PROFILE

1967

Annual Report • Pharmaceutical Manufacturers Association Foundation, Inc.

Profile of Progress

How many angels can dance on the head of a pin? Questions as elusive as this one from medieval times are not without their counterparts today. A current, but not as perplexing a question, is how to measure the contribution of an activity to the "betterment of public health". This report will not discuss angels, dancing or otherwise, but will address itself to the specific question of the contributions of the Pharmaceutical Manufacturers Association Foundation in 1967 to the "betterment of public health." The events and activities developed within the Foundation's second year provide excellent measures of achievement. The result of this measuring, of this summing up, is one which shows continued growth and progress.

Demands on the PMA Foundation's resources increased substantially in 1967. That this would happen was predictable—due in part to decreased availability of government research funds and in part to the greater awareness by the scientific community of the Foundation's existence. It has been disappointing not to be able to support all of the worthwhile activities which have come to the Foundation's attention. Priorities were applied, and rightly so, to reach wise decisions on the use of the funds provided the Foundation by its many contributors.

The beginning made by the Foundation in its short existence is still small, but it has become more significant during 1967. This progress was not achieved by accident. It is the result of the generosity and combined efforts of many groups and individuals. Sincere expressions of thanks are due to the Foundation's advisory committees for the thoughtful advice provided to the Board of Directors, to the many contributors for their continuing financial support, and to the individuals who submitted the many well conceived research projects for consideration.

Whence the Foundation?

For those of you, who through this Annual Report, learn of the Pharmaceutical Manufacturers Association Foundation 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 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 of distinguished membership, 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 uncovering 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 31, 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 of PMA Member Firms and Associates, industrial concerns, organizations and individuals with an interest in health care.

A seven-man Board of Directors was elected for the Foundation from the membership of the PMA Board of Directors, a continuing requirement, and the President of the PMA was designated as Foundation President. The Foundation is incorporated in the District of Columbia. Contributions to the Foundation are deductible for federal income tax purposes under a ruling by the Internal Revenue Service.

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. The broadness of this goal made it immediately necessary to adopt certain guidelines to promote the wise and properly directed use of the limited resources available. To arrive at these guidelines, the Foundation relied heavily on special committees of the Medical, Research and Development, and Biological Sections of the Pharmaceutical Manufacturers Association, and a variety of other professional and scientific sources. The areas of interest agreed to initially, and which still govern the distribution of funds, are *support of fundamental research in drug toxicology,* and *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 most directly advancing the purposes of the Foundation.

For the information of future applicants for support, it is important to indicate those areas which the experience of these first two years has shown cannot or should not be supported within existing guidelines.

(1) Support of research on specific drugs. This exclusion is not meant to preclude support of projects which, of necessity, use a number of drugs or a class 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. This kind of activity is the proper concern of individual firms or research agencies.

(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 better be served by channeling the Foundation's available resources into other areas.

(3) Requests from individuals for funds for travel.

(4) Requests for funds to cover entertainment costs.

As of 1968, a policy has been instituted which restricts research support to no more than a two year commitment, but allows the grantee to request an extension for a third year at the end of the first year's activity, with a report of the first year's activity.

Organization and Administration

The PMA Foundation operates through a Board of Directors and three advisory committees. The Chairman of the Board is E. Gifford Upjohn, M.D., C. Joseph Stetler is President, Raymond M. Rice, M.D., is Vice-President, and Thomas E. Hanrahan is Executive Director.

E. Gifford Upjohn, M.D.

C. Joseph Stetler

Raymond M. Rice, M.D.

Thomas E. Hanrahan

At the PMA Annual Meeting in 1967, Henry W. Gadsden, President, Merck & Co., Inc., was elected to the Board of Directors of the Foundation to fill the vacancy created by the resignation of Mr. John G. Searle, Chairman of the Board and Chief Executive Officer, G. D. Searle & Co. Mr. Gadsden was elected Secretary-Treasurer.

In continuing to seek the most worthwhile activities for support, the Board of Directors has had the advice of extremely knowledgeable individuals, serving on three advisory committees.

The Scientific Advisory Committee has the responsibility of making recommendations to the Board of Directors on all grant requests and on self-initiated undertakings. To increase its effectiveness, the Chairmen of the Medical and the Research and Development Sections of the PMA were invited to serve on the Committee.

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The Advisory Committee to the "Faculty Development Awards in Clinical Pharmacology" program is charged with making recommendations to the Board of Directors on all applications received for these awards, as well as those applications received under the "Medical Student Traineeships in Clinical Pharmacology" program.

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San Francsico Medical Center
University of California
San Francsico, California

The Advisory Committee to the "PMA Foundation Fellowship Awards in Pharmacologic-Pathology" program is the newest advisory group. It is responsible for making recommendations to the Board of Directors on all applications received under this program.

Activities

Over $1.3 million have been authorized to date by the PMA Foundation for a variety of workshops, conferences, research activities and training programs. A table showing these approved programs and the individual or group sponsors appears on pages 22-23. These activities have provided a significant beginning for the Foundation.

Workshops and Conferences

An important continuing activity was the Foundation's support of pertinent meetings. These conferences and workshops have provided excellent educational opportunities for the participants. Support was authorized in 1966 for various meetings held in 1967. These included a second workshop on drug metabolism at George Washington University; an international symposium on comparative pharmacology in Washington, D.C.; an invitational interdisciplinary conference on immunology and pharmacology in Washington, D.C.; and a workshop on biochemical approaches to clinical pharmacology at Vanderbilt University. Meetings approved for support in 1967 are described below.

Neonatal Concerns

One meeting, supported in part, was a symposium conducted by the Teratology Society, May 26, 1967, in Estes Park, Colorado, on the subject of "Developmental Mechanisms Associated with Congenital Deformity." Approximately $2,600 was provided for the meeting by the Foundation. Representatives from the pharmaceutical industry, departments of pediatrics, the National Institutes of Health, and various academic research centers attended. Those responsible for the symposium said they believed it to be a highly successful scientific meeting.

Clinical Investigation

Another meeting, supported by a grant of $1,000, was a round table discussion held October 25, 1967, on "Control of Clinical Evaluations" under the chairmanship of Professor Maxwell Finland, Harvard Medical School. Participants in the discussion were from government, universities and pharmaceutical companies. The meeting, attended by 650, was held in Chicago, and was part of the Seventh Interscience Conference on Antimicrobial Agents in Chemotherapy. The proceedings are expected to be published in *Antimicrobial Agents in Chemotherapy—1967*, which should be available in July, 1968.

