Pharmaceutical Manufacturers Association Foundation, Inc. 1978 Annual Report

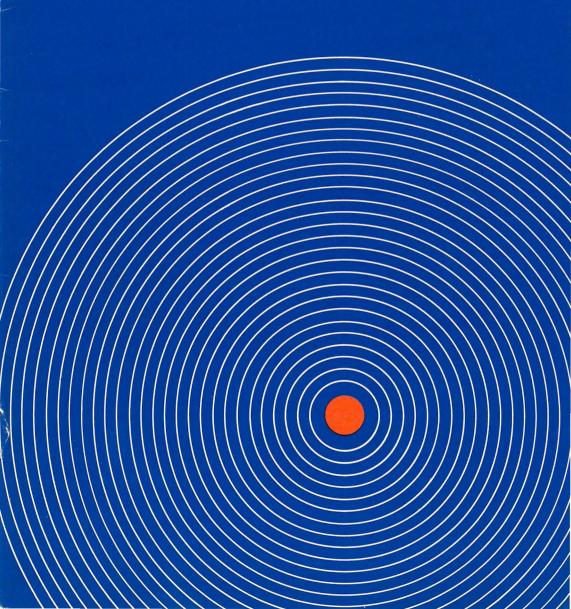


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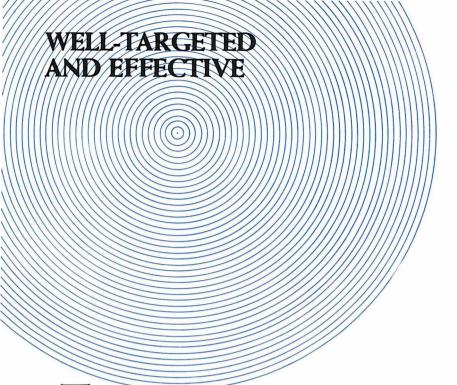
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Applications (inside back cover)



his conclusion emerges strongly from any evaluation of the eight regularly-offered programs of the PMA Foundation. Measured by career advancement, a primary goal of the Foundation since its inception in 1965, these programs have been highly successful. So to that extent alone, the PMA Foundation has contributed notably to the progress of pharmacology and clinical pharmacology in the United States.

On the clinical side, the major PMA Foundation program confers faculty awards in clinical pharmacology. Of the 40 scientists supported under this program from 1966 through 1977, the time of the last general survey, 36 continued to be active in academic careers, one had joined the pharmaceutical industry, one the military medical corps and two had entered private practice. The 36 individuals in academe had achieved impressive stature: 13 are full professors, 12 are associate professors and 11 are assistant professors

(the most recent awards). In addition, two are chairmen of departments of pharmacology. This is an extraordinary record given the time period for academic advancement and considering that, as awardees, they come into the program as instructors or assistant professors.

Other prestigious awards testify to their continuing professional recognition. Six faculty awardees have received Burroughs Wellcome Scholar Awards. Four others won NIH Career Development Awards, two Established Investigator Awards from the American Heart Association and one a Howard Hughes Medical Investigator Award.

Additionally, a most telling fact is that 25% of the academic clinical pharmacology units in the United States are directed by those who were aided by the Foundation's faculty program.

On the basic science side, the major PMA Foundation effort goes into faculty awards in pharmacology,

research starter grants for beginning investigators and interdisciplinary fellowships. Information gathered in 1977 from 103 of those grantees under the research starter grant and faculty award programs showed that 97 of them hold faculty appointments in 47 medical schools, 10 schools of pharmacy and five other professional schools. The other six are in government or other research institutions.

These two programs have provided support to about 12% of the full-time pharmacology faculty members in the United States.

The interdisciplinary fellowship program grew out of the recognition in 1968 by the PMA Foundation that the training then offered in departments of pharmacology, anatomy and pathology did not fully prepare scientists to interface effectively with other disciplines. The Foundation believed that the major advances in the 1970's would be made at these points of interface. The fellowship program was developed to interest individuals trained in one of these fields to learn the principles and research methods of the other.

The Foundation's prediction as to the future direction of research in pharmacology has proven to be accurate. The 1967 Annual Review of Pharmacology contained relatively few reports of truly interdisciplinary research, although several of the authors showed a growing awareness of the need for correlation of

morphological and pharmacological observations. The reviews in the 1979 volume, by contrast, identify 11 areas of interdisciplinary efforts in pharmacology and morphology.

Of the 27 fellows surveyed in 1977 who had completed their fellowships, 25 continue to be involved in research similar to that fostered by the fellowship. They are applying the skills of the complementary field in their current research. These 25 scientists have published frequently in well-respected journals on research related to the projects undertaken while they were PMA Foundation grantees, thereby, contributing further to the movement of interdisciplinary research.

These few results are among many which the Foundation has developed. Information of this kind, site visits to many former and current awardees and yearly meetings with them have demonstrated, we believe, that the Foundation's programs are well on their way to achieving their goals. The Foundation's ability to offer these useful programs is possible only because of the financial base provided by the many contributors and the excellent advice offered by the advisory committees. To these groups rightly go the lion's share of credit, as the Foundation continues to strengthen the biomedical community efforts in research, education and training in increasingly effective wavs.

REACHING OUT

ho needs another meeting? Apparently, a majority of the awardees of the postdoctoral programs offered by the PMA Foundation do. Comments received from the approximately 100 attendees at a yearly meeting hosted by the Foundation indicate that they are uniformly pleased with the opportunity to meet with their colleagues and the more senior scientists who assist on the Foundation's advisory committees. The ninth in a series of these meetings was held in December, 1978.

