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Pharmaceutical Manufacturers Association Foundation



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REPORT OF THE CHAIRMAN



Harvey S. Sadow, Ph.D.

It will seem unusual for the Report of the Chairman of the Pharmaceutical Manufacturers Association Foundation to be coming from someone other than Irwin Lerner, since he has served notably—and reported—in that capacity, for the previous six years. It was with sincere appreciation for Irwin's contributions to the Foundation and particularly, the knowledge that he would continue to serve on the Board of Directors that I was encouraged to accept the Chairmanship. Thus, for the first time, here is my Report as the Chairman of the PMA Foundation for 1988:

In reporting to the many constituencies of the Foundation, it must be noted that I have had the benefit of an outstanding group of officers and board members. They are:

- 1. Vice Chairman—Albert Bowers, Ph.D., Chairman and Chief Executive Officer, Syntex Corporation.
- 2. Immediate Past Chairman—Irwin Lerner, President and Chief Executive Officer, Hoffmann-La Roche, Inc.
- 3. President—Maurice Q. Bectel
- 4. Secretary/Treasurer (through Nov.)—Hazen L. Richardson, Vice President, Medical Products Department, E.I. du Pont de Nemours & Co.
- 5. Secretary/Treasurer (beginning Dec.)—David B. Sharrock, President and Chief Operating Officer, Merrell Dow Pharmaceuticals Inc.
- 6. Directors: Richard J. Kogan, President and Chief Operating Officer, Schering-Plough Corporation. Joseph J. Ruvane, Vice Chairman, Glaxo Inc. David B. Sharrock*
 7. En Offician Council J. Maximum ff. President. Planmanutical
- 7. Ex Officio—Gerald J. Mossinghoff, President, Pharmaceutical Manufacturers Association.

In addition, the Foundation's Bylaws were amended in 1988 to provide for a larger Board of Directors, thereby providing the Foundation with broader input. Joining the Board in December, 1988 are the following three new Directors:

Sheldon G. Gilgore, M.D., Chairman, President, and Chief Executive Officer of G.D. Searle & Co.

Hubert E. Huckel, M.D., Chairman and President of Hoechst-Roussel Pharmaceuticals Inc.

Klaus Heinz Risse, Ph.D., President and Chief Executive Officer of Miles Inc.

^{*} Served as a Director through November, and assumed the office of Secretary-Treasurer in December, 1988.

The Foundation's Board of Directors was not the only area of activity which was expanded during 1988. Contributions received, grants awarded, and categories of grants were all record-setters.

Contributions Received: The Treasurer's Report will detail the dollar amounts and provide comparisons with previous years. Nineteen eighty-seven saw contributions exceed \$2 million for the first time—a major milestone, indeed—and 1988 continued to build on previous years, with total contributions of \$2.3 million.

Grants Awarded: Foundation grants were awarded in 1988, primarily to young scientists and researchers just getting started in their careers. What a privilege and pleasure it is to be able to provide support for these bright, dedicated, young scientists!

Grant Categories: During 1988, the number of categories for grant awards was increased from ten to twelve, with the addition of an Undergraduate Fellowship Program in Pharmaceutics and an innovative approach to awards, Research on Drugs for Rare Diseases, which will be supported through grants in *any* of the eleven single subject areas.

All of these developments make the PMA Foundation an exciting adjunct to the Pharmaceutical Manufacturers Association, and, of course, I feel honored to be a part of it.

Foundation Roots

Thanks to the farsighted leadership of the research intensive pharmaceutical industry, the Pharmaceutical Manufacturers Association, in 1965, established the PMA Foundation. The objectives were—and continue, essentially unchanged to this day—to assist young scientists in pursuing their educational and research objectives. Typically, these scholars are in their late 20's or early 30's and have multiple degrees, combining such academic backgrounds as chemistry, medicine, pharmacy, veterinary medicine, or dentistry, with the Ph.D. scientific research degree.

The Foundation's niche in supporting research, however, lies in the uniqueness of the recipients, who are in the early stages of their careers. The Foundation's grants go to young scientists and researchers before they have acquired the experience and reputation usually needed to obtain support from the National Institutes of Health and other similar sources.

Tracking Recipients

Starting with a modest number of grant recipients in 1966, the first year of award, the Foundation award recipients now total over 1,100. The Foundation is, indeed, accomplishing its primary objective: to increase the pool of talented scientifically qualified people, either conducting research in the health sciences or educating future health scientists.

In 1987-88, we conducted a survey of the previous awardees and received a gratifyingly high response. With a median age of 40, 78% have earned their Ph.D. degree. Some 13% hold combined Ph.D./M.D. degrees and 63% have at least one year of formal, postdoctoral education. The respondents are located at 121 different educational/research locations. Eighty-five percent are in academic settings, of whom 25% are full professors and 38% are associate professors. 83% are engaged in pharmaceutically-related research and/or development and 7% are full-time health science educators. And, we, at the Foundation, are proud of every one of them.

Future Growth

With new award categories on one hand, and the negative impact of ever-tightening government budgets on health science research support on the other, the PMA Foundation finds ever-increasing demand for its assistance. It is sad that, at this time, we can fund only one out of every four meritorious, qualified applications. Fortunately, we continue to receive increasing support from the researchintensive pharmaceutical companies which make up the PMA.

We realize that the pharmaceutical industry has a broad commitment to research. As we all know, just during this past year, the pharmaceutical industry's investment in research and development was a record \$6.5 billion-which, for the first time, exceeded the amount spent by the National Institutes of Health (\$6.3 billion) on all types of biomedical research. Many PMA companies have also established-and funded-their own foundations. Certainly, these PMA member companies support, in addition, other foundations, charities, and many worthy causes. It is, therefore, highly significant that they support the PMA Foundation through their voluntary contributions which, in turn, allow the Foundation to support young health care scientists and researchers and their projects. We firmly believe that this generous support will grow in the next few years, to the Foundation's \$5 million goal. With that level of support, the Foundation can, as we believe it should, more adequately fulfill its mission as a critical participant in the provision of improved health care.

To the Foundation's Officers and Board members, ... to President Bectel and his dedicated staff, ... and to the Scientific Advisory Committee and the many committed scientists whose input makes the awards program possible, but especially to the contributing members of PMA, I express my deep and sincere appreciation.

Harvey S. Sadow, Ph.D. Chairman Board of Directors

REPORT OF THE PRESIDENT

N ineteen eighty-eight represented a year of change, a year of growth, and a year of challenge for the PMA Foundation.

Change

After six years as Chairman, Irwin Lerner passed the gavel to Harvey S. Sadow. The transition was smooth and the Foundation's growth trends continued, attesting to the calibre of both chairmen. Chairman Lerner was at the helm as I began my tenure as President, however, and I would be negligent were I not to publicly thank him for his leadership and wise counsel.

New Chairman Harvey Sadow assumed office in 1988 and has an agenda that will aggressively move the Foundation forward on the growth trend. He too offers invaluable guidance as the Board of Directors oversees the directions of the Foundation, the activities of its staff, and the coordination of the Scientific Advisory Committee, as we attempt to balance contributions, awards, and needs.

Another key player on the team is the Foundation's Scientific Advisor, a consultant to the Foundation Board and President, and one who oversees the scientific input into the award selection process. In 1988, longtime Scientific Advisor I. C. Winter, M.D., Ph.D. retired and was warmly honored at the Annual Awardees Banquet. He is succeeded by Edward J. Cafruny, M.D., Ph.D.

Dr. Cafruny is no stranger to the PMA Foundation. He has served the Foundation since 1970, most recently as Chairman of the Basic Pharmacology Advisory Committee. He is currently a Distinguished University Professor at the Graduate School of Biomedical Sciences, University of Medicine and Dentistry of New Jersey. He is former Dean and Professor of Pharmacology at the same institution. Ed Cafruny is already making his mark on the activities of the Foundation and I welcome him aboard.

Growth

In 1987, the foundation surpassed the \$2 million mark for the first time. In 1988, the voluntary contributions from the research-intensive pharmaceutical industry exceeded \$2.3 million.

In addition to financial growth, we have been involved in award category "growth"—from nine categories in 1985 to 12 categories in 1988. That involves growth not only in the categories themselves, but in Scientific Advisory Subcommittees to assess each award application, in dollars to fund each category, and in the number of applications and awards. Managing that multiplicity of growth components has demanded the attention of the Officers, Board, and staff, including scientific consultants.