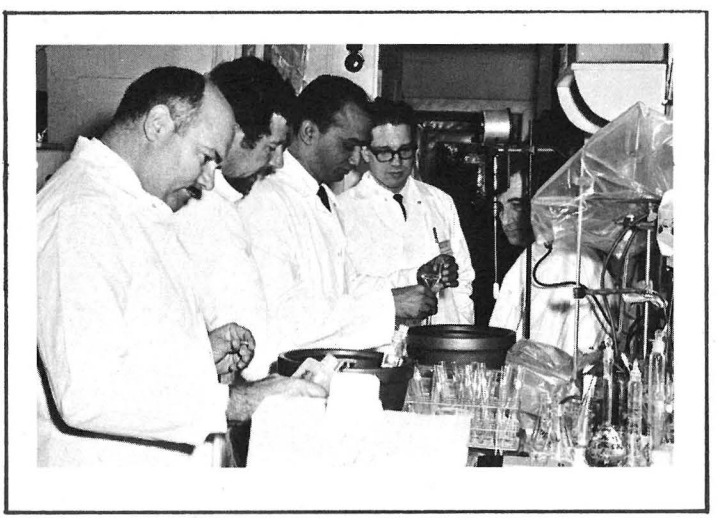
Autoradiography

A conference wholly supported by a Foundation grant of $14,650, dealing with "High Resolution Autoradiography of Diffusible Substances," is scheduled at the University of Chicago, Center for Continuing Education, June 2-4, 1968. Its goals are to provide a critical review by experts in the fields of autoradiography, histochemistry, and electron microscopy, leading to devel-

opment of guidelines for the use of autoradiography in the study of diffusible compounds. The conference chairman is Lloyd J. Roth, Ph.D., Chairman, Department of Pathology, University of Chicago. The conference and published papers will be of interest to pharmacologists and toxicologists concerned with the localization of drugs and toxic substances in tissue, as well as to biochemists concerned with the localization of enzymes and other tissue constituents.

Drug Metabolism

The Foundation has agreed to support and co-sponsor a Third Workshop on Drug Metabolism, scheduled for June 24-28, 1968, at the University of California, San Francisco Medical Center. Other sponsors are the University of California Schools of Medicine and Pharmacy, and the Drug Research Board of the National Research Council. The Foundation is providing up to $20,000 in full support of this meeting. It is being held because of the continued high quality of applicants who could not be accommodated in the limited enrollment of the first two workshops. As in the earlier ones, this



Drs. Cipriano Cueto, W. R. Jondorf, Krishna C. Agrawal, O. John Lorenzetti and Arthur G. Bolt (left to right) are engaged in an experiment measuring the effects of a number of variables on rat liver microsomal drug metabolizing enzymes. Samples are being prepared for the colorimetric estimation of drug metabolites. This was one of the experiments being conducted for the Second Workshop on Drug Metabolism held at the Department of Pharmacology of The George Washington University School of Medicine.

workshop is directed to pharmacologists, biochemists, toxicologists, teratologists, and clinical pharmacologists, who wish to gain further knowledge of approaches and techniques used in drug metabolism studies. These three workshops were designed for those without a previous working knowledge of drug metabolism. The workshop director is E. Leong Way, Ph.D., Professor of Pharmacology, School of Medicine, University of California, San Francisco Medical Center.

Pharmacology-Clinical Pharmacology

Scheduled to continue over a four-year period are a series of summer sessions entitled, "An Institutional Supplementary Training Program for Graduate Students in Pharmacology." An award of $176,880 was made to the American Society of Pharmacology and Experimental Therapeutics to support this undertaking. Programs in advanced pharmacology for Ph.D. candidates, drawn from schools across the United States and Canada, will be offered, with one six-week course per summer in an academic setting. Content of the courses, though not necessarily in the order given, will be: toxicology; drug disposition, stressing the biochemical mechanisms of drug action; neuropharmacology and behaviorial pharmacology; and cardiovascular autonomic pharmacology and renal pharmacology. Emphasis will be given to clinical pharmacology, as it relates to the subjects and drugs to be discussed.

The purpose of this program is to overcome a basic problem in pharmacology education, arising from the fact that many departments are not large enough to have all of the areas of pharmacology represented as major research and teaching interests. Because of this, graduate students tend to receive specialized training to the point where they are not fully aware of some of the other major problems in pharmacology. It is hoped that the broader exposure in the summer sessions will give the student a better perspective for continuing a career in teaching and research in pharmacology. The first such program is to be held in the summer of 1969.

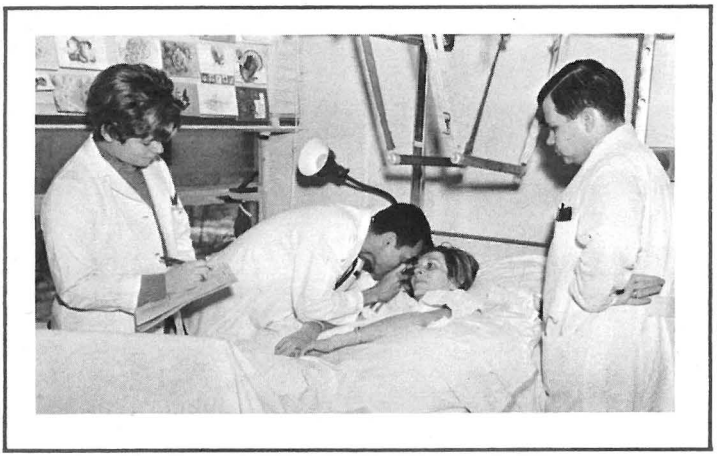
Research Grants

Another aspect of the Foundation's activities is its support of fundamental research in drug toxicology. Within this particular category the Foundation made five research awards in 1966, which continued into 1967. The recipients were: (1) Division of Clinical Pharmacology, Lemuel Shattuck Hospital Medical Service-Tufts University School of Medicine, Boston, Massachusetts; (2) Stanford Research Institute, Menlo Park, California; (3) Institute for Developmental Research, Children's Hospital Research Foundation, University of Cincinnati, Cincinnati, Ohio; (4) Renal and Electrolyte Division, Georgetown University Hospital, Washington, D.C.; and (5) the Registry of Tissue Reactions to Drugs, Armed Forces Institute of Pathology, Washington, D.C.