Donald van Roden, Chairman of the PMA Foundation Board of Directors, opened the meeting with a review of some of the survey data which had been collected on the present activities of former awardees. The keynote speaker for the general session was Daniel W. Nebert, M.D., Chief, Developmental Pharmacology Branch, National Institute of Child Health and Human Development. who covered the topic "Genetic Differences in Drug Metabolism Influencing Individual Risk for Drug Toxicity or Cancer." In separate sessions, the clinical pharmacologists, the fellows in pharmacologymorphology and the faculty awardees in basic pharmacology developed their own programs. The clinical pharmacology session featured a wideranging discussion on issues facing the field led by Louis Lasagna, M.D., Chairman and Professor, Department of Pharmacology and Toxicology, University of Rochester. The session was moderated by Leon I. Goldberg, M.D., Ph.D., Chairman, Clinical Pharmacology Advisory Committee and Chairman, Committee on Clinical Pharmacology, University of Chicago.

The pharmacology-morphology fellows divided their time between discussions of the research efforts of some current fellows and Michael D. Gershon, M.D., Professor and













Chairman, Department of Anatomy, Columbia University, discussing "The Third Division of the Antonomic Nervous System."

The faculty awardees in basic pharmacology examined the issue of academic tenure. Edward J. Cafruny, M.D., Ph.D., Dean of the Graduate School of Biomedical Sciences, Professor of Pharmacology, College of Medicine and Dentistry of New Jersey, led the discussion.

In addition to the exchange of information which takes place during these meetings, the advisory committee members assess how well each program

is progressing.

Also in 1978, a similar, but shorter, meeting with the research starter grantees and advisory committee members was held during the fall meeting of the American Society for Pharmacology and Experimental Therapeutics. The speaker was Richard S. Johnston, Director of Space and Life Sciences, Lyndon B. Johnson Space Center, National Aeronautics and Space Administration, who discussed space medicine studies conducted to date by the National Aeronautics and Space Administration. He presented a forecast of future life sciences research in space. with special attention to studies involving the pharmaceutical sciences.

To augment the Foundation's perspective on the progress of its programs, Dr. I. C. Winter, consultant to the Foundation, made a number of site visits to current and former grant recipients. He obtained first-hand information on the relevance of current programs, identified other needs the Foundation might consider for funding and gained some insight into how the academic community views the Foundation's activities.

All of these efforts, reaching out as they do to those whom the Foundation has been privileged to assist in their career development, contribute to the ways the Foundation responds to needs in the biomedical field.













ACTIVITIES

Since its formation in 1965, about \$9 million has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects and educational programs. Of this amount approximately \$2.7 million has been used to support research and about \$5.8 million has gone into educational awards. The remaining \$475,000 has provided financial assistance for scientific meetings, along with a small portion for publications.

Virtually all of the 1978 grants and awards were made within programs sponsored by the Foundation. These include two faculty level programs of salary and fringe benefit support, four fellowship programs—two postdoctoral, one at the advanced predoctoral level and one at the medical student level—plus a program of research starter grants for beginning investigators wishing to move into areas of independent research. A special toxicology workshop was sponsored by the Foundation as well.

Through these programs the Foundation in 1978 assisted 54 individuals, all of whom were helped at a crucial time in their career development. The Foundation has, in its twelve years of existence, helped about 525 individuals through its research and educational support programs.

EDUCATION AND TRAINING PROGRAMS

To further its objectives in the field of education, the PMA Foundation sponsors four programs in clinical pharmacology, one in the combined field of pharmacology-morphology, one in pharmacology or toxicology and one in basic pharmacology. Each program is intended to achieve a specific goal, either for a particular rung on an individual's career ladder or in a particular discipline.

CLINICAL PHARMACOLOGY

The four 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 benefits support of full-time junior faculty members. The level of support varies, in keeping with the salary structure of the applicant university. The Foundation has set a ceiling of \$30,000 on the amount of its participation in the total yearly salary and fringe benefit for any candidate.

With the new awards scheduled to begin July 1, 1979, a total of 47 individuals have been supported under this program since 1967. They apply for a two-year period, with a third year option.

Recipients of the three awards to begin July 1, 1979 are:



Thorir D. Bjornsson,. M.D.

• Thorir D. Bjornsson, M.D., Assistant Professor, Department of Pharmacology, Duke University Medical Center. Dr. Bjornsson's primary research area of interest is the clinical pharmacology of antithrombotic drugs. He will study the clinical pharmacokinetics of heparin in patients, including determinations of its anticoagulant, platelet, and lipolytic effects. He will also initiate studies on the clinical pharmacokinetics of the antiplatelet drugs sulfinpyrazone and dipyridamole and the kinetics of their antiplatelet effects. In these studies, particular attention will be paid to the relative significance of pharmacokinetic variability and pharmacodynamic variability in the intersubject variation and in pharmacologic response and also, possible determinants of such variabilities.

Dr. Bjornsson will have teaching responsibilities in basic and clinical pharmacology. He will also participate in the Clinical Pharmacology Consultation Service.



Robert F. O'Dea, Ph.D., M.D.

• Robert F. O'Dea, Ph.D., M.D., Assistant Professor, Departments of Pharmacology and Pediatrics, University of Minnesota Medical School. Dr. O'Dea is involved in studies dealing with the regulation of blood pressure. The project will examine how certain molecular regulators, which have been previously shown to be involved in secretory processes, may control the release of renin in the response to signals directed to specific receptors on the kidney cells. These regulatory molecules include protein carboxymethylase, an enzyme which may alter the electrical charges on membranes and cyclic GMP. a "transducer" or information-carrying molecule which is intimately linked to other calcium-dependent processes in cells. These basic studies will complement an ongoing clinical research program pertaining to the treatment of high blood pressure in children with special emphasis on the role of renin in this disease.



Stephen P. Spielberg, M.D., Ph.D.