While we can measure growth in the number of applications, we are still striving to improve on our record of actual awards being made. In 1987, the Foundation was able to fund 59 awards, or 30%



Maurice Q. Bectel

of those requested. In 1988, the awards totalled 51, or 30% of the qualified applications. It is in actual awards *made* that the Foundation is now focusing.

Challenge

That is the challenge which the Foundation is addressing as Issue One. We are both proud and appreciative of the support given the Foundation by the PMA member companies—the research-intensive pharmaceutical industry. Moving from a contribution level of \$1.5 million the previous two years to one exceeding \$2 million took a major commitment on the part of the Foundation leadership and the PMA companies, many of which significantly increased their voluntary contributions from the previous year. They deserve—and receive—our heartfelt thanks.

Activities

In 1988, the Foundation continued some programs and added others. The PMA Foundation newsletter, *Tracking 22*, initiated in 1987 as *Tracking 21* to designate the year of activity for the Foundation, provided Foundation constituencies with two activity reports. Such events as Officer changes, Board expansion, category additions, and award news were reported in the pages of *Tracking 22*.

Over 100 participants attended the 1988 Annual Awardee Meeting, held again in Washington, D.C. Distinguished scientists from across the country participated and Robert F. Furchgott, Ph.D., Former Chairman of the Department of Pharmacology at the SUNY Health Science Center, presented the major address, "Endothelium-Dependent Vasodilitation and the Nature of the Endothelium-Derived Relaxing Factor."

The annual meeting of the American Society for Pharmacology and Experimental Therapeutics was held in Montreal, Quebec and again saw the Foundation host a program and reception on October 8, 1988. Over 100 ASPET attendees and previous Foundation awardees heard world-renowned pharmacologist Adrien Albert, Ph.D., D.Sc. of Australia present a paper on "Xenobiosis, and the Genesis of Selective Medication."

The May meeting of the Pharmaceutical Manufacturers Association Foundation Board of Directors was again held in conjunction with the PMA Annual Meeting, held April 24-27, 1988 in Phoenix, Arizona. Outgoing Chairman Lerner presented the Chairman's Report at the First General Session of the PMA Annual Meeting.

In my 1987 annual report, I reported a banner year. Nineteen eighty-eight did not disappoint me in that it too set new records, new yardsticks by which we will measure 1989 and beyond. I am now in my fourth year as President of the PMA Foundation and am confident that the growth and successes will continue, but only with the continued leadership, teamwork, quality research applicants and, certainly most importantly, support from the research-intensive PMA member companies.

Maurice Q. Bectel President

1988 ON RECORD

he Pharmaceutical Manufacturers Association Foundation is a nonprofit, tax exempt organization, established in 1965 to promote public health through scientific and medical research. It provides funding for basic research on drugs and for educational training programs in basic and clinical pharmacology, toxicology and pharmaceutics. Since its formation, approximately \$24 million has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects, and educational programs. Of this amount, slightly more than \$5 million has been used to support research and approximately \$19 million has gone into educational awards. The Foundation continues to provide limited financial assistance for scientific meetings and small amounts for publications.

Virtually all of the 1988 grants and awards were made within programs sponsored by the Foundation. These include three faculty-level programs of salary and fringe benefit support, four fellowship programs, two postdoctoral — two at the advanced predoctoral level and one at the medical student level — plus a program of research starter grants for beginning investigators wishing to move into areas of independent research. An award to assist in expediting the research efforts of new clinical pharmacology units or those with new directors is also available.

Through these programs in 1988, the Foundation assisted an additional 51 individuals. All of these individuals were supported at a critical time in their professional development. The Foundation has, in its 23 years of existence, assisted more than 1,100 individuals through its research and educational support program. A twenty-year historical perspective outlining Foundation activities was prepared in 1985 and is available from the PMA Foundation office.

Meetings and Other Activities

1988 ASPET Meeting

Because of the mutual areas of subject interest, the PMA Foundation sponsors a scientific symposium and reception at the annual meeting of the American Society for Pharmacology and Experimental Therapeutics (ASPET). The 1988 PMAF Symposium and Reception were held October 8 in Montreal, Quebec, with over a hundred PMAF supporters attending.

Highlights of the 1988 gathering included a presentation by world-renowned Australian pharmacologist Adrien Albert, Ph.D., D.Sc., speaking on "Xenobiosis, and the Genesis of Selective Medication." The Foundation also used the ASPET meeting as an ideal opportunity to recognize the contributions of Walter F. Riker, Jr., M.D., to the development of the Foundation and its programs. Dr. Riker had served as a charter member of the PMAF Scientific Dr. Adrien Albert (center), principal speaker at the PMA Foundation Lecture at ASPET, enjoys a relaxing moment with attendees E. Leong Way, Ph.D. (left), member of the Basic Pharmacology Advisory Committee, and Irwin M. Weiner, M.D., chairman, Basic Pharmacology Advisory Committee.



Advisory Committee and throughout its 23-year history and recently retired as Chairman and Revlon Professor of Pharmacology at Cornell Medical College.

Annual Meeting: Other Board Changes

At the May, 1988 PMA Foundation Board of Directors Meeting, new officers were elected and installed. After six years' service as Chairman of the Board of the PMA Foundation, Irwin Lerner stepped down from that post at the conclusion of the meeting. Mr. Lerner, President and Chief Executive Officer of Hoffmann-La Roche Inc., was presented an inscribed, crystal glass mortar and pestle in recognition of his service to the Foundation.

Elected and installed to succeed Lerner was Harvey S. Sadow, Ph.D., Chairman of the Board of Boehringer Ingelheim Corporation of Ridgefield, Connecticut. Serving with Dr. Sadow for Foundation terms 1988-89 are Albert Bowers, Ph.D., re-elected Vice Chairman of the Board, and Hazen L. Richardson, who was reelected Secretary-Treasurer. Dr. Bowers is Chairman and Chief Executive Officer of Syntex Corporation, Palo Alto, California. Mr. Richardson was Vice President, Medical Products Department, E. I. duPont de Nemours & Company of Wilmington, Delaware, until his retirement in December, 1988, at which time he resigned his Foundation post. David B. Sharrock, President and Chief Executive Officer of Merrell Dow, Cincinnati, Ohio, was named Secretary-Treasurer for the remainder of the term. He had been serving a term on the Board as a Director.

Also serving on the Foundation Board for 1988-89 are Irwin Lerner, who serves a term as Past Chairman, and Directors Richard J. Kogan, President and Chief Executive Officer of Schering-Plough Corporation, and Joseph J. Ruvane, Jr., Vice Chairman of Glaxo Inc. PMA President Gerald J. Mossinghoff serves as an ex-officio member of the Foundation Board. Maurice Q. Bectel continued to serve the PMA Foundation as its President and principal staff officer throughout 1988, as he had the previous year. At the October, 1988, meeting of the PMA Foundation Board of Directors, significant Bylaws changes were adopted. The Foundation's Board was expanded through the addition of three new directors. Enlarging the Board will provide greater exposure by industry executives to the Foundation and its objectives. Although the PMA Foundation and the Pharmaceutical Manufacturers Association are separate corporate entities, each with its own operation and purposes, the Foundation's Bylaws require that Foundation Board members must also serve on the PMA Board of Directors.

Elected to serve as new Foundation Board members are:

• Sheldon G. Gilgore, M.D., Chairman, President, and Chief Executive Officer of G. D. Searle & Co.

• Hubert E. Huckel, M.D., Chairman and President of Hoechst-Roussel Pharmaceuticals Inc.

• Klaus Heinz Risse, Ph.D., President and Chief Executive Officer of Miles Inc.

Two New Grant Programs Added in 1988

1988 saw the expansion of the Foundation's Grant Awards Program from ten to twelve separate categories. The PMA Foundation Board took action to authorize an additional specific category for an award, then took precedent-setting action to establish a new grant concept.

Research on Drugs for Rare Diseases is the new grant concept award in that an applicant for any of the other eleven award categories may qualify for this award if the research is in the areas commonly called "rare diseases" or "orphan drugs." In other words, an application for any one of the Award Categories 1-11 (see chart) could be approved for the "Research on Drugs for Rare Diseases" category.