In 1967 new awards were granted to the Institute of Experimental Pathology and Toxicology of the Albany Medical College of Union University, Albany, New York; the Clinical Pharmacology Section, Department of Medicine, University of Southern California, Los Angeles, California; and the Department of Pediatrics, University of Utah, Salt Lake City, Utah. With these, the number of research efforts receiving support from the Foundation total eight. These research grants fall into five categories. They are:

Drug Surveillance

The Foundation currently supports three activities involved to some degree in adverse drug reaction reporting programs. Two of these, the studies at the Lemuel Shattuck Hospital in Boston and at the University of Southern California, are sufficiently different in approach that the Foundation believed much could be gained by supporting both. The third, the Registry of Tissue Reactions to Drugs, AFIP, is totally unlike in approach than the first two. These three are as follows:



Nurse monitor on location. A full-time nurse monitor is appointed to each of the wards under observation in the drug surveillance program at the Lemuel Shattuck Hospital.

A grant to the Clinical Pharmacology Division, Lemuel Shattuck Hospital Medical Service-Tufts University, of $27,439 for one year represents a renewal of a grant which expired August 31, 1967. This award brings to $53,209 the amount of support provided by the Foundation. These additional funds will enable the Division to continue its program of monitoring each drug routinely prescribed to patients in four 30-bed wards in the Lemuel Shattuck Hospital. Nurses are used in the study as monitors to work with the attending physicians in the wards. Their roles are to record the reasons of the doctors for beginning or stopping drugs at the times these decisions are made. Hershel Jick, M.D., Director of the Clinical Pharmacology Division, is the principal investigator. The research group believes that the additional year of support will permit them to gather sufficient information to seek long term support from other sources.

This study seeks to incorporate, within a predetermined design, the systematic collection of data to yield a number of different types of information such as:

- Total patient exposure to each drug, including dose and route of administration.
- Total recognized incidents of adverse reactions.
- A measure of efficacy to toxicity, taking into account the reason for which the drug is being used.
- An estimate of the degree of certainty regarding whether a given drug produced a given reaction.
- A description of the reaction.
- The identity of specific genetic populations more likely to develop adverse or beneficial effects from a given drug.
- A full listing of all other drugs which each patient received, enabling an analysis of drug interaction to be performed.

Studies have been set up in the laboratories to measure various genetically determined blood and plasma protein factors. These will be correlated with the drug effects.

Some of the conclusions reached during the first year of this study include:

- The drug surveillance program, as originally planned, is feasible and can be done efficiently.
- The expansion to other hospitals has been achieved.
- The computer handling of the inflow of data is possible and productive.
- Precise denominator and numerator data for large numbers of drugs can be collected.
- Important clues to the identification of subpopulation groups by means of blood groups is being obtained.
- A framework exists for the introduction of double-blind controlled studies within the drug surveillance program. One such study concerning analgesics has almost been completed, and has yielded interesting and statistically significant results.

A grant to the University of Southern California of $48,000 was made to support in part a study of adverse drug reactions at the Los Angeles County General Hospital. The program is under the direction of Robert F. Maronde, M.D., Chief, Clinical Pharmacology Section at the University of Southern California. It is part of a larger project divided into two studies: (1) an adverse drug reaction study of hospitalized patients, and (2) an inquiry into drug ordering and dispensing in an outpatient population.

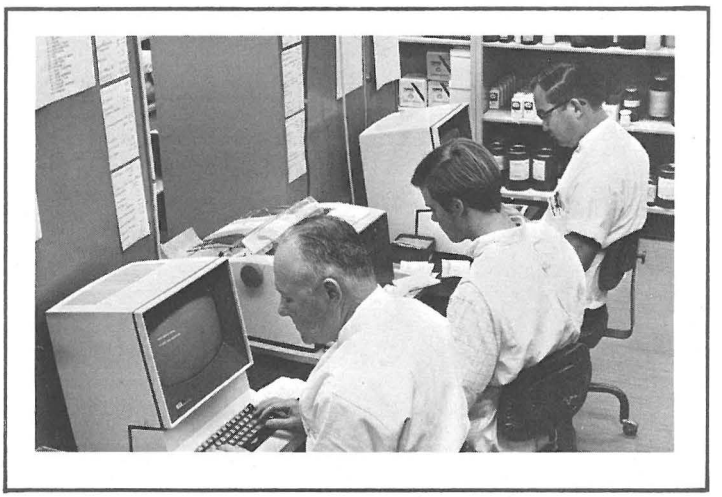
In the adverse drug reaction study on hospitalized patients, certain basic assumptions have been made. Some of these are:

- Voluntary reporting by physicians of adverse drug reactions has been shown to be inadequate.
- The information gained in interviewing physicians regarding adverse drug reactions in their patients is often worthless, since this will only lead to the recording of commonly known reactions and may not distinguish disease-related events or interactions of drugs from an adverse reaction to a particular drug.
- Only by the acquisition and proper analysis of valid data regarding patient-related events, may new or previously unrecognized reactions be found, events attributed to drugs that are truly disease-related be properly delineated, or interactions of drugs in the causation of adverse reactions be recognized.
- To assure the validity of the data, the most appropriate method is an epidemiologic approach by a team of physicians, combined with the development of proper input and output techniques for the computer file.

Approximately 2,000 patients are admitted yearly to the one medical ward within the Los Angeles County General Hospital involved in this phase of the project. Each patient admitted to this medical ward will be seen daily by one of six members of the physician surveillance team. The role of the physician surveillance team is to note patient events. Such recording of events is not limited to recognized side effects of a drug or to incidents that are unexpected. The reporting technique will encourage the physicians to include events outside the specific areas of concern that they believe are significant.

In the companion study of process control over the ordering of drugs for an outpatient population, the Los Angeles County General Hospital Outpatient Clinic, with over 700,000 outpatient visits per year, provides a good setting for this study. In excess of 300 interns and 300 resident physicians, plus other house staff physicians, rotate through the clinic service annually. No other county hospital provides services to patients attending this facility. Medications are dispensed free of charge or at a greatly reduced rate to the patients, so that over 90% of the outpatients' drugs originate from this out-

patient area, and one pharmacy serves the entire clinic. Integral parts of this study are the computer programs written for cathode ray terminal ordering of prescriptions. All drug information is entered into the patient's computer file, when the pharmacists enter the prescription.



Pharmacists operating two IBM 2260 Cathode Ray Tube Display Stations, in daily use at the Los Angeles County General Hospital Outpatient Pharmacy.

A grant of $23,700 was made to support of the Registry of Tissue Reactions to Drugs, Armed Forces Institute of Pathology, Washington, D.C., for its second year of operation. The Registry is co-sponsored and equally supported by the American Medical Association, the Food and Drug Administration, the National Institutes of Health, and the PMA Foundation. Nelson S. Irey, M.D., is the Registrar, and Miles E. Foster, M.D., a pathologist, is the other physician member of the Registry's staff. The Registry obtains biopsy and autopsy tissue specimens from suspected drug reaction cases, subjects them to microscopic examinations, and reports its findings to the pathologist who submitted the material for review. During the first two years the number of cases obtained by the Registry totalled slightly over 700. From the files of the AFIP, the Registry has nearly 9,000 cases which are related to some kind of suspected drug reaction, and which are available for study when desired.

