucleotide phosphodiesterase. Earlier efforts by Dr. Strada have discovered that different cells contain entirely different patterns of these isozymes, each of which differ with regard to substrate specificity, physio-chemical properties, and sensitivity to endogenous activators and inhibitors.

Recipients of faculty awards which began July 1, 1973 are:

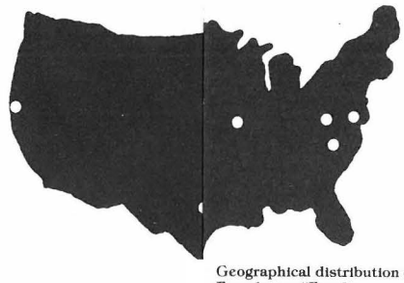
• Kenneth L. Dretchen, Ph.D., Instructor of Pharmacology, Georgetown University, School of Medicine and Dentistry. He is studying the way the neuromuscular junction works in the living animal and the way it is affected by disease and by drugs. The results of his research should add to understanding of synaptic transmission. The technique used involves intracellular electrodes to record neuromuscular phenomena in the **in vivo in situ** cat muscle, without adding chemicals. Virtually all other studies by other investigators have been done with intracellular electrodes in muscles removed from the body and kept alive in artificial solutions. The results of these kinds of studies have provided a great deal of information on how nerves and muscles work, but, the fact that the tissues were isolated from the body sometimes made it difficult to interpret results in terms of what actually happens in the living animal.

He is teaching pharmacology to medical and dental students in addition to his research.

• Robert I. Glazer, Ph.D., Assistant Professor of Pharmacology, Emory University, Woodruff Medical Center. His research is in the area of chemical carcinogenesis. Investigations are being undertaken aimed at analyzing the interactions between hepatocarcinogens and the synthesis of nucleic acids. In addition, biochemical studies of this nature are being used to assess the efficacy of antineoplastic drugs using appropriate experimental animal tumor systems. It is hoped that these investigations will lead to a further understanding of the molecular events involved in initiating and reversing neoplastic processes.

He is also responsible for training medical, graduate and other health personnel in the field of pharmacology.

• Theodore A. Slotkin, Ph.D., Assistant Professor, Department of Physiology and Pharmacology, Duke University Medical Center. He is conducting research on the synthesis, uptake, storage and secretion of catecholamines in adrenergic neurons and the adrenal medulla with particular reference to interactions on subcellular levels among the peripheral autonomic nervous system, the central nervous system and the cardiovascular system. In addition to independent investigations in pharmacology, Dr. Slotkin is participating in the teaching programs in pharmacology at Duke. These include courses and seminars for medical students, graduate students and allied health personnel as well as overseeing the research projects of graduate students and post-doctoral fellows.

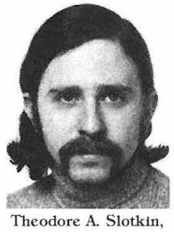


Geographical distribution of Foundation "Faculty Development Awards in Pharmacology" program, 1973-1974
● One

Kenneth L. Dretchen, Ph.D.

Robert I. Glazer, Ph.D.

Steven B. Mizel, Ph.D.



Theodore A. Slotkin, Ph.D.

Nancy J. Russel, Ph.D.

Pharmacology-Morphology. The aim of the Fellowship Awards in Pharmacology-Morphology 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 tissues and cellular structure.

The awards are for two years each and, in exceptional circumstances, may be extended for an additional year. The level of support is variable and is aimed at keeping within the existing stipend levels for similarly trained individuals within the applicant university. Since 1968 when the first fellowships were offered, 24 awards have been made.

The fellowship program is designed to support individuals interested in studying the actions of drugs in relation to morphologic approaches (cytology, histology, ultrastructure, pathology). Although the program requires that a candidate be qualified primarily either in a morphologic specialty or in pharmacology, training in the complementary discipline need not be formal. The aim is to have the candidate gain familiarity with a new disciplinary approach by using his primary discipline as a medium for acquiring the second.

Recipients of awards which began July 1, 1973 are:

• Steven B. Mizel, Ph.D., Postdoctoral Fellow, Department of Biochemistry, Colorado State University, Ft. Collins. Dr. Mizel is investigating the biochemical and pharmacological properties of neurotubule protein in differentiating normal and neoplastic nerve cells. The levels of neurotubule protein in the developing normal and neoplastic nerve cells will be quantitated by polyacrylamide gel electrophoresis and by the ability of neurotubule protein to selectively bind the antimitotic agent, colchicine. It is intended also to measure the interaction of several agents such as colchicine, vinblastine, vincristine, and podophyllotoxin with neurotubule protein during differentiation in normal and neoplastic nerve cells. Differences in the biochemical and pharmacological properties of neurotubule protein in the normal and neoplastic nerve cells may then be correlated with the state of neoplasia.