1988 Foundation honorees reminisce over their experiences since the founding of the PMA Foundation in 1965. Left in photo is Walter Franklyn Riker, Jr., M.D., who was cited by the Foundation as a "Distinguished Teacher, Research Scientists, and Physician." At right is Irwin C. Winter, M.D., Ph.D., long-time member and former chairman of the Foundation's Scientific Advisory Committee and, from 1975-88, Scientific Consultant to the Foundation.

Undergraduate Research Fellowship Program in Pharmaceutics is the second new award category authorized in 1988. This award, set to begin in 1990, recognizes that a shortage is occurring now—and will worsen in the future—for Ph.Ds in the field of pharmaceutics. This is problematic, not only for the pharmaceutical industry, but for the health sciences and the public at large, as we enter the end of the twentieth century.

See the adjacent chart for a chronological listing of all twelve Foundation Award Categories.

Survey on PMA Foundation Completed

Begun in late 1987, a comprehensive analysis of a survey undertaken of nearly 700 Foundation grant awardees was completed during 1988. Objectives of the project were to:

- Develop a baseline for demographic data on awardees;
- Develop an overview of awardees' accomplishments; and
- Solicit awardees suggestions for program improvements.

An extremely high response rate was experienced—over 50% returned the comprehensive questionnaire. An impressive 83% of the respondents are employed at educational institutions and are engaged in pharmaceutical research. An additional 7% are full-time health science educators. The remaining 10% are engaged in other health field pursuits, such as practice, administration, or consulting.

Copies of the Survey Critique are available through the PMA Foundation office.

Awardee Meeting Held in Washington

Downtown Washington, D.C., was the location for the February 10-11, 1988 Annual PMA Foundation Awardee Meeting. Over 130 guests attended and heard keynote speaker Robert F. Furchgott, Ph.D. Dr. Furchgott is former Chairman of the Department of Pharmacology at the SUNY Health Science Center in Brooklyn.

Accompanying photographs provide additional information regarding the 1988 awardee meeting.



Irwin C. Winter, M.D., Ph.D. (left), receives the plaudits of PMA Foundation Board Chairman Irwin Lerner, President and Chief Executive Officer of Hoffmann-La Roche. The presentation was a portrait of Dr. Winter, in recognition of his many contributions to the Foundation.

Na Yea	me of Program/ r of First Awards	Number of Awards Budgeted Yearly/ Length of Award	Program	Budget	Deadline Announcement Date Starting Times
Cli	nical Pharmacology Advisory Commi	ttee	5.0		
(1)	Faculty Awards in Clinical Pharmacology (1967)	3 budgeted/ 3 years	\$360,000 \$ 40,000	total per award per year	October 15 December 15 July 1
(2)	Fellowships for Careers in Clinical Pharmacology (1973)	4 budgeted 2 years	\$192,000 \$24,000	total per award per year	October 15 December 15 July 1
(3)	Medical Student Research Fellowships (1974-Amended 1982)	6 budgeted 3 months to one year	\$ 36,000 \$ 500	total per month maximum \$6,000	January 15 March 15 July 1
(4)	Development Grants for Clinical Pharmacology Units (1978)	1 budgeted 3 years to use funds	\$ 50,000	per award	January 15 March 15 July 1
Bas	sic Pharmacology Advisory Committe	e			
(5)	Faculty Awards in Basic Pharmacology/Toxicology (1973)	3 budgeted 2 years	\$180,000 \$ 30,000	total per award per year	September 15 December 15 July 1
(6)	Research Starter Grants (1972)	20 budgeted 2 years	\$400,000 \$ 10,000	total per award per year	September 1 November 15 January 1
(7)	Advanced Predoctoral Fellowships in Pharmacology/Toxicology (1978)	12 budgeted 2 years	\$240,000 \$ 10,000	total per award per year	September 15 December 15 January-July 1
Pha	armacology-Morphology Advisory Co	mmittee			
(8)	Fellowships in Pharmacology- Morphology including Cell Biology (1968)	3 budgeted 2 years	\$126,000 \$21,000	total per award per year	January 1 March 15 July 1
Tox	icologic-Pathology Advisory Subcom	mittee		- M. G L L L L L L L.	
(9)	Faculty Awards in Toxicologic- Pathology (1982)	2 budgeted 2 years	\$120,000 \$ 30,000	total per award per year	September 1 November 15 July 1
Pha	armaceutics Advisory Subcommittee				
(10) Advanced Predoctoral Fellowships in Pharmaceutics (1987)	8 budgeted 2 years	\$160,000 \$ 10,000	total per award per year	September 1 November 15 January-July
(11) Undergraduate Fellowships in Pharmaceutics (1990)	12 budgeted 1 year	\$ 60,000 \$ 5,000	total per award	September 1 November 15 January-July

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

Winter Recognized at Retirement

Irwin C. Winter, M.D., Ph.D., was recognized at the Awardee Dinner for his many contributions to the Foundation. "I.C." served the Foundation as chairman of the Scientific Advisory Committee during the early growth stages, 1970-75. At the time, he was Vice President of Medical Research at G. D. Searle & Co.

After retiring from Searle, he became the scientific consultant to the Foundation and served in that capacity until retiring from that post in early 1988.

PMA Foundation Chairman Irwin Lerner acknowledged I. C. Winter's unique contributions to the Foundation at the banquet and presented him with a striking portrait.

Miller Retires From Board

William R. Miller, Vice Chairman of the Board of Bristol-Myers Company, retired from the PMA Foundation Board of Directors at its May, 1988, meeting. He had served the Foundation since 1983, including a term as Secretary-Treasurer.

Board Chairman Irwin Lerner presented a plaque to Mr. Miller in recognition of his service to the Foundation.



Scientific interchange is fostered by the PMA Foundation at such events as the Annual Awardee Meeting. Rochelle D. Schwartz, Ph.D. (left) and one of the more than 130 attendees actively participate during the Poster Session.



Education and Training Programs

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

Clinical Pharmacology

Faculty Awards in Clinical Pharmacology

The four clinical pharmacology programs provide opportunities at the student, fellow and faculty levels. Through the Faculty Development Awards in Clinical Pharmacology program, the Foundation makes three-year awards to medical schools for salary and fringe benefits support of full-time junior faculty members. The Foundation has set a ceiling of \$40,000 on the amount of its participation in total yearly salary and fringe benefits for any individual candidate.

With the awards scheduled to begin July 1, 1989, 84 individuals have been supported under this program since 1967.

Recipients of the three awards to begin July 1, 1989 are:

Patrick Taylor Horn, M.D., Ph.D., Assistant Professor, University of Chicago, Committee on Clinical Pharmacology. Dr. Horn's research is entitled, "Sympathetic Nervous System Control of Regional Blood Flows," which is a study into mechanisms through which an animal's nervous system automatically and selectively controls blood flow to different regions of the body. Studies are planned that will investigate the distribution of postsynaptic alphaadrenoceptor subtypes on vascular smooth muscle and the role that the receptor distribution plays in the response of the regional vascular beds to sympathetic control. This research will also investigate the intracellular actions initiated by dopamine receptor activation in vascular smooth muscle. Additionally, he will investigate the physiologic role of inhibitation of impulse transmission through sympathetic ganglia produced by catecholamines. Carl C. Peck, M.D. (left) and John Beary, III, M.D., exchange ideas over dinner at the 1988 Annual Awardee Meeting. Dr. Peck is Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration and Dr. Beary is Senior Vice President of Science and Technology, Pharmaceutical Manufacturers Association.



Patrick Taylor Horn, M.D., Ph.D.



Ralph A. Kelly, M.D.



Lawrence G. Miller, M.D.

Dr. Horn will also perform clinical studies on blood pressure in children. Twenty-four hour ambulatory blood pressure recordings will be obtained from normal and hypertensive patients. The reduction of blood pressure during sleep will be compared between the two groups and the results in children compared to the recently obtained results in adults.

Ralph A. Kelly, M.D., Assistant Professor, Harvard Medical School. Dr. Kelly will investigate whether an endogenous ligand exists for the cardiac glycoside binding site on NaK-ATPase — the molecular machinery that constitutes the cellular sodium pump. The evolutionary longevity of this binding site has led to much speculation that NaK-ATPase acts as a "receptor" for hormone or autacoid.