• Stephen P. Spielberg, M.D., Ph.D., Assistant Professor, Departments of Pediatrics and Pharmacology and Experimental Therapeutics, The Johns Hopkins University, School of Medicine. Dr. Spielberg's research interests are in the area of mechanisms of and genetic control of drug toxicity from electrophilic drug metabolites in humans. Model systems employing human lymphocytes and fibroblasts and a microsomal drug-activating system will be used to assess individual susceptibility to toxicity in: 1) patients with known inborn errors of glutathione metabolism; 2) mono- and dizygotic twins to examine genetic control of detoxification processes in the human population; 3) patients (and their relatives) who have experienced idiosyncratic drug reactions (e.g. hepatotoxicity) to establish the mechanism and heritability. The goal of the studies is to develop non-invasive approaches to understanding pharmacogenetic differences in humans.

Those individuals whose awards began in July, 1978 are:

- Robert M. Graham, M.B., B.S., Instructor, Departments of Pharmacology and Internal Medicine, University of Texas, Southwestern Medical School.
- Fred E. Karch, M.D., Assistant Professor, Department of Pharmacology and Toxicology, University of Rochester, School of Medicine and Dentistry.
- Juan J. L. Lertora, M.D., Ph.D., Assistant Professor, Departments of Medicine and Pharmacology, Northwestern University, Medical School.
- Aubrey R. Morrison, M.B., B.S., Assistant Professor, Departments of Medicine and Pharmacology, Washington University, School of Medicine.

The individual who entered the second year of his award in July, 1978 is:

• Raymond L. Woosley, Jr., M.D., Ph.D., Assistant Professor, Departments of Medicine and Pharmacology, Vanderbilt University, School of Medicine.

Those individuals whose awards continued for a third year beginning July 1, 1978 are:

- Werner A. Bleyer, M.D., Assistant Professor, Departments of Pediatrics and Medicine, University of Washington, School of Medicine.
- Robert C. Boerth, M.D., Ph.D., Associate Professor, Departments of Pediatrics and Pharmacology, Vanderbilt University, School of Medicine.
- Curt R. Freed, M.D., Assistant Professor, Departments of Medicine and Pharmacology, University of Colorado Medical Center.

The individual who ended his award in June, 1978, is:

• Reynold Spector, M.D., Professor, Department of Internal Medicine, University of Iowa, College of Medicine.



Geographical distribution of Foundation awards under its "Faculty Development Awards in Clinical Pharmacology" program, 1967-1979

- One
- More than One

Fellowships for Careers in Clinical Pharmacology

The second program provides Fellowships for Careers in Clinical Pharmacology. This award offers clinicians an opportunity for intensive study in any of the basic sciences that fall within the general field of pharmacology. The program is open to physicians, dentists and veterinarians who are well into their clinical training and wish to pursue careers in clinical pharmacology. With the year or two of support offered by this fellowship program, depending on the particulars of the undertaking, the individual can pursue full time the basic pharmacologic sciences needed to complement his clinical skills.

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

Recipients of the two fellowships beginning July 1, 1979 are:



Richard C. Ahrens, M.D.

• Richard C. Ahrens, M.D., Fellow, Departments of Pediatrics and Pharmacology, University of Iowa, College of Medicine. Dr. Ahrens' research program will investigate questions related to acquired tolerance to beta adrenergic bronchodilators. He has developed a model using guinea pig tracheal strips to quantitate tolerance to beta adrenergic bronchodilators in vitro. He has also developed a protocol for examining the clinical significance of tolerance to inhaled beta adrenergic bronchodilators administered to asthmatic patients. It is expected that further development of the in vitro and in vivo models for examining tolerance will answer some of the clinically relevant questions regarding the degree of tolerance from various beta adrenergic bronchodilators, cross-tolerance between various beta adrenergic bronchodilators, and some of the implications with regard to the clinical use of this class of antiasthmatic drugs.



Claes M. Nilsson, M.D.

• Claes M. Nilsson, M.D., Postdoctoral Fellow in Hematology-Oncology, Cancer Research Institute, University of California, School of Medicine. Dr. Nilsson's research interests are two fold. One is to develop a highly sensitive and specific assay for drug-induced antibodies to platelets. The second is to characterize the nature of these immunological reactions which result in destruction of platelets. He will approach this problem in two ways. First, he plans to study the specificity of drug-induced platelet antibodies. Using radiolabelled anti-human IgG and anti-human C3, he will attempt to define whether antibodies bind to a particular drug/drug-protein complex; or to the platelet/platelet-drug complex. Second, he plans to determine either the specific platelet membrane antigen(s) these antibodies are directed against or the specific site on the platelet to which the antibody-drug complex binds. He will use polyarylamide gel electrophoresis of platelet membranes for these experiments.

Those individuals whose fellowships began July, 1978 are:

- Robert L. Blum, M.D., Postdoctoral Fellow, Division of Clinical Pharmacology and the Department of Computer Science, Stanford University, School of Medicine.
- Brian A. Jones, M.B., B.S., Postdoctoral Fellow in Departments of Medicine and Pharmacology, Cornell University Medical College.
- James R. Matson, M.D., Fellow, Pediatric Clinical Pharmacology/Nephrology, Departments of Pediatrics and Pharmacology, University of Iowa, College of Medicine.
- Douglas K. Reilly, M.D., Fellow in Clinical Pharmacology, Department of Pharmacology and Toxicology, University of Rochester, School of Medicine and Dentistry.