A primary function of the Registry in its first two years has been educational. An award-winning exhibit produced in 1966 has been presented at several scientific meetings. Another educational activity of the Registry is the "Drug Reaction Syllabus." Part I of this syllabus was written for use with the exhibit mentioned above. It contains a description of specific cases and the techniques used by the Registry. Nearly 3,000 copies have been distributed. Slides of tissue specimens have been prepared for use with Part I. Nearly 75 medical schools have requested the slide sets for use in teaching.

Part II of the syllabus was recently completed. In it, three major points covered in Part I are enlarged upon by the use of 20 cases to illustrate certain diagnostic points. It was prepared for use with a second exhibit developed by the Registry. Copies of the syllabus can be obtained by contacting the Registry.

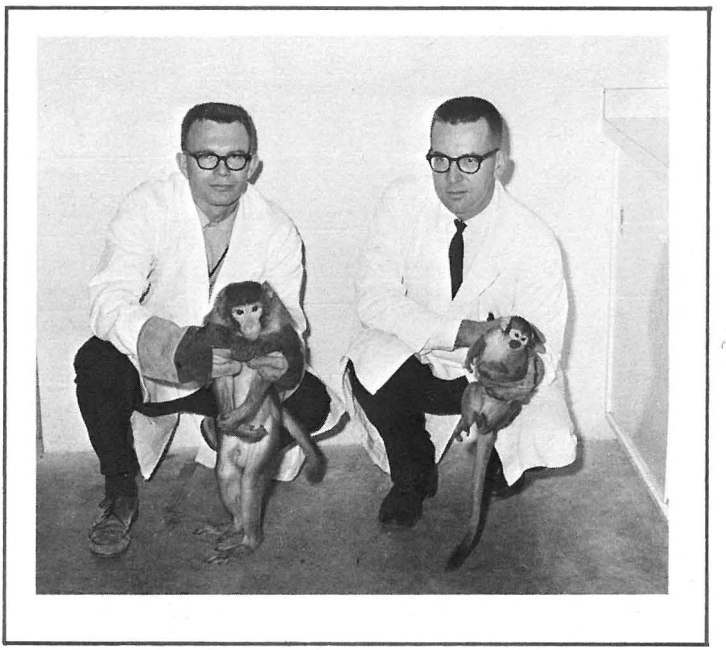
Placing third among scientific exhibitors, Nelson S. Irey, M.D., right, is shown receiving the Bronze Award from Ernest E. Simard, M.D., center, Salinas, California, president of the College of American Pathologists, and Albert L. McQuown, M.D., Baton Rouge, Louisiana, president of the American Society of Clinical Pathologists. The award was given for the display of the activities and accomplishments of the Registry of Tissue Reactions to Drugs of the Armed Forces Institute of Pathology. The presentation was made at the annual joint meeting of the societies September 17-23, 1966, Washington, D. C.

Animal-Human Predictability Studies

A two year grant of $59,885 to the Stanford Research Institute dating from September 1, 1966, is in its second year. It provides for a study of the metabolism of well known drugs in subhuman primates. Hopefully, the knowledge acquired in this work will enable scientists to make more accurate and realistic predictions of toxic and pharmacological effects of new drugs in humans.

The objectives of this undertaking are to investigate the comparative capacities of the rhesus and squirrel monkeys to metabolize and excrete commonly used drugs and to relate the results obtained to existing knowledge of the metabolic processes of the drugs in man. The rhesus monkey has been used frequently in drug studies, and much is known concerning the predictability of animal tests on the rhesus monkey to man. However, if the squirrel monkey is found to have similarities to the human, their smallness and more docile nature will make them a better laboratory animal, since they are easier to handle and less expensive to house and feed than the rhesus.

The work of the first year has involved extensive testing of two drugs, chloral hydrate and meperidine hydrochloride, and others will be investigated as the work progresses. A report on this investigation has been accepted by the American Society of Pharmacology and Experimental Therapeutics for presentation April 17, 1968, at its meeting in Atlantic City.



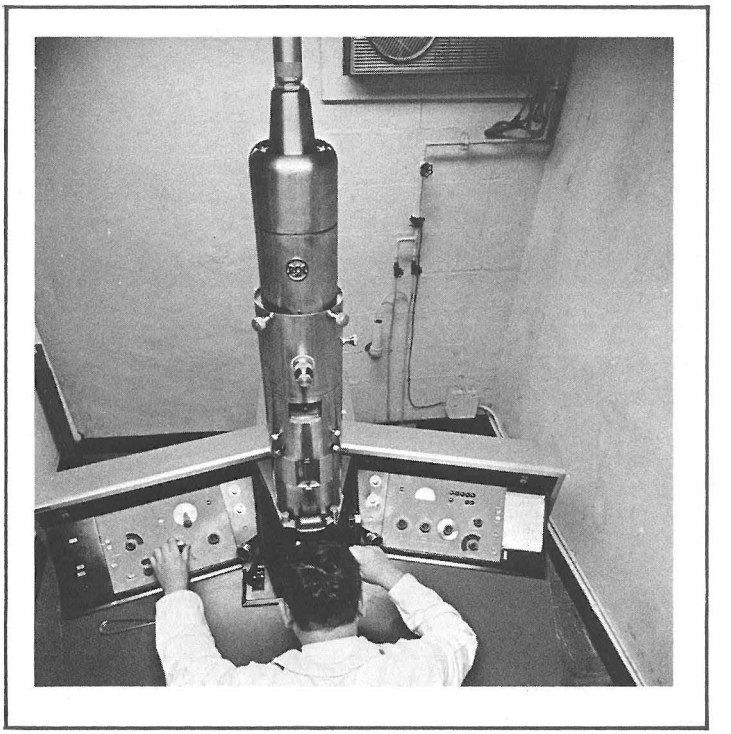
Rhesus and squirrel monkeys are being used by G. R. Gordon (left) and J. H. Peters, Ph.D., of Stanford Research Institute, Menlo Park, California, for studies on the "Metabolism of Well-Known Drugs in Subhuman Primates."