• Nancy J. Russell, Ph.D., Research Associate, Department of Pharmacology, University of Oregon Medical School, Portland. Dr. Russell is involved in the study of early functional and morphological changes that occur at the nerve terminals of bullfrog sympathetic ganglia 24-72 hours after surgical section of preganglionic fibers. The specific aim of the project is to localize the time at which synaptic transmission is still intact but neostigmine fails to induce repetitive firing. This represents the earliest sign of functional impairment in the presynaptic nerve terminal. Isolated ganglis with associated pre- and post-ganglionic fibers are placed on electrodes for extracellular recording of synaptic transmission. After the

functional effects of denervation have been recorded, the ganglia will be processed for electron microscopy. Thin sections will be examined for ultrastructural changes that may be related to functional changes.

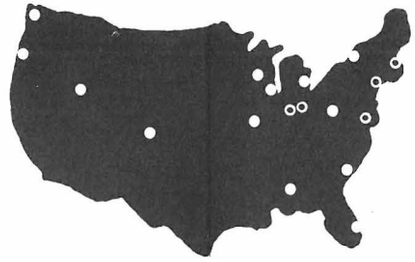
- Norman R. West, Ph.D., Postdoctoral Fellow in Anatomy, Washington University, School of Medicine, St. Louis. Dr. West is engaged in research dealing with organotypic nerve tissue cultures treated with a series of phenothiazine compounds in doses comparable to tissue levels found in vivo. Psychoactive agents, their metabolites and "inactive" congeners are being compared by studying alterations produced in nerve tissue as visualized in the living state with the light microscope and after fixation and embedding with the electron microscope.

Recipients of awards which began July 1, 1968 are:

- David W. Hiott, Ph.D., M.D., Teaching Fellow in Pharmacology, Medical University of South Carolina. His current research interests involve studies on the acute effects of high doses of drugs on the electron microscopic morphology of mammalian hearts.
- John O. Lindower, M.D., Ph.D., Associate Professor of Pharmacology, The Ohio State University, College of Medicine. Dr. Lindower is studying the effect of digitalis by correlating the changes the compound produces in heart cells. Isolated small animal hearts are perfused with the digitalis medium while a recording device measured the more forceful contraction that the drug produced in the heart. After the drug effect is demonstrated, small samples of the heart muscle are examined by the electron microscope to detect any changes produced by the drug.
- Timothy J. Mathew, M.B.B.S., Renal and Electrolyte Division, Georgetown University Hospital. He was engaged in studies directed to examination of platlets in the pathogenesis of transplant rejections. An attempt was made to alter histologic pattern rejection by using drugs directed at changing the platlet function. Following the conclusion of the fellowship. Dr. Mathew returned to Australia and has responsibilities as Physician to the Renal Unit, The Royal Melbourne Hospital.

Recipients of the awards which began July 1, 1969 are:

- Andrew K. S. Ho, Ph.D., Assistant Professor of Pharmacology, Wayne State University, College of Pharmacy. Current studies are being conducted into the effect of psychopharmacological agents in different regions of the brain. Experiments are being designed to eludidate the possible indirection between processes involving acetylcholine and biogenetic amines at the cellular and subcellular levels using techniques of bio-chemical pharmacology and histo-chemistry. The findings of these studies are correlated to the therapeutic use of these drugs and their effect on behavior.



Geographical distribution of Foundation "Fellowship Awards in Pharmacology-Morphology", 1968-1973
● One
○ More than one

Norman R. West, Ph.D.

- William J. Scott, Jr., D.V.M., Ph.D., Associate Professor of Research Pediatrics, University of Cincinnati, School of Medicine. Dr. Scott is currently attempting to determine the mechanism of teratogenic action of cytotoxic drugs in rats. In addition to studies designed to evaluate the teratogenic potential of numerous chemicals in primates, these animals are also being used to determine pharmacodynamic and teratogenic mechanisms in the primate embryo.

Recipients of the awards which began July 1, 1970 are:

- Roy J. Baerwald, Ph.D., Assistant Professor, Departments of Medicine and Pharmacology, University of Miami, School of Medicine. Dr. Baerwald is involved in studies of membrane structure and development utilizing the freeze-fracture technique with special reference to cell junctional complex development in excitable cells.
- Patricia J. Bingham, D.Phil., Associate in Pharmacology, University of Rochester, School of Medicine and Dentistry at the time of the award. During the fellowship, Dr. Bingham used autoradiography techniques to study the mechanism of action and localization of hormones and other agents which affect bone formation and resorption. She is now at the University of Melbourne, Australia, as Senior Research Officer in the Department of Medicine.
- Richard F. Hoyt, Jr., Ph.D., Assistant Professor, Department of Anatomy, Boston University Medical School. Dr. Hoyt is conducting research on hydrocortisone-induced changes in the histochemistry, fine structure, and secretory activity of rat pituitary cells in tissue culture. The cells in question are cloned strains derived from functional, pituitary tumors. They secrete both growth hormone and prolactin into the culture medium. In response to treatment with hydrocortisone, secretion of growth hormone by these cells rises while the secretion of prolactin is depressed. Light and electron microscopy and immunohistochemical methods are being applied to cell cultures grown with and without hydrocortisone in an attempt to define morphological changes that accompany alterations in secretory function.
- Carole Davis Kimmel, Ph.D., in the Division of Toxicology, Kettering Laboratory Department of Environmental Health, College of Medicine, University of Cincinnati when the award was made. Dr. Kimmel is engaged in research aimed at elucidating the mechanism of teratogenic action of compounds capable of interacting with metals. Studies are being carried out with salicylates, but primary emphasis is being placed on the actions of a known metal chelator, EDTA, and its interaction with both essential and toxic metals. This direction of research was taken to provide a model for investigating compounds, such as salicylates which are not easily demonstrated to be chelating agents. Dr. Kimmel is currently Senior Staff Fellow, National Institute of Environmental Health Services, NIH, Research Triangle Park, North Carolina.