Those individuals whose fellowships entered the second year of awards in July, 1978 are:

- Thomas P. Green, M.D., Postdoctoral Fellow, Department of Pharmacology, and Medical Fellow, Department of Pediatrics, University of Minnesota, Medical School.
- Stanley J. Szefler, M.D., Fellow in Clinical Pharmacology, Department of Pharmacology, State University of New York, School of Medicine.
- Walter M. Williams, M.D., Ph.D., Fellow in Clinical Pharmacology, Departments of Pharmacology and Medicine, University of Chicago, School of Medicine.

The individual who ended his award in June, 1978 is:

• William P. Arnold, III, M.D., Assistant Professor, Department of Anesthesiology, University of Virginia, School of Medicine.



Geographical distribution of Foundation "Fellowships for Careers in Clinical Pharmacology" program, 1973-1979

- One
- o More than One

Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology

The third program is the Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology. This program, which began in 1974, provides students an opportunity to spend one year full-time in an investigative project in pharmacology-clinical pharmacology. To meet the full-time requirement, the student must interrupt his formal medical training, but he must also intend to continue his schooling at the conclusion of the fellowship. It is hoped that by having students become involved extensively in investigative projects at a point when career choices are still relatively flexible, that they will opt for research careers in clinical pharmacology. Twenty-eight awards have been made since 1974.

The PMA Foundation has had a medical student support program since 1968. The earlier program offered three month traineeships to enable students to become acquainted with the techniques used in clinical pharmacology.

The six students who received fellowships which began July 1, 1978 are:

• Stanley L. Barnwell, a second year medical student at the time of the award at Vanderbilt University. His principal advisor is B. V. Rama Sastry, D. Sc., Ph. D., Professor, Department of Pharmacology. Mr. Barnwell is studying the interrelationships between human placental acetylcholine (ACh), placental ACh release, amino acid uptake by placental villus under normal and experimental conditions in which isolated placental villus is exposed to nicotine, morphine and cocaine.

Specifically, the investigation will examine the occurrence of enkephalins like substances in placenta; study the role of these substances in placental release of ACh and examine the effect of the possible depression of ACh release on the amino acid uptake by placental villus.

- David M. Carlisle, a second year medical student at the time of the award at Stanford University. His principal advisor is Terrence F. Blaschke, M.D., Assistant Professor, Department of Medicine. Mr. Carlisle is concentrating on one aspect of ongoing studies of the effect of warfarin on the disposition and turnover of vitamin K_1 . Specifically, he will investigate the interconversion of vitamin K_1 and vitamin K_1 epoxide in a dog model. He will be studying the disposition of radiolabelled vitamin K_1 and vitamin K_1 epoxide in the absence of drugs and after the continuous oral administration of warfarin. Also, using kinetic techniques, he will study the extent of interconversion of vitamin K_1 and its epoxide in the presence or absence of warfarin.
- Mark A. Dayton, a freshman medical student at the time of the award at Indiana University. His principal advisor is R. Mark Wightman, Ph.D., Assistant Professor, Department of Chemistry. Mr. Dayton is investigating dopamine receptors in synaptosomes developing a flow cell for the study of

neurotransmitter release in synaptosome fractions and is studying neurotransmitter interactions in synaptosomes. The principal interests in this pharmacological probing of neuroreceptors are to measure the effect of neuroleptics in vitro, to examine the displacement of dopamine agonists with neuroleptics and to examine the presynaptic feedback mechanisms. An understanding of all of these features should lead to a clearer overall understanding of the mechanism of action of neuroleptics.

- Terence C. Gayle, a second year medical student at the time of the award at Tulane University. His principal advisor is Morris A. Spirtes, M.D., Professor, Department of Pharmacology. Mr. Gayle is examining research evidence that cyclic nucleotide involvement in the action of opiates and opiate-like substances is increasing. Enkephalins are two endogenous brain pentapeptides with strong opiate properties. Recent experiments have shown that the effects of opiates on cyclic nucleotide levels in various areas of the brain can also be affected by peptide hormones, specifically, melanocyte stimulating hormone (MSH) from the pituitary, and melanocyte release inhibiting factor (MIF-I). Mr. Gayle is involved in a series of experiments based upon the measurement of guanylate cyclase activity designed to investigate the biochemical aspects of enkephalins as well as the so-called "extra-hormonal" activity of MIF-I.
- Stephen P. Montgomery, a freshman medical student at the time of the award at Boston University working at Dartmouth Medical School. His principal advisor is Herbert L. Borison, Ph.D., Professor, Department of Pharmacology and Toxicology. Mr. Montgomery is participating in ongoing studies aimed at characterizing the responsiveness of brainstem respiratory chemoreceptors to alterations in acid-base composition of the cerebrospinal fluid. The study is being done in cats.
- Woodrow W. Wendling, a fourth year medical student at the time of the award at Temple University, School of Medicine. His principal advisor is Martin Black, M.D., Associate Professor, Department of Gastroenterology. Mr. Wendling's research is concerned with the mixed-function oxidase system of male Skh: (1CR) mice and Spraque-Dawley rats. He is attempting to further characterize the mixed function oxidase system in mice and rats, particularly interactions between cytochromes P-450 and B₅; as well as attempting to find an experimental model for the isoniazid-related liver injury that occurs in man.



Geographical distribution of Foundation "Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology" program, 1974-1978

- One
- o More than One

Clinical Pharmacology Unit Support

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

Those who received awards beginning July 1, 1978 are:

- Division of Clinical Pharmacology, University of California, Los Angeles. The division was formed within the Departments of Medicine and Pharmacology in August, 1977. The chief of the unit is Matthew E. Conolly, M.D. Dr. Conolly is also an Associate Professor in Medicine and Pharmacology. The research efforts are directed towards bronchial asthma, ischemic heart disease, liver disease of various types, hypertension and drug abuse.
- Division of Clinical Pharmacology, State University of New York at Stony Brook. This division was created within the Department of Pharmacological Sciences in September, 1976. The director is Ilene Raisfeld, M.D., Associate Professor of Clinical Pharmacology and Medicine. The present areas deal with the study of the mechanisms by which drug-induced pulmonary fibrosis can be minimized. She has also initiated a clinical project on the pharmacokinetics of haloperidol. Plans have been made for a clinical project involving narcotic antagonists.