Drug-Related Structural Studies

A grant of $100,000 over a four-year period was made to the Institute of Experimental Pathology and Toxicology of the Albany Medical College of Union University, Albany, New York. The principal investigator is Frederick Coulston, Ph.D., Director of the Institute. The funds will support the Institute's program of studies of the relation of structural changes in the subcellular organelles of important tissues to the actions of chemicals and drugs on various functional properties of these tissues. The study will correlate morphological changes determined by simple microscopy, histochemistry and electron microscopy, with the biochemical changes in tissues following acute and chronic administration of various pesticides and drugs.

Data presently available indicate that many pesticides and other chemicals produce early and predictable ultrastructural changes in the intestinal and liver cells. Many of these changes represent physiologic adaptation and are reversible within days. With the grant, further experiments are planned to relate these early changes to those found in some more chronic situations.

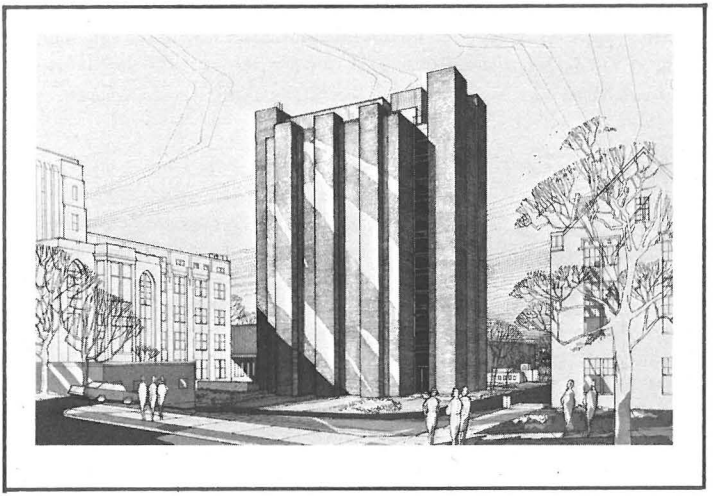
Foundation funds will enable the Institute to expand its efforts in studies with drugs. The experiments will not concern themselves necessarily with the toxicity of such drugs, but rather to demonstrate the manner in which a cell adapts itself to the presence of a new chemical in its environment. The comparative biochemical and ultrastructural studies to be performed under this award may enable the study group to predict with greater accuracy from animal data what drugs will do in man.



RCA electron microscope (EMU-3H), in air conditioned dark room, used at the Institute of Experimental Pathology and Toxicology, Albany Medical College, to study the effects of chemicals on tissue structure at high magnification (10,000 to 50,000 times).

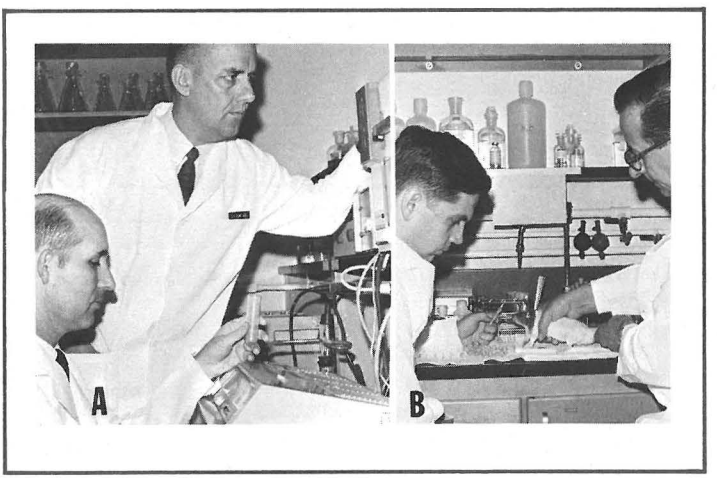
Pediatric-Fetal Pharmacology

A grant of $50,000 a year for five years to Josef Warkany, M.D., Professor of Research Pediatrics, on behalf of the Children's Hospital Research Foundation beginning January 1, 1967, is for partial support of the activities of the Division of Fetal Pharmacology of the Institute for Developmental Research. The Institute, presently under construction, will use its sixth floor to accommodate the activities of the Division of Fetal Pharmacology. These funds will provide the means to retain the necessary staff and secure equipment to make possible an early beginning of the basic research envisioned within the Division. While construction funds had been obtained for the Institute, research funds for the Division of Fetal Pharmacology were needed. During 1967, a director for the Division of Fetal Pharmacology was retained, Ernest F. Zimmerman, Ph.D., pharmacologist and molecular biologist, presently at Stanford University. He will join the Institute staff in July, 1968. The Institute is to be officially opened in the Spring of 1968. While the entire sixth floor of this building will be devoted to research in fetal pharmacology, other divisions within the Institute will engage in related fields.



The architect's sketch for the Institute of Developmental Research, Children's Hospital, University of Cincinnati, Cincinnati, Ohio. The Institute, which will open in the Spring of 1968, will devote its sixth floor to the activities of the Division of Fetal Pharmacology.

An award of $36,000 for a two-year period made to the Department of Pediatrics of the University of Utah, and Alan K. Done, M.D., Associate Professor of Pediatrics, is for "The Study of the Drug Potentiation of Kernicterus." Kernicterus, as it is studied in this investigation, is a condition of hyperbilirubinemia associated with jaundice and evidence of brain damage in the newborn. It is potentiated by certain widely used drugs which compete with bilirubin for binding to serum albumin, thereby increasing the level of



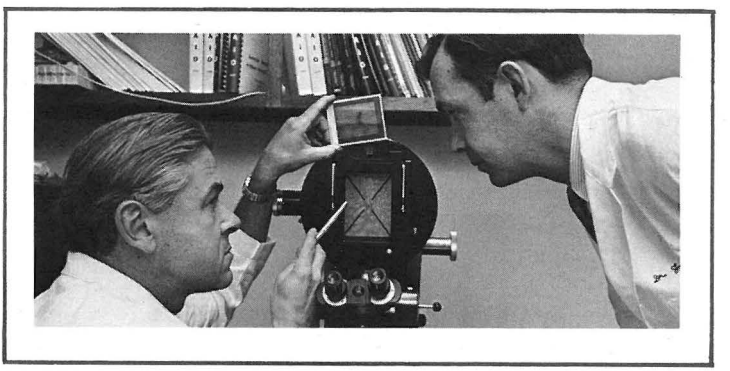
At the University of Utah Dr. Alan K. Done (standing) and technician, Arnold Peart, perform test tube experiments (A) which they hope to correlate with studies (B) conducted in congenitally-jaundiced rats by Anthony Temple (left) and Orville Pape. The hope is to develop ways of testing possible hazards posed to newborn infants by drugs which may potentiate a type of brain damage known as kernicterus.

circulating free bilirubin. A special strain of rat which has an inherited inability to conjugate bilirubin is being utilized as a test animal. The objective of the study is to develop a method by which drugs may be tested for their potential to promote development of kernicterus in the newborn.