• Robert E. Seegmiller, Ph.D., Assistant Professor in Zoology, Brigham Young University. Dr. Seegmiller is studying the niacin analogue 6-aminonicotinamide (6-AN), administered to day-4 chick embryos, and the resulting early fine structural and histological alterations in the developing limb and micromelia in embryos examined several days later. Effects of the drug specific to limb chondrogenesis correlate with the resulting micromelia. Studies underway will help to determine the mechanism of action of 6-AN in producing micromelia and should suggest means by which nicotinamide protects against the teratological effects of 6-AN.

Recipients of the awards which began July 1, 1971 are:

• Sharon E. Corey, Ph.D., Research Associate, Department of Pharmacology, West Virginia University Medical Center. Dr. Corey is engaged in research involving chronic treatment of rats with reserpine and resulting supersensitivity of the vas deferens to a variety of agents. Present work involves a quantitative electron microscopic analysis of the vas deferens to determine if similar reserpine treatment alters the number of nexal contacts between cells. A nexus, or "gap" junction is a fusion of cell membranes such that a "five" rather than a seven layer system of membranes results.

• William A. Croft, Jr., D.V.M., Division of Clinical Oncology, University of Wisconsin, resigned the last months of the award to undertake responsibilities on the university's faculty. Dr. Croft is investigating the development of leukemia induced in rats by a chemical that also has marked antitumor properties. The studies will attempt to determine whether the leukemia is related directly to the administration of the chemical, or to the release of a latent leukemia virus that may be present in rats. The rat, unlike the mouse, rarely develops leukemia. Thus, a study of this model may provide clues of importance in furthering the understanding of the development of leukemia.

• Penelope A. Fenner-Crisp, Ph.D., Adjunct Instructor, Department of Anatomy, Georgetown University, School of Medicine and Dentistry. Her studies deal with the effects of certain pharmacological and physiological substances upon fine structure morphology and the function of corpora lutea.

• Anita P. Hoffer, Ph.D., Instructor in Anatomy, Harvard Medical School. Her current research involves studies of the ultrastructural effects of U5897 on the rat epididymis. U5897, an alpha-monochlorohydrin, is a reversible antifertility drug which has a post-testicular site of action. A single high dose of this drug produces a lesion confined to the initial sement of the epididymis whereas lower doses given daily produce reversible infertility without producing a lesion. Ultrastructural and motility studies on epididymal sperm of normal and U5897-treated rats are also being carried out.

• Michael C. Lowe, Ph.D., Assistant Professor, Department of Pathology, University of Washington Medical School, Seattle is studying the mechanisms involved in the production of cardiomyopathies by catecholamines.

• Asa K. Thureson-Klein, Ph.D., Assistant Professor of Pharmacology, University of Mississippi Medical Center is studying noradrenaline storage vesicles of sympathetic nerves, stressing the pharmacological effects on the uptake sorage and relase of catacholamines from the vesicles.

Recipients of awards which began July 1, 1972 are:

• Anna B. Drakontides, Ph.D., Assistant Professor, Department of Anatomy, New York Medical College, is conducting studies to ascertain whether exogenously applied acetylcholine (ACh), and related drugs, reach the post junctional membrane in the innervated state. In addition, she is seeking to ascertain if the observed denervational "hyperresponsiveness" to ACh reflects a post junctional response not previously observed and which may be due to structural changes that have exposed this membrane. These studies are being conducted using the rat phrenic nerve preparation in situ.

• James L. Lessard, Ph.D., Assistant Professor of Research Pediatrics, University of Cincinnati, College of Medicine. Dr. Lessard is studying the molecular basis of palate shelf movement, specifically determining whether the contractile protein action is involved in the process.

• Juliet Morgan, Ph.D., Research Associate, Department of Medicine, University of Chicago, Pritzker School of Medicine. Dr. Morgan is studying the influence of various stilbenes on the ultrastructural characteristics and lipid composition of cell membranes isolated from normal and dystrophic muscle cells grown in tissue culture.

• Myron L. Seligman, Ph.D., Postdoctoral Fellow, Department of Pathology, New York University Medical Center. Dr. Seligman will study the effects of prostaglandins on the molecular anatomy of membranes using magnetic resonance techniques and electron microscopy.