BASIC PHARMACOLOGY

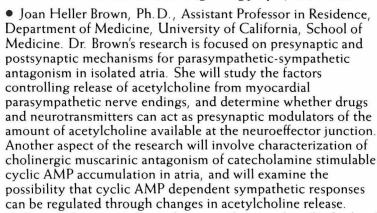
Faculty Development Awards in Basic Pharmacology

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

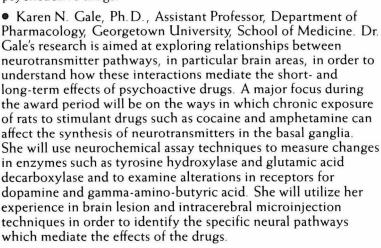
pharmacology who give promise of outstanding accomplishments.

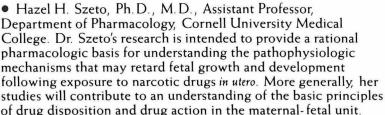
The first awards, which are for a two-year period, were made in 1973. The program provides salary and fringe benefits. The Foundation has set a ceiling of \$25,000 on the amount of its participation in the total yearly salary and fringe benefit for any candidate beginning with the 1980 awards. The total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

Those who received awards beginning July 1, 1979 are:



Her teaching in undergraduate, graduate and medical school pharmacology courses will be in the areas of autonomic pharmacology, regulation of central aminergic neurons, and psychoactive drugs.







Joan H. Brown, Ph.D



Karen N. Gale, Ph.D.



Hazel H. Szeto, Ph.D., M.D.

Dr. Szeto plans to investigate the pharmacokinetics and pharmacodynamics of methadone, 1-acetylmethadol (LAAM) and heroin using the maternal-fetal unit of the pregnant ewe. She will first quantitatively determine the mode of distribution and elimination of methadone, LAAM and heroin in both the mother and fetus after acute and chronic administration. Particular attention will be directed to the distribution of these drugs and their metabolites to the fetal brain, and their elimination by fetal urinary excretion.

Those who began their award in July, 1978 are:

- Yvonne C. Clement-Cormier, Ph.D., Assistant Professor, Departments of Pharmacology and Neurobiology, University of Texas Medical School, Houston.
- Linda F. Quenzer, Ph.D., Assistant Professor, Department of Pharmacology, University of Connecticut Health Center.

Those who entered the second year of their award in July, 1978 are:

- R. Adron Harris, Ph.D., Assistant Professor, Department of Pharmacology, University of Missouri, School of Medicine.
- Michael E. Maguire, Ph. D., Assistant Professor, Department of Pharmacology, Case Western Reserve University, School of Medicine.

Those who ended their award in June, 1978 are:

- Sue Piper Duckles, Ph.D., Assistant Professor, Department of Pharmacology, University of California, School of Medicine.
- Garrett J. Gross, Ph.D., Associate Professor, Department of Pharmacology, Medical College of Wisconsin.
- Daniel A. Koechel, Ph.D., Associate Professor, Department of Pharmacology and Therapeutics, Medical College of Ohio.



Geographical distribution of Foundation "Faculty Development Awards in Pharmacology," 1973-1979

- One
- O More than One

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

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

The fellowship program provides a stipend of \$3,900 a year, payment of tuition and \$500 for incidentals directly associated with the thesis research preparation. The program has been funded to provide seven fellowships each year. However, three extra fellowships were authorized for 1979. A total of twenty fellowships have been made.

Those who received fellowships which begin between January-August, 1979, are:

- Arleen Chase, Department of Pharmacology, Boston University, School of Medicine. Ms. Chase's thesis advisor is Dr. Ladislav Volicer, Professor of Pharmacology. The thesis is concerned with the effect of vasoactive drugs on cyclic nucleotide levels in aortic smooth muscle cells maintained in tissue culture. The study is to determine if changes in cyclic nucleotide mechanism in vascular smooth muscle cells may be causally involved in the pathogenesis of hypertension; and if changes in cyclic nucleotide levels reflect changes in vascular reactivity which are known to occur in hypertension.
- Elaine M. Faustman, Department of Pharmacology and Toxicology, Michigan State University, College of Human Medicine. Ms. Faustman's thesis advisor is Dr. Jay I. Goodman, Associate Professor of Pharmacology. The thesis is a study of the assessment of carcinogen-induced methylation of DNA-purines in different fractions of hepatic chromatin.
- Robert N. Fontaine, Department of Pharmacology, University of Missouri, School of Medicine. Mr. Fontaine's thesis advisor is Dr. Friedhelm Schroeder, Assistant Professor of Pharmacology. The thesis is examining the dependence of drug permeabilities on the phospholipid composition of mammalian cell plasma membranes. The ultimate goal is to elucidate the mechanism by which the plasma membrane can determine or control penetration of relatively lipophilic drugs.
- Richard H. Kennedy, Department of Pharmacology, University of Nebraska, College of Medicine. Mr. Kennedy's thesis advisor is Dr. Thomas E. Donnelly, Jr., Associate Professor of Pharmacology. The thesis is examining several aspects of the propranolol withdrawal syndrome. Using isolated rat atrial and ventricular muscle, Mr. Kennedy will attempt to determine the nature of the proposed supersensitivity by examining the positive chronotropic and inotropic effects of catecholamines and other agents in saline control vs. propranolol-treated tissue.