Dialyzable Drugs

A grant of $20,000 per year for up to five years to the Renal and Electrolyte Division, Georgetown University Hospital, is in the first year. George E. Schreiner, M.D., Professor of Medicine and Director of Renal and Electrolyte Division, is the principal investigator. This award is to support research relating to the hemodialysis of drugs, and a proposed registry of drug dialysis findings, to be developed in co-operation with the American Society for Artificial Internal Organs. Hemodialysis is the removal of certain elements (in this case drugs) from the blood by diffusion through a semipermeable membrane. The artificial kidney utilizes this procedure.

This list of dialyzable poisons and drugs has increased rapidly since hemodialysis was first used for the treatment of drug poisoning. Broader application of dialytic techniques and greater interest in research on poisons encouraged the research group to bring this subject up to date in a publication which appeared in *Transactions of the American Society for Artificial Internal Organs,* Vol. 8, 1967. The article covers a series of known dialyzable poisons and drugs, such as barbiturates, tranquilizers and other sedatives , analgesics, halides, metals, alcohols, antibiotics, and others.



George E. Schreiner, M.D., (left) and John F. Maher, M.D., Georgetown University Hospital, discussing a renal biopsy from a patient with mercury poisoning.

Clinical Pharmacology

To attain its objectives in the field of clinical pharmacology, the Foundation has sponsored two programs. Increased numbers of medical personnel to conduct clinical studies must be trained. The two clinical pharmacology programs, one with hoped for immediate results, and the other more long range, have provided opportunities for a number of individuals to extend their career commitments in the field of clinical pharmacology or to acquaint themselves with the techniques of clinical pharmacology. The "Faculty Development Awards in Clinical Pharmacology" and the "Medical Student Traineeships in Clinical Pharmacology" proved to be highly successful and much sought after awards in 1967.

Through the "Faculty Development Awards in Clinical Pharmacology" program, the Foundation makes two-year awards to medical schools for salary support of full time junior faculty members in the field of clinical pharmacology. To best meet the needs of the applicant universities and the candidates they sponsor, the level of support offered through the program is variable. It is aimed at keeping within the existing salary structure of the applicant university for similarly trained individuals. The Board of Directors has established a fund of $100,000 for this program.

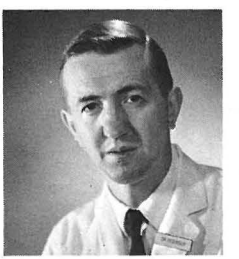
The recipients of awards in 1967 which will begin July 1, 1968, and the purposes for which the awards will be used, are:

William Y. W. Au, M.D., Assistant Professor of Pharmacology and Medicine at the University of Rochester School of Medicine and Dentistry, will continue his research on the effect of hormones and other agents affecting bone metabolism. Dr. Au, a native of Oahu, Hawaii, a graduate of Boston University and Boston University Medical College, will play a central role in the expansion of the medical school's clinical pharmacology unit at the Rochester General Hospital.

Arthur H. Hayes, M.D., a faculty member at the Cornell University Medical College, will extend his training in the cardiovascular field. Dr. Hayes studied at Oxford University as a Rhodes scholar prior to receiving his medical degree at Cornell in 1964. He will study the mechanisms of the action of cardiovascular drugs in animals and man. His aim is to test the validity of animal models for human problems and, in appropriate instances, to extend his work to include parallel basic studies of drug action in man, continuing until practical and ethical limitations prevent further human experiments.

William Y. W. Au, M.D.

Arthur H. Hayes, M.D.



Donald S. Robinson, M.D.

Donald S. Robinson, M.D., presently a clinical investigator at the National Heart Institute, National Institutes of Health, will use this award to pursue his interests in the clinical application of biochemical pharmacology. Dr. Robinson received his medical degree from the University of Pennsylvania, and in July of 1968 will join the University of Vermont College of Medicine as Assistant Professor of Pharmacology and Medicine. Among a variety of other activities, Dr. Robinson will coordinate a comprehensive study of the drug therapy of depressed patients. He will also be responsible for organizing and activating a Division of Clinical Pharmacology.

These three awards bring to six the number of faculty members being supported by the Foundation through this program. The individuals who received awards in 1966, which began July 1, 1967, and will continue until June 30, 1969, are:

John L. McNay, M.D., Emory University
Faruk S. Abuzzahab, Sr., M.D., University of Minnesota
John S. Holcenberg, M.D., University of Washington, Seattle

Dr. McNay is doing research in renal physiology and pharmacology; Dr. Abuzzahab is conducting research in both basic and clinic psychopharmacology; and Dr. Holcenberg is extending his interests in biochemical approaches to clinical pharmacology.

John L. McNay, M.D.

Faruk S. Abuzzahab, Sr., M.D.

John S. Holcenberg, M.D.

The "Medical Student Traineeships in Clinical Pharmacology" program offered for the first time in 1966, with awards beginning in 1967, provided 20 students in 14 medical schools across the United States with opportunities to become better acquainted with the basic techniques applied in the field of clinical pharmacology. It is hoped that as a result of such an experience at least some of these students may retain their interest and will continue along this path as a career. The program provides $1,000 to each student for a three-month period of work in a clinical pharmacology unit, primarily concerned with research and training. A yearly fund of $20,000 has been authorized for this program, which is again being offered for awards to begin June, 1968.

A number of highly interesting reports have been submitted by the trainees. One of the first reports received informed the Foundation that the experience under the traineeship has prompted the student to pursue a combined M.D.-Ph.D. in pharmacology. Generally the reports reflected a new

respect for the field of clinical pharmacology as a career. Students receiving these awards for 1967 are listed below:

University of California on behalf of
Mr. Jeffrey S. Stoff

Emory University, School of Medicine on behalf of
Mr. Robert R. M. Gifford

Georgetown University, School of Medicine on behalf of
Mr. Richard S. Kruse

Hahnemann Medical College on behalf of
Mr. Philip L. Bonnet and Mr. Harris S. Vernick

University of Iowa on behalf of
Mr. William W. Lukensmeyer and Mr. John D. Miller

University of Kansas on behalf of
Mr. Jack L. Croughan and Mr. Danny M. Westphal

Loma Linda University on behalf of
Mr. Dale E. Kearbey

University of Nebraska on behalf of
K. C. Wong, Ph.D.