Sarah A. Tjioe, Ph.D., Instructor, Department of Pharmacology, the Ohio State University, College of Medicine. Dr. Tjioe is studing the subcellular brain neuron and glial changes that develop under the influence of psychoactive drugs.

Research Grants

An important aspect of the PMA Foundation's early efforts has been support of fundamental research in drug toxicology.

Since 1966 a total of 26 general research grants have been made for this purpose. Support on 20 of these has terminated. The remaining 6 grants which continued over various periods of time through 1973 were:

Medical College of Georgia, Department of Cell and Molecular Biology, Augusta, Georgia

University of Illinois, Department of Microbiology, Urbana, Illinois

University of Illinois at the Medical Center in Chicago, Department of Pediatrics

State University of New York in Buffalo, Department of Pediatrics

The University of Texas Medical Center in Dallas, Department of Pediatrics

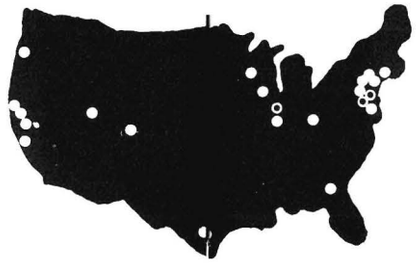
Stanford University Medical Center, Department of Pediatrics, Stanford, California

These six grants fall into the following categories.

Animal-Human Predictability Studies. A grant of $8,000 over a two year period beginning March 1, 1971 made to Edward W. Voss, Jr., Ph.D., Associate Professor, Department of Microbiology, University of Illinois to allow the continuation of immuno-chemical studies with lysergic acid (LSA) and lysergic acid diethylamide (LSD) concluded in 1973.

Clinical Pharmacology. A grant of $40,000 over a two year period which began March 1, 1971, made to John J. Miller, III, M.D., Ph.D., Assistant Professor of Pediatrics, Department of Pediatrics, Stanford University School of Medicine for a study of the relation of drugs to the lupus syndrome concluded in 1973.

Drug Metabolism. A grant of $30,000 over a two year period beginning November 1, 1971 made to Edward Bresnick, Ph.D., Chairman, Department of Cell and Molecular Biology, Medical College of Georgia for study of the mechanisms by which the mixed-function oxidase system is regulated during liver development concluded in 1973. A second aspect of the study deals with research aimed at understanding the mechanisms by which environmental factors such as polycyclic hydrocarbons are able to induce the drug metabolising enzyme system.



Geographical distribution of Foundation general research grants, 1966-1973
● One
○ More than one
◑ Outside U. S.

Fetal and Neonatal Pharmacology. A grant of $30,000 over a two year period which began February, 1971 was made to Charles E. Mize, M.D., Ph.D., Assistant Professor of Pediatrics and Biochemistry, The University of Texas, Southwestern Medical School at Dallas for a study of selective antibiotic action on mammalian membrane assembly. The co-investigator is Howard G. Worthen, Professor of Pediatrics. The grant concluded in 1973.

A grant of $58,000 over a two year period beginning May 1, 1970, made to Richard E. Behrman, M.D., then Professor of Pediatrics, Department of Pediatrics, University of Illinois at the Medical Center (Chicago) concluded in 1973. The study aims to characterize the pharmacologic effect of phenobarbital on fetal and newborn monkeys by evaluating the effects on blood pressure, heart rate, ECG, cardiac output, oxygen consumption and organ blood flows. Dr. Behrman accepted the Chairmanship of the Department of Pediatrics at the College of Physicians and Surgeons in late 1971, but remained a consultant to the study.

Nutritional Deficiencies – Drug Action. A grant of $44,590 over a two year period, which began April 15, 1971, was made to Sumner A. Yaffe, M.D., Professor of Pediatrics, Department of Pediatrics, State University of New York at Buffalo, to study the effect that malnutrition may have on the activity of hepatic drug-metabolizing enzymes. Both acute and long-term effects of nutritional deficiency are being studied. This grant concluded in 1973.

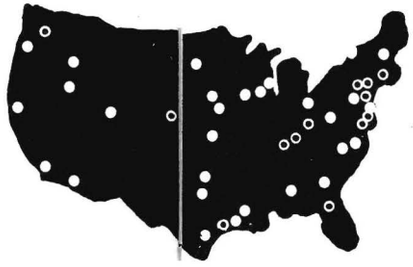
Research Starter Grants

A program of Research Starter Grants was offered for the first time in 1971. These grants are intended to provide financial support for beginning investigators. The program offers a sum of $5,000 a year for two years, with the second year contingent upon a continuing need for the funds. The research areas of interest within this program are in the fields of pharmacology, clinical pharmacology and drug toxicology. The program allows for up to 20 new research grants each year.

This approach is designed to assist investigators starting independent research efforts. It is motivated by the belief that a very real need exists among beginning investigators for "starter" funds. Experiences recorded during the first three years of the program have proved this to be the case.