- Peter K. Nelson, Department of Pharmacology, Tulane University, School of Medicine. Mr. Nelson's thesis advisor is Dr. James W. Fisher, Professor and Chairman, Department of Pharmacology. The thesis is studying the potential role of prostaglandins in erythroid differentiation, participating directly at bone marrow sites or indirectly through a manipulated release of erythropoietin (a glycoprotein hormone effecting erythropoiesis). Additionally, the research will assess the feasibility of prostaglandins, especially the E-series, functioning as transducers in the detection of an oxygen deficit and its translation into physiologic phenomena.
- Linda M. Parsons, Department of Pharmacology, Stanford University, School of Medicine. Ms. Parsons' thesis advisor is Dora B. Goldstein, Professor. The thesis is aimed at testing the hypothesis that both acute and long-term tolerance to the atoxic effects of ethanol are at least partially the result of adoptive changes in the plasma membrane lipid composition. Using the mouse red blood cell (RBC) as a model membrane system, cholesterol and phospholipid values will be determined after long or short-term ethanol exposure. Further studies will focus on quantitation of the five major phospholipid classes present in these RBC membranes.
- Steven L. Peterson, Department of Pharmacology, University of California School of Medicine. Mr. Peterson's thesis advisor is Dr. Larry G. Stark, Associate Professor of Pharmacology. The thesis is involved in a study of anticonvulsants and the development of kindled seizures. The plan is to evaluate the effects of chronic anticonvulsant administration on the progressive development of amygdaloid seizures. The work involves rats in a dose-response study of phenobarbital, carbamazepine, diazepam, sodium valproate and phenytoin.

The second part of the research will involve a study of the relationship of kindling, sleep states and anticonvulsants.

- ullet James B. Reese, Department of Medicine, University of California, School of Medicine. Mr. Reese's thesis advisor is Dr. Steven E. Mayer, Professor of Medicine. The thesis is studying two related systems of the heart, the glycogenolytic pathway and the contractile mechanism. The basis of the research stems from the observation that PGE1 induced increases in cardiac cAMP concentration activates protein kinase without activating the glycogenolytic enzymes or increasing the inotropic state of the heart. The explanation for this phenomenon is being examined
- Adelaide M. Siegl, Department of Pharmacology, Thomas Jefferson University, Jefferson Medical College. Ms. Siegl's thesis advisor is J. Bryan Smith, Ph.D., Associate Professor. The thesis is aimed at characterizing the receptors for prostaglandin I_2 and prostaglandin D_2 present in platelets and investigating their interaction with the platelet adenyl cyclase system.

• Susan Trieser, Department of Pharmacology, Georgetown University, School of Medicine. Ms. Treiser's thesis advisor is Kenneth J. Kellar, Ph.D., Assistant Professor. The thesis is examining the effect of lithium on various neurotransmitters. Most commonly, the noradrenergic, dopaminergic and serotonergic transmitter systems have been implicated as possible sites of action of lithium. Within each transmitter system both the acute and chronic effects of lithium on both presynaptic and postsynaptic sites need to be considered and the thesis is concentrating on this aspect.

Those who entered the second year of their fellowships in 1979 are:

GALE L. CRAVISO
New York University
School of Medicine
PAUL E. DRIEDGER
Harvard Medical School
CLIFFORD C. HALL
University of Wisconsin
School of Medicine
DENNIS M. HIGGINS
University of Connecticut
School of Medicine
VIVIAN Y. HO HOOK
University of California
School of Medicine

STANLEY R. JOLLY
Medical College of Wisconsin
MICHAEL R. PALMER
University of Colorado
School of Medicine
TODD M. SAVARESE
Brown University
WILLIAM L. STRAUSS
State University of New York
School of Medicine
LARRY A. WALKER
Vanderbilt University
School of Medicine



Geographical distribution of Foundation awards under the "Fellowships for Advanced Predoctoral Training in Pharmacology/Toxicology, 1978-1979

- One
- · More than One

Fellowship Awards in Pharmacology-Morphology

The aim of this program of fellowship awards 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. The level of support varies and is aimed at keeping within the existing stipends for similarly trained individuals within the applicant university. Since 1968, when the first fellowships were offered, 40 awards have been made.

The program requires that a candidate be qualified primarily either in a morphologic speciality or in pharmacology. However, training to be achieved under the fellowship in the complementary discipline need not be formal. The candidate's

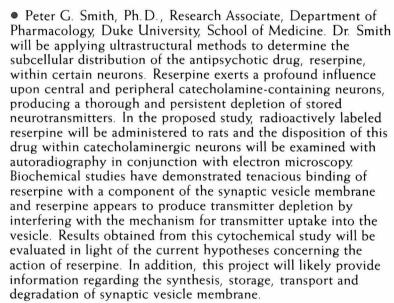
program should result in a familiarity with a new discipline approach by using his primary discipline as a medium for acquiring the second.

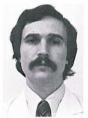
The recipients of fellowships which began in July, 1978 are:



Virginia S. Seybold, Ph. D.

• Virginia S. Seybold, Ph.D., Postdoctoral Fellow, Department of Anatomy, University of Minnesota, Medical School. Dr. Seybold will be trained to use and develop immunohistochemical techniques at the light and electron microscopic level. These morphological techniques will be used to analyze circuits in the brain that contain specific neuropeptides are putative transmitter substances. Dr. Seybold will use these immunochemical methods to study the role of peptidergic primary afferent neurons as well as other peptidergic circuits in the spinal cord in the etiology of peripheral diabetic neuropathy. In addition, she will employ these methods to extend her previous studies of neuroendocrine control mechanisms.