The second thrust of Dr. Kelly's research investigates the role of the mitochondrion in the maintenance and defense of cellular calcium and proton homeostasis under physiologic conditions and in defending the cell during anoxic or hypoxic stress. Specifically, he will determine whether matrix calcium serves as a regulator of myocardial energetics under physiologic conditions, and whether the mitochondria acts as a buffer for cytosolic calcium during during cellular anoxia.

Lawrence G. Miller, M.D., Assistant Professor, Tufts University School of Medicine. Dr. Miller's research involves molecular determinants of benzodiazepine action. While substantial information is available concerning acute effects of benzodiazepines, relatively little is known concerning chronic drug effects. Dr. Miller's present proposal seeks to extend studies already performed demonstrating alterations in receptor binding and function during chronic benzodiazepine administration by utilizing two major technical advances: culture of neurons *in vitro* and assessment of gene expression through molecular biological techniques. These studies will be performed both in animals and in culture and establish techniques that can be directly applied to drug design and receptor regulation in human disease states.

Individuals whose awards began July 1, 1988 are:

Francesca Catella, **M.D.**, Instructor, Department of Pharmacology, Vanderbilt University. Dr. Catella ended her award in June, 1989, to take a position at a pharmaceutical company located in Italy.

Thomas C. Shea, M.D., Assistant Professor, Department of Medicine, Oncology, University of California, San Diego.

John Tangney Sullivan, M.D., Instructor of Medicine, Roger Williams Medical Center (moved to Johns Hopkins University as Assistant Professor in early 1989).

Individuals who entered the second year of their awards in 1988 are:

Matthew E. Knight, M.D., Assistant Professor, Pediatrics and Pharmacology, University of Florida.

Ullrich Schwertschlag, M.D., Assistant Professor of Medicine, Duke University Medical Center. Dr. Schwertschlag ended his fellowship and became an Associate Research Physician with Eli Lilly Research Laboratories in late 1988. Lyle Amos Siddoway, M.D., Assistant Professor, Medicine, Division of Clinical Pharmacology, The Johns Hopkins Hospital (moved to Georgetown University in early 1989).

Individuals who entered the third year of their awards in 1988 are:

William J. Elliott, M.D., Ph.D., Assistant Professor of Medicine, University of Chicago.

Theodore Wang, M.D., Assistant Professor of Medicine, Tulane Medical Hospital and Clinic.

Concluding their awards in 1988 are:

Desmond Fitzgerald, M.D., Instructor in Medicine and Pharmacology, Vanderbilt University.

Douglas G. Roberts, M.D., Assistant Professor of Pediatrics and Pharmacology, Wayne State University School of Medicine.

William Steven Dalton, M.D., Ph.D., Clinical Instructor, Section of Hematology/Oncology, Department of Internal Medicine, Health Sciences Center, The University of Arizona.

Phyllis I. Gardner, M.D., Assistant Professor of Medicine, Stanford University Medical Center.

Ruth Margrit Ruprecht, M.D., Ph.D., Assistant Professor, Dana-Farber Cancer Institute, Harvard Medical School.

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, individuals can pursue full-time study in the basic pharmacologic sciences needed to complement their clinical skills.

The program was amended in 1982 to allow an individual to apply for a fellowship two years in advance of the activation date of the award. For example, those applying for a fellowship in the Fall of 1989 may request that the fellowship begin July 1990 or July 1991.

The first awards under this program were made in 1973. Since that time, 45 fellowships have been awarded.

Recipients of the two fellowships beginning in 1989 are:

David W. Rudy, M.D., Indiana University, postdoctoral fellow. Dr. Rudy's research is two-part: The first is entitled "Stereoselective Disposition of Ibuprofen Enantiomers and Their Effects on Renal Function in Normal Volunteers." He aims to determine the pharmacokinetics of the R and S enantiomers of ibuprofen, investigate the conversion of the R-enantiomer to the S-enantiomer, and to assess the effects of the different enantiomers on renal function. The second project, "Bumetanide Infusion in Chronic Renal Failure," will compare the efficacy, pharmacokinetics, pharmacody-



David W. Rudy, M.D.



Daniel Ward, D.V.M.

namics, and the development of diuretic tolerance of bumetanide administered either as a continuous IV infusion or as intermittent IV boluses.

Daniel Ward, D.V.M., University of Georgia, postdoctoral fellow. Dr. Ward's research is divided into three areas: the clinical pharmacology consultation service (CPCS), the ocular pharmacology research program, and clinical duty. The CPCS will occupy approximately 50% of the fellowship program, and will involve consultation therapeutic drug monitoring of cases presented to the Department of Small Animal Medicine. The ocular pharmacology research program will occupy approximately 40% of the fellowship year and will consist of continued research into ocular anti-inflammatory drugs and ophthalmic uses of cyclosporine A. Clinic duty will occupy the remaining 10% of the fellowship and will concentrate on consultations involving pharmacologic management of cases presented to the ophthalmology section of the Department of Small Animal Medicine.

Individuals who began their awards in July of 1988 are:

Li Wang, M.D., Department of Pharmacology/Toxicology, Children's Hospital (Ohio State University).

Daniel David Gretler, M.D., Departments of Medicine and Pharmacology, University of Chicago.

Individuals who entered the second year of their awards in 1988 are:

Dawn Merton Booth, D.V.M., Department of Veterinary Physiology and Pharmacology, College of Veterinary Medicine, Texas A&M University.

Christian Leon Hadrzynski, M.D., Pediatric Clinical Pharmacology, University of Texas Medical Branch at Galveston. Dr. Hadrzynski accepted a position with a pharmaceutical firm in France and ended his fellowship in December 1988.

Individuals whose awards concluded in 1988:

Patrick Taylor Horn, M.D., Ph.D., Division of Clinical Pharmacology, University of Minnesota.

Richard D. Huhn, M.D., Clinical Pharmacology, Department of Medicine, Brown University.

Therese M. Kitt, M.D., Department of Pharmacology, Internal Medicine, University of Iowa.

Thomas C. Shea, M.D., Cancer Pharmacology Division, Harvard University, Dana-Farber Cancer Institute.

Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology

The third program is the Medical Student Research Fellowships in Pharmacology-Clinical Pharmacology. This program, which began in 1974, offers students an opportunity to spend up to one year fulltime conducting an investigative project in pharmacology-clinical pharmacology. The minimum period of the award is three months and maximum is two years. It is hoped that by having students become involved in investigative projects at a point when career choices are still relatively flexible, they will eventually choose research careers in clinical pharmacology. Ninety awards have been made since 1974.

Individuals whose awards will begin in July of 1989 are:

Harold S. Cooper, University of Pennsylvania, School of Medicine, received a one-year fellowship. His principal advisor is Martin Wax, M.D, Assistant Professor of Pharmacology and Ophthalmology.

Lee Madeline, Vanderbilt University, School of Medicine, received a three-month fellowship. His principal advisor is David Robert, M.D., Professor of Medicine and Pharmacology and Director, Clinical Research Center.

Aloke Kumar Mandal, Department of Pharmacology, Georgetown University, School of Medicine, received a one-year fellowship. His advisor is Richard A. Gillis, Ph.D., Professor, Department of Pharmacology, Georgetown University.

Lynne I. Portnoy, Department of Clinical Pharmacy, Ferris State University, has a six-month fellowship. Ms. Portnoy's principal advisor is Dr. Dennis Mungall, Associate Professor of Pharmacy.

Individuals whose awards began in July of 1988 are:

David Allan Brousseau, University of Pennsylvania, has a twelvemonth fellowship. His principal advisor is Dr. Glen N. Gaultion, Assistant Professor, Department of Pathology.

Aloke Kumar Mandal, Georgetown University, has a twelve-month fellowship. His principal advisor is Richard A Gillis, Ph.D., Professor, Department of Pharmacology.

Craig van Horne, University of Colorado, School of Medicine, has a twelve-month fellowship. His principal advisor is Barry J. Hoffer, M.D., Ph.D., Professor, Department of Pharmacology.

Scott B. Shappell, Baylor College of Medicine, has a twelve-month fellowship. His principal advisor is Jerry R. Mitchell, M.D., Ph.D., Professor of Medicine and Pharmacology.

Paul Joseph Utz, Stanford University School of Medicine, has a twelve-month fellowship. His principal advisor is Gerald R. Crabtree, M.D., Assistant Professor, Pathology, Howard Hughes Medical Institute.