The 23 research starter grants, beginning January 1, 1974 went to schools of pharmacy, schools of medicine and veterinary schools in all parts of the United States. **The schools and the recipients of the research starter grants for 1974 are:**

Margaret A. Acara, Ph.D.,
School of Medicine,
State University of New York
Harold L. Altshuler, Ph.D.,
Baylor College of Medicine
William J. Cooke, Ph.D.,
School of Medicine,
University of Massachusetts
John W. Dailey, Ph.D.,
Medical School, George
Washington University
H. Frederick Dalske, Ph.D.,
College of Medicine,
University of Nebraska
Laurence M. Demers, Ph.D.,
College of Medicine,
Pennsylvania State University
Vincent W. Dennis, M.D., School
of Medicine, Duke University
Kenneth L. Dretchen, Ph.D.,
Schools of Medicine and
Dentistry, Georgetown
University
Joel D. Feinblatt, Ph.D.,
University of Massachusetts
Medical School
Edward J. Flynn, Ph.D.,
College of Medicine and
Dentistry of New Jersey
Morley D. Hollenberg, Ph.D., M.D.,
Johns Hopkins University
School of Medicine
Gary E. Isom, Ph.D.,
College of Pharmacy,
Idaho State University
Michael C. Koss, Ph.D.,
College of Medicine,
University of Oklahoma
Health Sciences Center
Richard J. Morrow, Ph.D.,
College of Pharmacy,
Drake University
Thomas L. Pazdernik, Ph.D.,
College of Medicine,
University of Kansas
Mark A. Peppercorn, M.D.,
Harvard Medical School
Richard E. Peterson, Ph.D.,
Medical College of Wisconsin
Robert E. Seegmiller, Ph.D.,
College of Biological and
Agricultural Sciences,
Brigham Young University
Ellen K. Silbergeld, Ph.D.,
School of Hygiene and Public Health,
Johns Hopkins University
Sheldon Stolman, Ph.D.,
College of Osteopathic Medicine,
Michigan State University
Samuel J. Strada, Ph.D.,
University of Texas Medical School
Jack W. Strandhoy, Ph.D.,
Bowman Gray School of Medicine,
Wake Forest University
George J. Traiger, Ph.D.,
School of Pharmacy,
University of Kansas



Geographical distribution of Foundation awards under the "Research Starter Grants" program, 1972-1974
● One
O More than one

Of the 23 research starter grants awarded January 1, 1973, 17 grantees demonstrated a need for the second year of support. Six individuals had successfully gained larger amounts of funds from other sources during the year, providing them with the resources to further their independent research careers. **The 17 grantees who were provided a second year's $5,000 grant are:**

Verna L. Armstrong, Ph.D.,
College of Pharmacy,
University of Cincinnati
Kenneth Blum, Ph.D.,
University of Texas Medical
School at San Antonio
David R. Brown, Sc.D.,
School of Pharmacy,
University of Maryland
Clinton N. Corder, Ph.D., M.D.,
School of Medicine,
University of Pittsburgh
Arthur L. Craigmill, Ph.D.,
College of Pharmacy,
Washington State University
Harold L. Crossley, Ph.D.,
School of Dentistry,
University of Maryland
Jean D. Deupree, Ph.D.,
College of Medicine, University
of Nebraska Medical Center
Michael R. Franklin, Ph.D.,
College of Pharmacy,
University of Utah
Matthew J. Friedman, M.D., Ph.D.
Dartmouth Medical School
Robert L. Gulley, Ph.D.
University of Miami Medical
School
Martin D. Hamburg, Ph.D.,
Cornell University
Medical College
Daniel A. Koechel, Ph.D.,
Medical College of
Ohio at Toledo
Chang-seng Liang, M.D.
Boston University School
of Medicine
Joseph O. Owasoyo, D.V.M.
School of Veterinary
Medicine, Tuskegee Institute
Philip Posner, Ph.D.
College of Medicine
University of Florida
Janice L. Stickney, Ph.D.
School of Medicine
Michigan State University
Carol T. Walsh, Ph.D.
Boston University School
of Medicine

Foundation Finances

The Board of Directors of the PMA Foundation decided at the outset of the Foundation's activities that, as a minimum, total annual contributions of $500,000 would be sought, with larger amounts anticipated thereafter. For 1973 and each year until a further increase is deemed necessary, the Board of Directors increased the contribution goal to $750,000. In requests for voluntary support to PMA Member Firms, a guideline is suggested (an amount equal to .015% of the firm's domestic and international pharmaceutical sales).

Income. The total income in 1973 was $818,938. Of this amount $749,800 came from contributions. The balance of $69,138 came from investments and refunds on unexpended balances from grants.