Peter G. Smith, Ph.D



James A. Weyhenmeyer, Ph.D

• James A. Weyhenmeyer, Ph.D., Postdoctoral Fellow, Department of Physiology and Biophysics, University of Iowa, College of Medicine. Dr. Weyhenmeyer will examine the localization of endogenous angiotensin II in neurons and specific regions of the central nervous system by indirect immunofluorescence, and the identification of catecholamine containing nerve terminals and cell bodies in angiotensin II-rich regions of the central nervous system by histofluorescence and radioisotopic-enzymatic assay. Intraventricular infusion of P113, an angiotensin II antagonist, will be examined by indirect immunofluorescence to further identify possible sites of action of angiotensin II. In order to produce a highly specific immunofluorescence assay, antisera to angiotensin II and P113 will be produced by a new method of intradermal injection of

minute quantities of antigen with an osmotic minipump. Rat whole brain and cells in tissue culture will be evaluated for the presence or absence of endogenous angiotensin II. Sections of rat whole brain will be examined with and without intraventricular infusion of angiotensin II for norepinephrine and dopamine. The significance of this study is to define central sites of action of angiotensin II and to determine what effect angiotensin II will have on catecholamine containing nerve terminals in blood pressure and ADH responsive regions of the central nervous system.



Geographical distribution of Foundation "Fellowship Awards in Pharmacology-Morphology," 1968-1978

- One
- More than One

Those individuals who entered the second year of their fellowships in July, 1978 are:

- Douglas E. Chandler, Ph.D., Postdoctoral Fellow, Department of Physiology, University of California, School of Medicine.
- Carole L. Jelsema, Ph.D., Assistant Professor, Department of Pediatrics, Medical College of Wisconsin.
- Michael P. Marietta, Ph.D., Postdoctoral Fellow, Department of Pharmacology, Pennsylvania State University, Milton S. Hershey Medical Center.
- Mark F. Nelson, Ph.D., Postdoctoral Fellow, Department of Pharmacology, The Johns Hopkins University, School of Medicine.

Those individuals whose fellowships concluded in June, 1978 are:

- Cheryl F. Dreyfus, Ph.D., Research Associate, Department of Anatomy, Columbia University, College of Physicians and Surgeons.
- Susan B. Stearns, Ph.D., Assistant Professor, Department of Anatomy, State University of New York, Upstate Medical Center.

Special Fellowship

A special postdoctoral fellowship, on a pilot basis, was authorized to be undertaken at the International Institute for Cellular and Molecular Pathology (ICP), Brussels, Belgium. The ICP is under the direction of nobel-prize winner, Dr. Christian de Duve. ICP's aim is to apply the discoveries and techniques of modern biology to medicine and therapeutics. It endeavors to achieve this aim through a close association of mission-oriented

research units, devoted to a wide variety of medical problems.

The staff is multi-disciplinary and includes experts in such fields as biochemistry, cell biology, genetics, immunology, microbiology, molecular biology and virology. There is equal stress placed on the basic and applied aspects of research merged in a single approach. Among others, there are research units engaged in cancer chemotherapy, cancer immunotherapy, male contraceptives, antiinflammatory agents, the chemotherapy of tropical diseases and cellular uptake and subcellular localization of drugs.

The fellowship began September 1, 1978, and extends until August 31, 1980. A stipend is offered, along with research funds and travel funds for the fellow and family to Brussels and back to the United States.

The recipient of this fellowship is J. Thomas Hjelle, Ph.D., who at the time of selection was completing some initial postdoctoral training at the Roche Institute of Molecular Biology. At ICP, Dr. Hjelle is involved in testing the various published methods for the isolation and growth of endothelial cells. He has learned the fluorescence assay and experimental procedure for the determination of accumulation of the anthracycline antitumor drugs by culture cells. He has also studied the metabolism of these cells and their amino acid derivatives by the cultured vascular cells.



J. Thomas Hjelle, Ph.D.

RESEARCH GRANTS

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



Geographical distribution of Foundation general research grants, 1966-1979

- One
- O More than One
- Outside U.S.

RESEARCH STARTER GRANTS

As part of the change of emphasis in 1971 which sought to direct monies more toward the development of the individual, a program of Research Starter Grants was initiated. These grants are intended to provide financial support for beginning investigators. The program currently offers \$6,000 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 pharmacology, clinical pharmacology and drug toxicology. The program allows for approximately 20 research starter grants each year. The first awards were made in 1972. A total of 192 research starter grants have been made, including the 24 awards beginning January 1, 1979.

The recipients of the grants beginning January 1, 1979 are:

FREDDIE K. CARR Ph. D. Philadelphia College of Osteopathic

Medicine

ANDREW T. CHIU, Ph.D. University of Oklahoma College of Medicine

MARTIN S. COHEN, M.D.

University of California (San Francisco)

School of Medicine IAN N. CREESE, Ph. D.

University of California (San Diego)

Medical School

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PATRICE G. GUYENET. Ph. D.

University of Virginia School of Medicine

M. MARLENE HOSEY, Ph. D.

University of Health Sciences

The Chicago Medical School PAUL M. IUVONE, Ph.D.

Emory University

School of Medicine

JACK H. KAPLAN, Ph.D. University of Iowa

College of Medicine

DAVID D. Ku, Ph. D. University of Alabama

School of Medicine ALICE A. LARSON, Ph.D.