Clinical Pharmacology Unit Support

This program assists directors of clinical pharmacology units established within a two-year period preceding the award, or units that have acquired a new director during that period. The grant provides a total of \$50,000 which may be used at any time over a three-year period. The purpose of the program is to provide supplementary funds to assist the unit's research efforts until other research grants are obtained. The first grants were made in 1978. The total number of awards made to date is seventeen. No awards were made for 1989.

The awards beginning July 1, 1988, were made to:

John E. Nelson, M.D., Ph.D., Director, Clinical Pharmacology Center, Loyola University Medical Center, Stritch School of Medicine. The broad mission of Dr. Nelson's Clinical Pharmacology Center is to improve patient care through enhanced understanding of drug therapy. Research interests of CPC core faculty are clinical pharmacokinetics, bioelectric impedence and drug distribution volume, assessment of renal function in pharmacokinetic studies, testing the multi-compartmental pharmacokinetic model, determination of free water diffusion coefficients, and the pharmacology of hypoxic pulmonary hypertension.

Raymond L. Woosley, Jr., M.D., Ph.D., Director, Clinical Pharmacology Unit, and Professor and Chairman, Department of Pharmacology and Professor of Medicine, Georgetown University School of Medicine. The goal of the Clinical Pharmacology Center will be to teach the principals of rational therapeutics at all levels of medical education. With the critical national need for trained clinical pharmacologists, the postdoctoral training program of the Center will receive special emphasis. The close proximity of the Center to the NIH and the FDA provides special opportunities for interaction with these two agencies. Specific research projects are biochemical factors in the toxicity of amiodarone, comparative antiarrhythmic actions and toxicity of des-oxoamiodarone and amiodarone, identification of biochemical predictors of amiodarone toxicity, and determinants of inter-individual variation in the response to drugs.

Basic Pharmacology

Faculty Development Awards in Basic Pharmacology

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

The first awards were made in 1973 and continue to be for a twoyear period. The program provides salary and fringe benefits. The Foundation has set a ceiling of \$30,000 on the amount of its participation in the total yearly salary and fringe benefits for awardees. The total number of awards made to date is 46.

Those who will receive awards beginning July 1, 1989 are:

Peter J. R. Cobbett, Ph.D., Assistant Professor, Department of Pharmacology, Michigan State University. Dr. Cobbett's research involves, "Excitatory amino acid transmission in the neuroendocrine hypothalamus: pharmacological and mechanistic studies." It has been established that the hormones vasopressin and oxytocin are secreted into the blood by neurons of the hypothalamus and have critical roles in the maintenance of body volume and of reproductive functions. Dr. Cobbett's goal is to investigate the role of amino acids and dipeptides as excitatory neurotransmitters within the hypothalamic nuclei containing these neurons. He will examine



Peter J.R. Cobbett, Ph.D.

the electrophysiological effects of putative amino acid agonists, including glutamate, aspartate and N-methyl-D-asparate (NMDA), and of competitive and non-competitive antagonists for the multiple amino acid receptor subtypes on single neurons and on individual membrane ion channels to determine the nature of the amino acid receptors and receptor-channel complexes. Dr. Cobbett will perform more extensive studies which, all in all, will permit the effects of various compounds currently under investigation for therapeutic uses in stroke and epilepsy, but with other target sites in the central nervous system to be examined.

Robert A. Nicholas, Ph.D., Assistant Professor, University of North Carolina at Chapel Hill. A primary objective of Dr. Nicholas' research is to learn about the structures of the penicillin-binding proteins (PBPs) of *Escherichia coli* and to understand how the structures of the PBPs relate to and affect their function in the synthesis of the cell wall peptidoglycan. These experiments combine the techniques of molecular biology with those of biochemistry and crystallography. Since PBPs are the killing targets for b-lactam antibiotics, the need to learn more about their structures provides a compelling reason for the continuing study of these proteins. An understanding of the molecular basis of b-lactam recognition should contribute to the rational design of new antibiotics. A greater understanding of the molecular events occurring in cell wall synthesis may also create a foundation for other areas of antibiotic research.

K. Kee Wan, Ph.D., Assistant Professor, Northwestern University Medical School. Dr. Wan's research involves "antihistamine receptor monoclonal antibodies." Cellular responses to histamine are mediated through specific histamine receptors which are coupled to second messenger systems. However, very little is known about the structures and properties of these receptors. The aim of Dr. Wan's research is to generate antihistamine receptor monoclonal antibodies using the auto-antiidiotype route and to use these antireceptor antibodies to isolate and to characterize various classes of histamine receptors. The study involves raising antireceptor antibodies by injecting experimental animals with histamine conjugated to a carrier protein, without prior biochemical purification of the receptor protein(s). These antiidiotype anti-receptor antibodies will then be further characterized followed by using them to probe the structure-function relationships of the different histamine receptors in the brain and in other tissues. These antireceptor antibodies will also be used alone or in combination with other techniques, including gene cloning techniques, to isolate the histamine receptors.

Those who received awards beginning July, 1988 are:

Serrine S. Lau, Ph.D., Assistant Professor, Department of Pharmacology, University of Texas at Austin.

Paul H. Ratz, Ph.D., Assistant Professor, Eastern Virginia Medical School.

Jonathan G. Scammell, Ph.D., Assistant Professor, Department of Pharmacology, University of South Alabama, College of Medicine.



Robert A. Nicholas, Ph.D.



K. Kee Wan, Ph.D.

Those who entered the second year of their awards in 1988 are:

Edward T. Morgan, Ph.D., Assistant Professor, Department of Pharmacology, Emory University.

Rick G. Schnellmann, Ph.D., Assistant Professor, Department of Physiology and Pharmacology, The University of Georgia.

Rochelle D. Schwartz, Ph.D., Assistant Professor, Department of Pharmacology, Duke University.

Concluding their awards in 1988 are:

Kelvin W. Gee, Ph.D., Assistant Professor, Department of Pharmacology, University of Southern California.

Jonathan Maybaum, Ph.D., Assistant Professor, Department of Pharmacology, University of Michigan.

Fellowships for Advanced Predoctoral Training in Pharmacology or Toxicology

This program, offered initially in 1977, is designed to assist those candidates who expect to complete the research for their doctoral dissertations.

For 1988, the fellowship program provides a stipend of \$6,552 a year, payment of tuition, and \$500 a year for incidentals directly associated with preparation of the dissertation. For 1989, in order to increase the number of awards budgeted from eight to twelve, the Basic Pharmacology Advisory Committee decided to eliminate the tuition and raise the stipend to \$10,000, retaining the \$500 per year expense money. A total of 137 fellowships have been awarded since 1977.

Those who will receive fellowships which begin between January and August, 1989 are:

Joseph Affholter, Stanford University, Department of Pharmacology. His advisor is Dr. Richard A. Roth, Assistant Professor of Pharmacology. Mr. Affholter will investigate the functional *(in vivo)* and biochemical *(in vitro)* interactions of insulin and the insulin degrading enzyme.

Jeffrey H. Boatright, Emory University, Department of Pharmacology. His advisor is P. Michael Iuvone, Ph.D., Associate Professor of Pharmacology. Mr. Boatright's research involves the regulation of the retinal dopaminergic system by melatonin.

Gretchen Feussner, State University of New York, Health Science Center, Syracuse. Her advisor is Mary Lou Vallano, Ph.D., Assistant Professor, Pharmacology. Ms. Feussner will examine $Ca^{2+}/$ calmodulin-dependent protein kinase II in the rat hippocampus.

Theresa M. Filtz, University of Pennsylvania, School of Medicine, Department of Pharmacology. Ms. Filtz's advisor is Perry B. Molinoff, M.D., Professor and Chairman, Department of Pharmacology. Her research will focus on the solubilization and purification of dopamine D-l receptors. **Carlotta Eileen Groves,** University of Georgia, College of Veterinary Medicine, Department of Physiology and Pharmacology. Ms. Groves' advisor is Rick G. Schnellmann, Ph.D., Assistant Professor, Department of Physiology and Pharmacology. She will study membrane blebbing in halocarbon-induced nephrotoxicity.