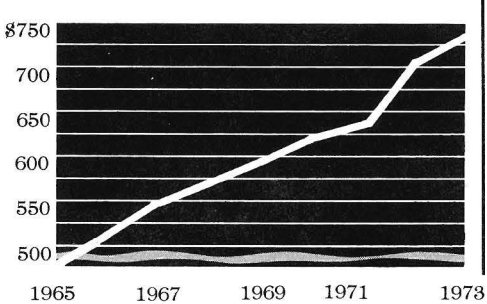
Contributions were received from approximately three of every four PMA Member Firms. Contributions were also received during 1973 from several individuals and groups in the health field.

Expenditures. Grants, Foundation-sponsored programs and administrative expenses for 1973 amount to $735,419. Of this amount, $641,232 represented expenditures for grants and Foundation-sponsored programs. There was a fund balance of $1,083,193 as of December 31, 1973. This figure, however, does not reflect the tentatively authorized, undisbursed amounts for some of the grants and programs described earlier. The Foundation reports these amounts as expenditures when the funds are distributed. As of December 31, 1973, this contingency liability totaled $1,229,000. Some of these grants represent amounts to be paid over the next two years. During 1973 the estimated amount to be paid on this tentative commitment is $666,000.

Financial Reports. The Foundation's financial position as of December 31, 1973 has been audited by the accounting firm of Ernst & Ernst. Copies of this statement will be supplied upon request.

Financial statements have been issued to contributors quarterly during 1973. These reports are prepared by the Washington, D. C. accounting firm of Buchanan & Company. Quarterly reports will continue to be distributed during 1974.

PMA Foundation Contribution Income 1965-1973 (Thousands)



Statement of Income and Expenditures
For the year ended December 31, 1973

Income

Contributions – Note a	$749,800
Income from Investments	56,335
Miscellaneous Income	12,803
TOTAL INCOME	$818,938

Expenditures

Grants – Note b

Clinical Pharmacology Faculty	$259,480
Clinical Pharmacology Fellowship Program	12,000
Faculty Development Awards in Basic Pharmacology	26,585
Medical College of Georgia	15,000
Medical Student Traineeships in Clinical Pharmacology	20,000
National Academy of Sciences Conference on Carcinogenesis	8,000
Workshop on Biochemical Approaches to Clinical Pharmacology	13,250
Pharmacology-Morphology Program	101,917
Research Starter Grants	185,000
	$641,232
Administrative expenses	94,187
TOTAL EXPENDITURES	$735,419
Excess of income over expenditures	$ 83,519
Fund balance at January 1, 1973	$999,674
Fund balance at December 31, 1973	$1,083,193

Note a – The Foundation received contributions of $121,500 prior to December 31, 1973 which the Foundation considered applicable to 1974 and, therefore are not recorded as income in 1973.

Note b – The Foundation has committed itself, subject to review, to make certain grants. At December 31, 1973 the amounts still to be disbursed with respect to these grants aggregated $1,229,000 of which approximately $666,000 is expected to be disbursed during the year 1974. No liability has been reflected for these amounts at December 31, 1973.

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 agreed to initially, and which still govern the distribution of funds, are support of fundamental research in drug toxicology, and the support of programs of research and training for personnel in clinical pharmacology and drug evaluation.

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 which 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 23

General research support of the type described in the Research Section, pages 22-23, is still offered, but on a scale much reduced from that which characterized the Foundation's earlier years.

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

Beginnings

For those of you who, through this Annual Report, learn of the Pharmaceutical Manufacturers Association Foundation, Inc. for the first time, a brief resume of the history which led to its formation is in order.

One event most influential in promoting the establishment of the PMA Foundation was the work and Final Report of the Commission on Drug Safety, a study group formed by the Pharmaceutical Manufacturers Association in the fall of 1962. The Commission was charged to make a study of the entire problem of drug safety and to come forth with recommendations. It carried out its work during the time of the urgency of the thalidomide situation. Special attention was given by the Commission initially to drug-induced fetal malformations. It became evident, however, that the most profitable line of inquiry would be to attack the overall problem of drug safety. This Commission composed of experts from universities, industry and government, arrived at a series of recommendations.

A continuing theme expressed in a variety of ways by these authorities was that the pharmaceutical industry should show more interest in the conduct of basic studies in drug toxicology, with the suggestion that co-operative sponsorship of such fundamental projects would have the greatest potential for undercovering new information. To make such studies possible, the Commission suggested a number of alternative mechanisms.

One was to establish a foundation. This, as well as many of the Commission's other recommendations, was considered by the PMA Board of Directors for some months following publication of the Commission's report. On May 13, 1965, the PMA announced the establishment of the PMA Foundation. The initial operating funds were supplied by the PMA, and sustaining support for the Foundation has come from voluntary contributions from PMA Member Firms and Associates, industrial concerns, organizations and individuals with an interest in health care research.

Organization and Administration

The PMA Foundation operates through a Board of Directors and four advisory committees. The Chairman of the Board is Daniel C. Searle, Chairman of the Executive Committee and Chief Executive Officer, G. D. Searle & Co., C. Joseph Stetler is President and Thomas E. Hanrahan is Executive Director. In July, 1973, Mr. Searle was elected Chairman of the Board to succeed H. W. Blades, Chairman of the Board, Wyeth Laboratories, Robert B. Clark, President, Hoffmann-La Roche Inc., was elected Vice Chairman and Donald van Roden, President, Smith Kline & French Laboratories, elected Secretary, Treasurer.