New York University School of Medicine on behalf of
Mr. Glenn S. Hammer

University of Rochester on behalf of
Mr. Werner A. Bleyer

Saint Louis University on behalf of
Mr. Jeffrey A. Leinicke and Mr. Gary A. Peasley

Temple University on behalf of
Mr. Kenneth M. Kessler

Vanderbilt University, School of Medicine on behalf of
Mr. William J. Anderson

Yale University on behalf of
Mr. Gary S. Farnham, Miss Lesley Nan Forman and Mr. Karl O. Wustrack

Pharmacologic-Pathology

A postdoctoral program offered by the Foundation, with the first awards to be made for the year beginning July 1, 1968, is the "PMA Foundation Fellowship Awards in Pharmacologic-Pathology." Through this program it is hoped that individuals will be encouraged to conduct studies aimed at relating drug action with drug-induced morphologic changes. It is intended to provide the opportunity for individuals to combine training in fields such as pathology, cytology, histology, or ultrastructure with pharmacology. If the primary training of a candidate is related to structure, then training under the program would be in pharmacology. If the initial training is pharmacologic, the opportunity for training and research in a structural discipline will be provided. It is anticipated that two or three awards will be possible under this program each year. A total of $70,000 has been set aside to fund this program.

These fellowship awards are similar to the faculty development awards in clinical pharmacology in that they are for two years each, with the stipend level variable, aimed at keeping within the existing stipend levels for similarly trained individuals within the applicant university.

SUMMARY OF PROGRAMS AND AWARDS OF THE PMA FOUNDATION 1965-1967

Institution or Program	Amounts Authorized	Payments up to December 31, 1967	Unpaid Amounts as of December 31, 1967	Estimated Amounts to be paid in 1968
Meetings				
Clinical Investigation				
American College of Cardiology [1]	$ 5,000	$ 5,000		
American Society of Microbiology	1,000	1,000		
Drug Metabolism				
New York University Medical Center [1]	18,060	15,025.16[2]		
George Washington School of Medicine [1]	18,000	18,000		
University of California Schools of Medicine and Pharmacy	20,000		$ 20,000	
Pharmacology				
Symposium on Comparative Pharmacology [1]	3,000	3,000		
National Academy of Sciences [1]	11,800	11,800		
Vanderbilt University [1]	20,090	20,090		
American Society of Pharmacology and Experimental Therapeutics	176,880		176,880	$5,000
Teratology Society	2,581.40	2,581.40		
University of Chicago	14,650	14,650		
Research Grants				
Children's Hospital Research Foundation, Cincinnati	250,000	25,000	225,000	50,000
Georgetown—Kidney Fund	100,000	20,000	80,000	20,000
Institute of Experimental Pathology & Toxicology, Albany, New York	100,000	12,500	87,500	25,000
Lemuel Shattuck Hospital—Tufts University, Boston	53,209	39,489.50	13,719.50	13,719.50
Registry of Tissue Reactions to Drugs, AFIP	79,061.08	54,061.08	25,000	25,000
Stanford Research Institute	59,885	41,921	17,964	17,964
University of Southern California	48,000		48,000	24,000
University of Utah	36,000	18,000	18,000	18,000
Training Programs				
Medical Student Traineeships in Clinical Pharmacology	40,000	20,000	20,000	20,000
Faculty Development Awards in Clinical Pharmacology	217,008.80	55,204	161,804.80	107,821.40
Fellowship Awards in Pharmacologic-Pathology	70,000		70,000	35,000
TOTALS	$1,344,225.28[3]	$377,322.14	$963,868.30	$381,504.90

1. For a discussion of these activities, see the 1966 Annual Report. All other awards listed are described herein.
2. Adjusted to reflect grant refund of $3,034.84.
3. The difference of $3,034.84 in the total of authorized amounts (Column 1) and the sum of (Column 2 + Column 3) represents the $3,034.84 in refund of grant listed in footnote 2.

Foundation Finances

Contributions are accepted from private, corporate and individual sources. The Foundation does not accept contributions which are so restricted as to place their use outside the policies of the Foundation.

The Board of Directors of the Foundation decided that, as a minimum, contributions of $500,000 would be sought for each of the first three years of the Foundation's existence, extending through 1968, with larger amounts anticipated thereafter. In requests for support to the PMA Member Firms, a guideline is suggested. Each firm is asked to consider a contribution equal to .015% of its domestic and international pharmaceutical sales.

Income

Total income in 1967 was $572,492.88. Of this amount, $543,392.00 came from contributions. The balance of $29,100.88 came from investments and a refund of an unexpended balance from a grant. The 1967 contributions represent an increase of approximately 10% over the amount received during the first contribution drive covering 18 months during 1965-66.

Contributions were received from approximately three out of every four of the 136 PMA Member Firms. Two out of every three of the PMA Associates joined in supporting the Foundation. Contributions were also received from a number of individuals and industry-related firms.

Expenditures

Expenditures for grants, Foundation-sponsored programs, and administrative expenditures for 1967 amounted to $345,222.86. Of this amount, $278,922.06 represent expenditures for grants and Foundation-sponsored programs. There was a fund balance of $621,167.82 at the year's end. This figure, however, does not reflect the liability for the authorized, undisbursed amounts for some of the grants and programs described earlier. The Foundation will report these amounts as expenditures when the funds are disbursed. As of December 31, 1967, this liability totaled $963,868.30. Some of these grants represent amounts to be paid over the next four years. Part of this liability will be met from anticipated income in 1968 and succeeding years. During 1968 the estimated amount to be paid on this liability totals $381,504.90.

Financial Reports

The Foundation's financial position as of December 31, 1967, has been audited by the accounting firm of Ernst and Ernst. Copies of this statement will be supplied upon request.

Financial statements have been issued quarterly during 1967. These reports have been prepared by the Washington, D.C., accounting firm of Buchanan & Company. These cumulative quarterly reports will continue to be distributed in 1968. A separate report covering the fourth quarter of 1967 was not distributed since the year's report is contained herein.