Devorah Gurantz, University of California, San Diego, Department of Pharmacology. Her advisor is Vincent E. Dionne, Associate Professor of Pharmacology. Ms. Gurantz' research will involve modulation of the neuronal nicotinic acetylcholine receptor during embryonic development.

Nancy W. Kleckner, University of North Carolina at Chapel Hill, Department of Pharmacology. Ms. Kleckner's advisor is Raymond J. Dingledine, Ph.D., Associate Professor of Pharmacology. Her research will deal with pharmacological studies of the NMDA/Glycine receptor expressed in xenopus oocytes.

Joseph William Polli, Pennsylvania State, University, M. S. Hershey Medical Center. His advisor is M. L. Billingsley, Ph.D., Associate Professor, Department of Pharmacology. Mr. Polli's research deals with the development regulation of calmodulin-binding protein expression in cortical aggregating cultures.

Julie Ann Poorman, University of Texas Health Science Center at Houston, Graduate School of Biomedical Sciences, Department of Pharmacology. Her advisor is David S. Loose-Mitchell, Assistant Professor of Pharmacology. Ms. Poorman's research deals with altered cholesterol metabolism in a hypercholesterolemia resistant rabbit colony.

G. William Rebeck, Harvard University, Laboratory of Toxicology. His advisor is Leona Samson, Assistant Professor of Toxicology. Mr. Rebeck will examine the response of E. coli and human cells to DNA alkylation damages.

Chen-Shian Suen, Mount Sinai School of Medicine of the City University of New York. His advisor is Sherwin Wilk, Professor of Pharmacology. Mr. Suen's research involves the regulation of thyrotropin releasing hormone-degrading enzymes.

Michael S. Vincent, Indiana University School of Medicine. Mr. Vincent's advisor is Joseph A. Near, Ph.D, Assistant Professor, Medical Sciences Program. Mr. Vincent will be studying the purification and characterization of soluble dihydrotetrabenzine binding activity.

Fellowship Awards in Pharmacology-Morphology

The aim of this program is to increase knowledge about the actions of drugs by direct study of their effects on cells and tissues; to correlate the morphological changes; and, concurrently, to uncover associations observed with functional parameters of cells and tissues.

The awards are 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. First offered in 1968, 73 awards have been made.

Karen J. Axt, Ph.D.



Melissa Rogers, Ph.D.



Paul R. Wade, Ph.D.

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

Recipients of the fellowships beginning July 1989 are:

Karen J. Axt, Ph.D., The Johns Hopkins University, Department of Neuroscience. Dr. Axt's research goal is to describe, both anatomically and pharmacologically, two distinct serotonergic forebrain projects from dorsal and media raphe nuclei, using the rat hippocampus as a model terminal region. At least two types of serotonergic nerve fibers have been described in the rat brain using 5-HT immunocytochemistry; "fine" fibers, which have small fusiform varicosities along their length, and "beaded" fibers characterized by large spherical varicosities. These fiber types can be differentially abated by neurotoxic amphetamines such as methylenedioxyamphetamine and p-chloroamphetamine. The fine fibers degenerate following drug administration, and the beaded fibers are spared. Thus, these substituted amphetamines are potentially useful tools for studying the anatomic organization of the morphologically distinct serotonin fiber types, their raphe origins, and their possible biochemical differences.

Melissa Rogers, Ph.D., Dana-Farber Cancer Institute, Harvard University. In order to understand the influence of retinoids on and differentiation, carcinogenesis, and morphogenesis, one must elucidate their mechanism of action. A useful model system has been the induction of embryonal carcinoma cell differentiation by the acid form of vitamin A, retinoic acid (RA). In particular, RA changes the highly malignant F9 cell line into benign, non-invasive cells resembling the extraembryonic endoderm of the mouse embryo. Dr. Rogers' experiments will further the understanding of RA action by extending the characterization of an RA-regulated gene previously studied using the in vitro F9 embryonal carcinoma system. In particular, she will determine the temporal and spatial expression pattern of the homeobox-containing gene, ERA-1/Hox-1.5 during mouse embryogenesis suing Northern blot hybridization and in situ hybridization. Moreover, she will determine the pattern of alternative splicing of this gene *in vivo* because the presence of alternative transcripts has important regulative implications.

Paul R. Wade, Ph.D., Columbia University, College of Physicians and Surgeons, Department of Anatomy & Cell Biology. Dr. Wade's research is entitled "Modulation by 5-hydroxytryptamine (5-HT) and its receptors of the aboral spread of excitation in the enteric nervous sytem." Although the activities of individual enteric neurons have been studied, neither the anatomy nor the function of enteric microcircuits is understood. 5-HT is a neurotransmitter of enteric interneurons. Specific actions of 5-HT on individual enteric neurons have been characterized using electrophysiological methods and these responses have been linked to different subtypes of 5-HT receptor. A physiological response linked to 5-HT is the mediation of slow EPSPs. Dr. Wade's research seeks to take advantage of the fact that only a subset of enteric ganglia ("5-HT ganglia") contain the cell bodies of serotonergic neurons to test two hypotheses: (1) That the ganglia of the myenteric plexus of the small intestine are heterogeneous. It is postulated that the pathways in the myenteric plexus that include "5-HT ganglia" are different from those that do not. Pathways will be traced using microinjection of novel anterograde and retrograde probes into ganglia that do or do not contain identified serotonergic neurons. (2) That "5-HT ganglia" and particular subtypes of 5-HT receptor are involved in the mediation of the descending excitation that accompanies the peristaltic reflex.

Those who began their awards in July 1988 are:

Dennis J. Paul, Ph.D., Department of Neurology, Memorial Sloan-Kettering Cancer Center. The title of Dr. Paul's research is "Autoradiographic Localization of Opioid Receptors in the CNS." Opioid receptor subtypes will be localized and quantified using direct and digital subtraction autoradiography. Anatomic localization will be determined with reference to genetic and development variables. He will also address the issues of pre- or post-synaptic localization and the rate of receptor turnover in the central nervous system. The goals of this project are to better understand the neuroanatomical determinants of opioid effects and to improve techniques for digital subtractions autoradiography.

Jean-Jacques Soghomonian, D.E.A., Medical College of Pennsylvania. Dr. Soghomonian is studying the regulation of gene expression for glutaminic acid decarboxylase (GAD), the key enzyme in the synthesis of GABA, in neurons of the basal ganglia. GAD mRNA will be detected by *in situ* hybridization histochemistry in single neurons of the striatum, pallidum and substantia nigra. Intact rats, and rats with a unilateral lesion of the nigrostriatal dopaminergic neurons will be treated with repeated injections of dopaminergic agonist and antagonists, including agents acting specifically on dopaminergic receptor subtypes. These experiments will give new insights into the role of dopamine in the long term regulation of GABA-ergic neurons in the basal ganglia. This is relevant to the search for a better treatment of diseases of the basal ganglia, especially by providing, using morphological techniques, new information on newly developed selective dopaminergic agents.

David W. Schulz, Ph.D., Harvard Medical School, Department of Biological Chemistry and Molecular Pharmacology. Dr. Schultz's research is entitled "Anatomical localization of binding sites for the nicotinic antagonist neuronal bungarotoxin in rat brain." The neurotoxin neuronal bungarotoxin (NBT) is known to block nicotinic activity at autonomic synapses, and Dr. Schultz's labs have recently demonstrated that NBT is also a functional nicotinic antagonist in rat brain. Therefore, he will use quantitative autoradiographic techniques in order to characterize the localization of iodinated NBT binding in the rat central nervous system. Because of evidence that nicotinic receptors may modulate the release of certain biogenic amines, particular emphasis will be placed on



Dennis J. Paul, Ph.D.



Jean-Jacques Soghomonian, D.E.A.



David W. Schulz, Ph.D.

determining the cellular localization of this population of nicotinic receptors through the use of selective lesioning techniques. (*Note that Dr. Schultz took a position with Pfizer, Inc. beginning August 1989 and ended his fellowship early.)

Individuals who entered the second year of their award in 1988 are: Barbara Christie-Pope, Ph.D., Vanderbilt University, Department of Pathology.

Britta A. Mattson, Ph.D., Tufts University, Department of Anatomy and Cell Biology.

Lisa A. Won, Ph.D., The University of Chicago, Department of Pharmacology and Physiological Sciences.