In reaching decisions on the most worthwhile activities for support, the Board of Directors has had the advice of extremely knowledgeable individuals serving on four advisory committees.

The Scientific Advisory Committee has the responsibility of making recommendations to the Board of Directors on all general research grant requests and on scientific priorities. Ira Ringler, Ph.D., Director of Research, Lederle Laboratories, is Chairman. To increase its effectiveness, the Chairmen of the Medical and the Research and Development Sections of PMA are invited to serve as members of the Committee.

The Clinical Pharmacology Advisory Committee is charged with making recommendations to the Board of Directors on all applications received for the faculty, fellowship and medical student programs in clinical pharmacology. The Chairman of this Committee is John A. Oates, M.D., Professor of Medicine and Pharmacology, Vanderbilt University, School of Medicine.

The Advisory Committee to the Fellowship Awards in Pharmacology-Morphology program has the responsibility for making recommendations to the Board of Directors on applications under this program. The Chairman of this Committee is Don W. Fawcett, M.D., Hersey Professor of Anatomy, Department of Anatomy, Harvard Medical School who succeeded Walter F. Riker, Jr., M.D., Chairman, Department of Pharmacology, Cornell University Medical College, in December, 1973.

The Basic Pharmacology Advisory Committee has the responsibility for making recommendations to the Board of Directors on all applications received under the research starter grant a program and the faculty awards in basic pharmacology program. The Chairman is Edward J. Cafruny, M.D., Ph.D., President, Sterling-Winthrop Research Institute.

Daniel C. Searle

C. Joseph Stetler

Thomas E. Hanrahan

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Daniel C. Searle, Chairman
Robert B. Clark, Vice Chairman
Donald van Roden, Secretary, Treasurer
C. Joseph Stetler, President
Thomas E. Hanrahan, Executive Director

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Indianapolis, Indiana

\+ Named to the Board, April, 1973
* Served until April, 1973
** Served until October, 1973
*** Named to the Board, October, 1973

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Director of Research
Lederle Laboratories
Pearl River, New York

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Head, Division of Clinical Pharmacology
University of Washington
Seattle, Washington

Edward J. Cafruny, M.D., Ph.D.
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Rensselaer, New York

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Department of Anatomy
Harvard Medical School
Boston, Massachusetts

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Professor of Medicine and Pharmacology
School of Medicine
Vanderbilt University
Nashville, Tennessee

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Vice President for Medical Affairs
Merck Sharp & Dohme Research Laboratories
West Point, Pennsylvania

Walter F. Riker, Jr., M.D.
Chairman, Department of Pharmacology
Cornell University Medical College
New York, New York

Joseph F. Sadusk, Jr., M.D.
Senior Vice President
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Morris Plains, New Jersey

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Professor and Chairman
Department of Pharmacology
School of Medicine
University of California
San Francisco, California

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Vice President-Research
Laboratory Sciences & Clinical Pharmacology
Merrell-National Laboratories
Cincinnati, Ohio

Irwin C. Winter, M.D., Ph.D.
Vice President, Medical Affairs
G. D. Searle & Co.
Chicago, Illinois

[1]Member until April, 1973

Ira Ringler, Ph.D.

John A. Oates, M.D.

Clinical Pharmacology Advisory Committee

John A. Oates, M.D., Chairman
Professor of Medicine and Pharmacology
School of Medicine
Vanderbilt University
Nashville, Tennessee

George N. Aagaard, M.D.
Professor of Medicine
Head, Division of Clinical Pharmacology
University of Washington
Seattle, Washington

John J. Burns, Ph.D.
Vice President for Research
Hoffmann-La Roche Inc.
Nutley, New Jersey

Glenn W. Irwin, Jr., M.D.[2]
Dean, School of Medicine
Indiana University
Indianapolis, Indiana

Walter F. Riker, Jr., M.D.[3]
Chairman, Department of Pharmacology
Cornell University Medical College
New York, New York

Ira Ringler, Ph.D.[4]
Director of Research
Lederle Laboratories
Pearl River, New York

Joseph F. Sadusk, Jr., M.D.
Senior Vice President
Warner-Lambert Company
Morris Plains, New Jersey

Albert Sjoerdsma, M.D., Ph.D.
Vice President, Research
Merrell International Research Center
Strasbourg, France

Alan B. Varley, M.D.
Medical Director, Pharmaceutical Marketing-Medical
The Upjohn Company
Kalamazoo, Michigan

Louis G. Welt, M.D.[5]
Professor and Chairman
Department of Internal Medicine
Yale University School of Medicine
New Haven, Connecticut

Irwin C. Winter, M.D., Ph.D.
Vice President, Medical Affairs
G. D. Searle & Co.
Chicago, Illinois