STATEMENT OF INCOME AND EXPENDITURES

January 1, 1967-December 31, 1967

Income

Contributions—Note a	$543,392.00
Income from investments	26,066.04
Refund of unexpended balance of prior year's grant	3,034.84
TOTAL INCOME	$572,492.88

Expenditures

Grants—Note b

Children's Hospital Research Foundation	$ 25,000.00
George Washington University	18,000.00
National Academy of Sciences	11,800.00
Tufts University	26,604.50
Teratology Society	2,581.40
Stanford Research Institute	29,882.30
Faculty Development Awards in Clinical Pharmacology	55,204.00
Medical Student Traineeships in Clinical Pharmacology	20,000.00
Georgetown—Kidney Fund	20,000.00
University of Utah	18,000.00
Institute of Pathology and Toxicology	12,500.00
American Society for Microbiology	1,000.00
Universities Associated for Research and Education in Pathology, Inc. (Registry of Tissue Reactions to Drugs, AFIP)	23,699.86
University of Chicago	14,650.00
	$278,922.06
Administrative expenses	66,300.80
	$345,222.86
Excess of income over expenditures	227,270.02
Fund balance at January 1, 1967	393,897.80
Fund balance at December 31, 1967	$621,167.82

Note a—
The Foundation received contributions of $94,557.00 prior to December 31, 1967, which the Foundation has considered as being applicable to 1968, and therefore are not recorded as income in 1967.

Note b—
The Foundation has committed itself, subject to annual review, to make certain research grants. At December 31, 1967, the amounts still to be disbursed with respect to these grants aggregated $963,868.30, of which approximately $381,504.00 is expected to be disbursed in 1968.

Contributors

PMA Member Companies

Abbott Laboratories
Alcon Laboratories, Inc.
Conal Pharmaceuticals, Inc.
Allergan Pharmaceuticals, Inc.
American Cyanamid Company
Davis & Geck
Fine Chemicals Department
Lederle Laboratories Division
American Home Products Corporation
Ayerst Laboratories
Ives Laboratories, Inc.
Wyeth Laboratories
Armour Pharmaceutical Company
Astra Pharmaceutical Products, Inc.
Baxter Laboratories, Inc.
Flint Laboratories
Hyland Division
Travenol Laboratories, Inc.
Wallerstein Company
Becton, Dickinson and Company
B-D Laboratories, Inc.
Boyle and Company
Bristol Laboratories
Burroughs Wellcome & Co. (U.S.A.) Inc.
Carbisulphoil Company
The Central Pharmacal Company
Chatham Pharmaceuticals, Inc.
CIBA Pharmaceutical Company
Cole Pharmacal Company, Inc.
Commercial Solvents Corporation
Crookes-Barnes Laboratories, Inc.
Cutter Laboratories
Hollister-Stier Laboratories
Difco Laboratories
Distillation Products Industries
(Eastman Kodak Company)
Dorsey Laboratories
(The Wander Foundation)
Endo Laboratories, Inc.
(Endo Foundation)
First Texas Pharmaceuticals, Inc.
C. B. Fleet Co., Inc.
Geigy Pharmaceuticals
Hoechst Pharmaceutical Company
Hoffmann-LaRoche, Inc.
Hynson, Westcott & Dunning, Inc.
Johnson & Johnson Association
Industrial Fund
Ethicon, Inc.
McNeil Laboratories, Inc.
Ortho Pharmaceutical Corporation
Knoll Pharmaceutical Company
Lakeside Laboratories, Inc.
Lemmon Pharmacal Company
Eli Lilly and Company
Mallard, Inc.
Mallinckrodt Chemical Works
Marion Laboratories, Inc.
* The S. E. Massengill Company
Merck & Co., Inc.
Merck Chemical Division
Merck Sharp & Dohme
Miles-Ames Foundation
Ames Company
Dome Laboratories
Neisler Laboratories, Inc.
Nion Corporation
The Norwich Pharmacal Company
(Norwich-Eaton Charitable Trust)
The P. J. Noyes Company, Inc.
Organon, Inc.
Parke, Davis & Company
S. B. Penick & Company
(S. B. Penick Foundation)
Chas. Pfizer & Co., Inc.
Philips Roxane Laboratories
Richardson-Merrell, Inc.
J. T. Baker Chemical Co.
The Wm. S. Merrell Company
The National Drug Company
Riker Laboratories
Rexall Drug Company
A. H. Robins Company, Inc.
William H. Rorer, Inc.
(Rorer Foundation)
Kinney & Company, Inc.
Rowell Laboratories
Rystan Company
Sandoz Pharmaceuticals
Savage Laboratories, Inc.
R. P. Scherer Corporation
Schering Corporation
White Laboratories, Inc.
G. D. Searle & Co.
Sherman Laboratories
Smith Kline & French Laboratories
(Foundation)
Norden Laboratories, Inc.
E. R. Squibb & Sons, Inc.
(Olin Mathieson Charitable Trust)
Strasenburgh Laboratories
Strong Cobb Arner, Inc.

Stuart Division
(Atlas Chemical Industries, Inc.)
The Upjohn Company
The Vale Chemical Company, Inc.
Walker, Corp & Co., Inc.
Wallace Pharmaceuticals
Wampole Laboratories
(Denver Chemical Manufacturing Co.)
Warner-Chilcott Laboratories
(Warner-Lambert Pharmaceutical Co.)
Warren-Teed Pharmaceuticals, Inc.
Winthrop Laboratories
Breon Laboratories, Inc.

PMA Associates

American Academy of General Practice
American Medical Association
Benzol Products Division, Cowles Chemical Co.
Clark O'Neill
The Dow Chemical Company
Gane's Chemical Works, Inc.
R. W. Greeff & Co., Inc.
Hazleton Laboratories, Inc.
Ivers-Lee, Division of Becton Dickinson and Company
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Modern Medicine Publications Foundation
Monsanto Company (Fund)
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The S.S.T. Corporation
Sheffield Tube Corporation
Sieber & McIntyre, Inc.
Robert E. Wilson, Inc.
The Yorke Medical Group
(The Reuben H. Donnelly Corp.)

Personal and Others

N. W. Ayer & Son, Inc.
(W. M. Armistead Foundation)
M. F. Charley, Chairman of the Board
of Directors, Standard Pharmacal Corp.
William N. Creasy
Frank J. Corbett, Inc.
Florence and Maxwell Geffen Foundation
MD Publications
** PMA Medical Section
Reader's Digest Foundation
Raymond M. Rice, M.D.
The Magazine of American Agriculture
The Scholl Mfg. Co.

** Contribution made in the memory of Francis C. Brown, Schering Corporation, and Rudy P. Neptun, S. B. Penick & Company.*

*** Contribution made in the memory of George R. Hazel, M.D., Abbott Laboratories.*

Applications

The Foundation welcomes requests for support and suggestions for projects from qualified institutions and individuals.

It is suggested that the requests for assistance take the form of a letter, outlining the subject, purposes, scope, principal researchers, curriculum vitae and bibliographies, budget and other sources of present or anticipated financing of the undertaking. Letters should be addressed to:

C. Joseph Stetler, *President*
Pharmaceutical Manufacturers Association Foundation, Inc.
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

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