Individuals who ended their fellowship in 1988 are:

Annette L. Kirchgessner, Ph.D., Columbia University, College of Physicians and Surgeons, Department of Anatomy and Cell Biology. Diane L. Rosin, Ph.D., Yale University, Department of Pharmacology.

Faith Winningham-Major, Ph.D., Vanderbilt University, Department of Pharmacology.

Faculty Awards in Toxicologic Pathology

With first awards given in 1983, this award was developed to attract scientists interested in analyzing, reviewing and questioning, where appropriate, the present state of the art in the field of toxicology. The goal of the program is to support veterinary and comparative pathologists who will devote two years to research with drugs. In the past, the Foundation has set a ceiling of \$25,000 on the amount of its contribution to total yearly salary and fringe benefits for any candidate. However, for 1989, that amount has been increased to \$30,000. Also, beginning in 1989, the Foundation will be granting two awards yearly in this program. Two awards were also made in 1989, bringing the total number to 13.

Beginning their awards July, 1989 are:

Deborah Gillette, D.V.M., Ph.D., Assistant Professor of Pathology, School of Veterinary Medicine, University of Pennsylvania. Dr. Gillette's research involves mechanisms of action of acute forestomach toxicity caused by two non-genotoxic carcinogens. The food additive butylated hydroxyanisole (BHA) and the chemical ethyl acrylate are two non-genotoxic compounds that elicit hyperplasia and inflammation of the squamous epithelium of the rat forestomach. This acute toxic reaction then progresses with repeated administration to development of tumors. There is some recent evidence that toxicity may be accompanied by glutathione (GSH) depletion. Dr. Gillette will investigate the possible mechanisms of forestomach toxicity including: (1) Histochemical mapping of the distribution of GSH in both glandular and squamous portions of the stomach; (2) Correlation of toxicity with peroxidative damage to the gastric mucosa as evidenced by production of conjugated dienes and malondialdehyde; (3) Comparison of the subcellular distribution of GSH in glandular and squamous portions of the stomach; 4) Examination of the effect of GSH depletion on chemi-



Deborah Gillette, D.V.M., Ph.D.

cally mediated forestomach injury; (5) Investigation of the effects of antioxidants on forestomach injury; and (6) Comparison of GSH transferase and carboxylesterase activities in normal and treated rats, both in forestomach and glandular mucosa.

Matthew A. Wallig, D.V.M., Ph.D., Assistant Professor of Pathology, College of Veterinary Medicine, Department of Pathobiology, University of Illinois at Urbana-Champaign. Nitriles can be present at significant levels in dietary preparations of cruciferous plants such as sauerkraut, cole slaw and brussel sprouts. Although these compounds can be toxic at high concentrations, they may have chemoprotective effects at lower doses against ingested toxins and carcinogens. This chemoprotective effect may be due to enhancement of an endogenous compound in tissues, glutathione (GSH), which is used by the body in detoxification reactions to neutralize reactive compounds or their metabolic intermediates. One such nitrile, CHB, although toxic to pancreas at high doses, enhances GSH in liver and pancreas and hence may be chemoprotective against toxins or carcinogens. Dr. Wallig plans to investigate the biologic effects of CHB to determine the mechanisms of GSH enhancement, define the dose of CHB necessary for GSH enhancement and test the actual chemoprotective potential of CHB against known toxins and carcinogens.

Beginning their awards July, 1988 are:

Evelyn Anne Kazacos, D.V.M., Ph.D., Purdue University, School of Veterinary Medicine, Department of Veterinary Microbiology, Pathology and Public Health.

James Arthur Render, D.V.M., Ph.D., Assistant Professor, Department of Pathology, Michigan State University.

Entering the second year of his award in 1988:

Michael W. Conner, D.V.M., Assistant Professor, Department of Pathology, Boston University. (Dr. Conner accepted a position with Smith Kline & French Laboratories in the fall of 1988 and ended his award.)

Those who ended their awards in 1988 are:

Merl F. Raisbeck, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Pathology, University of Missouri. Dr. Raisbeck moved to the University of Wyoming and extended his fellowship to end March 1989.

Dennis W. Wilson, D.V.M., Ph.D., Assistant Professor, Department of Veterinary Pathology, University of California, Davis.

Fellowship for Advanced Predoctoral Training in Pharmaceutics

The program was initiated in 1987 as a permanent program to assist candidates who have one or two years remaining in their predoctoral training, the time during which they are engaged in dissertation research.

The fellowship program provides a stipend of \$10,000 a year and \$500 a year for incidentals directly associated with the preparation



Matthew A. Wallig, D.V.M., Ph.D.

of the dissertation. The program has been funded to provide eight fellowships each year. Six fellowships were awarded in 1989 bringing the total number of awards given to 14.

Those who received fellowships beginning between January and August 1989 are:

Cynthia Ann Goates, University of Utah, Department of Pharmaceutics. Ms. Goates' advisor is Dr. Kristine Knutson, Assistant Professor, Department of Pharmaceutics. Her research will focus on the biophysical aspects of enhanced transdermal drug delivery the hydrophilic pathway.

Kathleen M. Lee, University of Michigan, College of Pharmacy, Department of Pharmaceutics. Her advisor is Dr. Gordon L. Amidon, Professor of Pharmaceutics. Ms. Lee's research involves predicting oral drug delivery.

William J. McLaughlin, Purdue University, Industrial and Physical Pharmacy. Mr. McLaughlin's advisor is Stanley L. Hem, Ph.D. Professor of Physical Pharmacy. His research will study coagulation, morphological changes and chemical transformation in mixed suspensions.

Tommy C. Morris, University of Wisconsin-Madison, Department of Pharmacy. His advisor is J. T. Carstensen, Professor. Mr. Morris will study thermal decomposition of indomethacin in the amorphous, crystalline and liquid states.

Inke Nathke, University of California, San Francisco, Department of Pharmaceutical Chemistry. Ms. Nathke's advisor is Frances M. Brodsky, D. Phil., Department of Pharmacy. Her research is entitled, "Molecular Control of Receptor Mediated Endocytosis."

Gail L. Zipp, University of Arizona, Department of Pharmaceutical Sciences. Her advisor is Nair Rodriguez-Hornedo, Ph.D., Assistant Professor. Ms. Zipp's research involves growth and nucleation kinetics of phenytoin: A model for mono-protic acids. Ms. Zipp moved her fellowship in July 1989 to Michigan University.



Distinguished guests Drs. Walter Riker and Adrien Albert are pictured at the ASPET program in Montreal. Over 100 participants attended to honor Dr. Riker and to hear Dr. Albert's featured presentation.



Research Grants

An important aspect of the PMA Foundation effort has been the support of fundamental research in drug toxicology. Between 1966 and 1971, 26 research grants of relatively large amounts for two to five years were made, principally to established investigators, either to extend existing research or to provide "seed" monies to follow a promising lead. In 1971 a change in emphasis within the Foundation shifted the bulk of the funds into educational support programs and, consequently, less into research. It is understood, however, that these educational programs place high emphasis on the research programs of the applicants for each award. In this sense, educational support programs are in fact also supporting research. The Foundation continues to accept requests for research support and suggestions for pertinent research projects since it is important that the potential within the Foundation for helping that particularly promising effort be maintained.

The Foundation will continue to review research applications that do not fall within the scope of its formal programs, but will not fund them unless they are deemed to be exceptional and novel approaches that have not generated support from conventional sources.

Ethical Considerations

The Scientific Advisory Committee as well as the program advisory committees of the PMA Foundation are sensitive to the appropriate use of experimental subjects, animals and humans, in research. In their deliberations, they consider all aspects of a proposal and may deny support for many reasons. Careful consideration is given to humane use and care of animal subjects. For human and animal research, the project review committee requires, in writing, a statement of adherence to prevailing standards of ethical research practices, including Institutional Review Board approval before initiation of any research project. In addition, for human research, assurance of informed consent will be required.

Research Starter Grants

As part of the change of emphasis in 1971 which sought to direct monies more toward the training of individuals, a program of Research Starter Grants was initiated. These grants are intended to provide financial support for beginning investigators. The program allows for approximately 20 research starter grants each year. The first awards were made in 1972. A total of 403 research starter grants have been made, including the 22 awards beginning January 1, 1989.