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University of Texas (San Antonio)

Health Science Center

Review of the need of the 26 research starter grantees whose awards began January 1, 1978 for a second year of the awards resulted in 15 of them having their awards continued. These are:

DANIEL E. FURST, M.D. University of California (Los Angeles) School of Medicine

GERALD GIANUTSOS, Ph.D. University of Connecticut College of Pharmacy

EDWARD HUA-SENG GOH, Ph.D. Indiana University School of Medicine KENNETH M. JOHNSON, Ph.D. University of Texas Medical Branch (Galveston) GEORGE L. KRAMER, Ph.D. Vanderbilt University School of Medicine LYMAN T. LAIS, Ph.D. Oregon State University School of Pharmacy BILLY R. MARTIN, Ph.D. Medical College of Virginia RICHARD MCGEE, JR., Ph.D. Georgetown University School of Medicine & Dentistry CHANDRA K. MITTAL, Ph.D. University of Virginia

MARIORIE MYERS-ROBFOGEL. Ph.D. University of Rochester Medical School DONALD E. NERLAND, Ph.D. University of Louisville School of Medicine RUSSELL E. SAVAGE, JR., M.D. Ohio University College of Osteopathic Medicine JAMES E. STRONG, Ph.D. Baylor College of Medicine DAVID A. TAYLOR, Ph.D. University of Colorado Medical School REGIS R. VOLLMER, Ph.D. University of Pittsburgh School of Pharmacy



Geographical distribution of Foundation awards under the "Research Starter Grants" program, 1972-1979

- One
- More than One

Other Support

School of Medicine

The PMA Foundation sponsored an invitational Workshop on Cellular and Molecular Toxicology October 8-11, 1978. This unique workshop is one of a series of three planned in the broad field of toxicology. The objective of the workshop was to stimulate research on the toxicology of drugs. The science of toxicology derives its impetus from the rational and theoretical body of information provided by molecular and cellular biologists. The workshop examined and updated this information and considered if and how it might be applied in the development of new and better methods for assessing the safety and potential toxicity of drugs. Further, the meeting sought to identify specific areas of research in such methodology and through publication, encourage such research.

The topics covered from the perspective of their implications to toxicology were: the cell surface; membrane systems of the cytoplasm, the cell nucleus, mutagenesis, lysosomes and lysosomal diseases.

A summary of the workshop is available from the Foundation. The formal proceedings of the workshop will be published as a regular issue of *Pharmacological Reviews* by September, 1979.

PURPOSE

he 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 21.

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

FOUNDATION FINANCES

The total income of the Foundation in 1978 was \$1,108,375. Of this amount, \$987,829 came from contributions. The balance of \$120,546 came from investments and refunds of unexpended balances from grants.

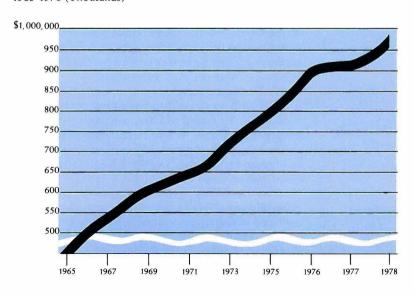
Contributions were received from approximately four out of every five PMA Member Firms. Contributions were also received during 1978 from individuals and other groups in the health field.

Grants, Foundation-sponsored programs and other expenses for 1978 amounted to \$1,073,122. Of this total, \$879,357 represented expenditures for grants and Foundation-sponsored programs. There was a fund balance of \$1,561,423 as of December 31, 1978. This figure, however, does not reflect the tentatively authorized, undisbursed funds for some of the grants and programs described earlier. The Foundation reports these amounts as expenditures when the funds are distributed. As of December 31, 1978, the contingency liability for 1979 was approximately \$955,500.

Financial Report. The Foundation's financial position as of December 31, 1978 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 1978. These reports are prepared by Washington, D.C. accounting firm of Buchanan & Company.

PMA Foundation Contribution Income 1965-1978 (Thousands)



Statement of Income and Expenditures For the Year Ended December 31, 1978

Income

Contributions—Note a	\$	987,829
Income from Investments		118,522
Miscellaneous Income		2,024
TOTAL INCOME		108,375
Expenditures		
Grants—Note b	_	
Clinical Pharmacology Faculty Awards	\$	207,505
Clinical Pharmacology Fellowships		90,325
Clinical Pharmacology Unit Support		51,000
Basic Pharmacology Faculty Awards		118,837
Medical Student Research Fellowships		35,000
Pharmacology-Morphology Fellowships		77,934
Research Starter Grants.		236,000
Advanced Predoctoral Fellowships		48,330
Special Fellowship—Brussels		14,426
	\$	879,357
Administrative, December Awardee Meeting		
and Toxicology Workshop Expenses	\$	193,763
TOTAL EXPENDITURES	\$1,	073, 122
Excess of income over expenditures Fund balance at January 1, 1978. Fund balance at December 31, 1978.	\$1,	526, 170

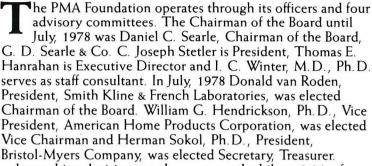
Note a—The Foundation received contributions of \$47,300 prior to December 31, 1978 which the Foundation considered applicable to 1979 and, therefore, are not recorded as income in 1978.

Note b—In addition to the amounts shown, the Foundation has committed itself, subject to annual review, to make certain grants. At December 31, 1978 the amounts still to be disbursed with respect to these grants during 1979 amounted to approximately \$955,572.

ORGANIZATION AND ADMINISTRATION

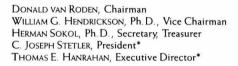


Donald van Roden



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.

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^{*}In April, 1979, Mr. Hanraban was appointed President and Mr. Stetler was named to the Board of Directors in his capacity as President of the PMA.

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⁷New Member October, 1978

^{*}Resigned May, 1978

New Member December, 1978

¹⁰Resigned October, 1978

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[&]quot;New Member December, 1978

¹²Term Expired December, 1978

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San Francisco, California

¹³New Members December, 1978

¹⁴New Member September, 1978

¹⁵ Term Expired December, 1978

¹⁶ Resigned May, 1978

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APPLICATIONS

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:

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