[2]Resigned May, 1973
[3]Resigned December, 1973
[4]Ex-officio as Chairman of the Scientific Advisory Committee
[5]Deceased January 13, 1974

Pharmacology-Morphology Advisory Committee

Don W. Fawcett, M.D., Chairman [6]
Hersey Professor of Anatomy
Harvard Medical School
Boston, Massachusetts

H. P. K. Agersborg, Jr., Ph.D.[7]
Associate Director of Research
Wyeth Laboratories, Inc.
Philadelphia, Pennsylvania

Kurt Benirschke, M.D.
Department of Reproductive Medicine
School of Medicine
University of California
La Jolla, California

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Head, Toxicology Section
Medical College of Virginia
Richmond, Virginia

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Abbott Laboratories
North Chicago, Illinois

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Wayne State University
School of Medicine
Detroit, Michigan

Walter F. Riker, Jr., M.D.[8]
Chairman, Department
of Pharmacology
Cornell University Medical College
New York, New York

William K. Riker, M.D.[9]
Professor and Chairman
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University of Oregon Medical
School
Portland, Oregon

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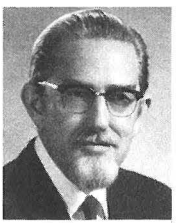
Director, Pathology & Toxicology
Research and Development Division
Smith Kline & French Laboratories
Philadelphia, Pennsylvania

Arnold M. Seligman, M.D.
Chief, Research Oncology
and Cell Biology
Sinai Hospital of
Baltimore, Inc. and
Professor of Surgery
The Johns Hopkins University
Baltimore, Maryland

Samuel W. Thompson, II, D.V.M.[9]
Manager of Pathology
CIBA-GEIGY Corporation
Summit, New Jersey

David A. Wood, M.D.
Director, Emeritus
Cancer Research Institute
University of California
San Francisco Medical Center
San Francisco, California

[6]Named Chairman, December, 1973
[7]New Members April, 1973
[8]Resigned December, 1973
[9]New Members December, 1973



Don W. Fawcett, M.D.

Edward J. Cafruny, M.D., Ph.D.

Basic Pharmacology Advisory Committee

Edward J. Cafruny, M.D., Ph.D., Chairman
President
Sterling-Winthrop Research Institute
Rensselaer, New York

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Vice President
Experimental Therapy
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Michigan State University
East Lansing, Michigan

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Warner-Lambert Company
Morris Plains, New Jersey

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Professor, Department of Pharmacology
The Medical College of Wisconsin
Milwaukee, Wisconsin

Walter W. Y. Chan, Ph.D.
Associate Professor
Department of Pharmacology
Cornell University Medical College
New York, New York

James R. Fouts, Ph.D.
Chief, Pharmacology-Toxicology Branch
National Institute of Environmental Health Sciences, N.I.H.
Research Triangle Park, North Carolina

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Chief, Laboratory of Chemical Pharmacology
National Heart and Lung Institute, N.I.H.
Bethesda, Maryland

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Department of Pharmacology
School of Medicine
University of California
Davis, California

Bernard L. Mirkin, Ph.D., M.D.
Director, Division of Clinical Pharmacology
University of Minnesota
Minneapolis, Minnesota

Robert A. Moe, Ph.D.[10]
Vice President, Research and Development
Searle Laboratories
Chicago, Illinois

Frank G. Standaert, M.D.
Professor and Chairman
Department of Pharmacology
School of Medicine
Georgetown University
Washington, D. C.

Aldo P. Truant, Ph.D.[11]
Vice President, Research and Development
Pennwalt Prescription Products
Rochester, New York

E. Leong Way, Ph.D.
Professor and Chairman
Department of Pharmacology
School of Medicine
University of California
San Francisco, California

Irwin C. Winter, M.D., Ph.D.[12]
Vice President, Medical Affairs
G. D. Searle & Co.
Chicago, Illinois

[10] New Members December, 1973
[11] Deceased September 5, 1973
[12] Resigned December, 1973

Contributors

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Abbott Laboratories
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William L. Searle
Ushkow Foundation Inc.

Application

The Foundation accepts requests for support and suggestions for pertinent research projects from qualified institutions and individuals. However, in 1971 the Foundation underwent a major shift in program direction, now emphasizing education and training support.

To expedite the handling of requests for research support, it is suggested that a brief one or two page letter be directed to the Foundation, outlining the intended project and an estimate of the funds involved. After review of this more informal request by members of the Scientific Advisory Committee to determine the degree of likelihood of the project falling within Foundation guidelines, a decision can be made as to whether a formal proposal is warranted.

Letters should be addressed to:

Thomas E. Hanrahan
Executive Director
Pharmaceutical Manufacturers
Association Foundation, Inc.
1155 Fifteenth Street, N. W.
Washington, D. C. 20005

Pharmaceutical Manufacturers
Association Foundation, Inc.
1155 15th Street, N.W.
Washington, D. C. 20005