The recipients of the grants beginning January 1989 are:

Aaron Barchowksy, Ph.D., Thomas Jefferson University, Jefferson Medical College

John L. Bixby, Ph.D., University of Miami, School of Medicine

Mary B. Boyle, Ph.D., University of Iowa, College of Medicine

Lisa A. Cassis, Ph.D., University of Kentucky, College of Pharmacy

Ching-Shih Chen, Ph.D., University of Rhode Island, College of Pharmacy

P. Jeffrey Conn, Ph.D., Emory University, School of Medicine

Margarita Luisa Contreras, Ph.D., Michigan State University, College of Human Medicine

Peter J. R. Cobbett, Ph.D., Michigan State University, College of Human Medicine

Edward I. Cullen, Ph.D., New York Medical College Beverley Greenwood, Ph.D., Medical College of Wisconsin Warren Heideman, Ph.D., University of Wisconsin, Madison College of Pharmacy

Anthony James Hickey, Ph.D., University of Illinois at Chicago, College of Pharmacy

Stephen R. Ikeda, M.D., Ph.D., Medical College of Georgia, School of Medicine

Mark D. Johnson, Ph.D., Medical College of Pennsylvania

Eric Hon-Cheong Lai, Ph.D., University of North Carolina at Chapel Hill

Steven R. Patierno, Ph.D., George Washington University, Medical School

Geoffrey Gordon Schofield, Ph.D., Tulane University, School of Medicine

Sidney A. Scudder, M.D., University of California, Davis Jill M. Siegfried, Ph.D., University of Pennsylvania, School of Medicine

Ethan Will Taylor, Ph.D., University of Georgia, College of Pharmacy Michael Jay Twery, Ph.D., University of Texas Medical Branch

Catherine A. White, Ph.D., University of Houston, School of Pharmacy

Based on need for funds, a review of the 15 research starter grantees whose awards began January 1, 1988 for a second year of the awards resulted in 11 awards being continued. They are:

Lowell B. Anthony, M.D., Vanderbilt University

David G. Beer, Ph.D., University of Kansas Medical Center

Robert D. Grubbs, Ph.D., Wright State University

Jerome A. Langer, Ph.D., University of Medicine & Dentistry of New Jersey Robert Wood Johnson Medical School

Janet A. Lovett, Ph.D., Oregon State University

Catherine A. Leslie, M.D., University of Virginia School of Medicine Craig B. Marcus, Ph.D., Purdue University

Marilyn E. Morris, Ph.D., State University of New York at Buffalo

Omar L. Sprockel, Ph.D., University of Cincinnati

Jason G. Umans, M.D., Ph.D., University of Chicago

Jennings F. Worley III, Ph.D., West Virginia University Medical Center



At the 1988 Annual Meeting of the Foundation, out-going and incoming chairmen share an informal moment. Left in photo is Irwin Lerner, President and Chief Executive Officer of Hoffmann-La Roche Inc., who had served the Foundation as Chairman of the Board since 1982. At right is Harvey S. Sadow, Ph.D., Chairman of the Board of Boehringer Ingelheim Corporation, who assumed the Chairmanship of the Foundation Board at the conclusion of the 1988 Annual Meeting.

REPORT OF THE TREASURER



David B. Sharrock Secretary-Treasurer

he total income of the Foundation in 1988 was \$2,377,300. Of this amount, \$2,237,704 came from contributions. The balance of \$139,596 came from investments, gain on sale of equities, and refunds of unexpended balances from grants.

Contributions were received from approximately four out of every five PMA Members Firms. Contributions were also received during 1988 from other groups in the health field.

Grants, Foundation-sponsored programs, special meetings and other expenses for 1988 amounted to \$1,990,667. Of this total, \$1,445,921 represent expenditures for grants. The total fund balance as of December 31, 1988 was \$3,903,662. This figure, however, does not reflect the tentatively authorized, undisbursed funds for some of the grants and programs described earlier. The Foundation reports these amounts as expenditures when the funds are disbursed. As of December 31, 1988, the contingency liability for 1988 was approximately \$2,618,993.

The Foundation's financial position as of December 31, 1988, has been audited by the Washington D. C. certified public accounting firm of Buchanan & Company.



Statement of Income and Expenditures For the Year Ended December 31, 1988				
Income				
Contributions Income from investments Miscellaneous Income Total Income	$2,237,704 \\ 118,778 \\ \underline{20,818} \\ 2,377,300$			
Expenditures				
Grants—Note A Clinical Pharmacology Faculty Awards Clinical Pharmacology Fellowships Clinical Pharmacology Unit Support Basic Pharmacology Faculty Awards Medical Student Research Fellowships Pharmacology-Morphology Fellowships Research Starter Grants Advanced Predoctoral Fellowships Toxicologic Pathology Faculty Awards Advanced Predoctoral Fellowships in Pharmaceutics	$268,444 \\ 146,694 \\ 75,546 \\ 136,640 \\ 30,000 \\ 135,398 \\ 250,000 \\ 276,408 \\ 54,657 \\ \hline 72,134 \\ 1,445,921 \\ \hline$			
Administrative, December Awardee	544 746			
TOTAL EXPENDITURES	$\frac{-944,740}{1,990,667}$			
Excess of income over expenditures Operating fund balance at January 1, 1988	386,633 1,605,942			
Operating fund balance December 31, 1988 Future Commitment Fund(Reserve Fund)	1,992,575			
(Note B) Total fund balance at December 31, 1987	$\frac{1,911,087}{3,903,662}$			
Note A-In addition to the amounts shown, the Foundation is committed, sub-				

Note A—In addition to the amounts shown, the Foundation is committed, subject to annual review, to make certain grants. At December 3l, 1988, the amounts still to be disbursed with respect to these grants amounted to approximately \$2,618,993 with approximately \$1,463,245 of this to be disbursed during 1989; 975,449 in 1990; and, 180,299 in 1991.

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

Income from Investments Gain on Sale of Stock	128,641 21,388
Less: Trust Commission Expense	150,029 21,118
Future Commitment Fund Balance at	128,911
January 1, 1988	1,782,176
Future Commitment Fund Balance at December 31, 1988	1,911,087

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 which govern the distribution of funds are support of fundamental research on drugs and programs for training personnel in basic and clinical pharmacology, toxicology and pharmaceutics.

Throughout the year, programs have been supported and developed which provide the means of achieving the goals of the Foundation. Many worthwhile proposals have been submitted. It has been necessary to limit support to those who hold the highest promise of advancing the purposes of the Foundation.

Those areas not supported within the existing guidelines are:

(1) Research on specific drugs. 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 28.

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 13.

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

ORGANIZATION AND ADMINISTRATION

Officers and Staff 1988



¹Harvey S. Sadow, Ph.D. Chairman of the Board Boehringer Ingelheim Corporation Ridgefield, Connecticut Chairman of the Board PMA Foundation



²**Albert Bowers, Ph.D.** Chairman and Chief Executive Officer Syntex Corporation Palo Alto, California *Vice Chairman PMA Foundation*

The PMA Foundation operates through its officers, Board of Directors and six advisory committees. In April, 1988, Harvey Sadow, Chairman of the Board of Boehringer Ingleheim was elected Chairman of the Board, Albert Bowers, Ph.D., Chairman, President and Chief Executive Officer, Syntex Corporation, was re-elected Vice Chairman and Hazen L. Richardson, Vice President, Medical Products Department, E. I. du Pont de Nemours & Co., was re-elected Secretary-Treasurer. At the December 7, 1988, Board Meeting in New York City, Hazen L. Richardson resigned as Secretary-Treasurer and David B. Sharrock was elected to fill his term.

Mr. Maurice Q. Bectel served as the Foundation's President. At the end of 1987, Dr. I. C. Winter retired as PMA Foundation consultant and Dr. Edward J. Cafruny became the PMA Foundation Scientific Consultant. C. Joseph Stetler again served as staff counsel.

- ¹ Elected Board Chairman May 1988
- ² Resigned from Board May 1989
- ³ Resigned from Board December 1988



³Hazen L. Richardson Vice President Medical Products Department E. I. du Pont de Nemours & Co. Wilmington, Delaware Secretary-Treasurer PMA Foundation



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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.

Inquiries should be addressed to:

Mr. Maurice Q. Bectel President Pharmaceutical Manufacturers Association Foundation, Inc. 1100 Fifteenth Street, N. W. Washington, D. C. 20005



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