news along the pike

NOVEMBER 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

VOLUME 5, ISSUE 11

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Product Quality Research Institute Launched

Virginia-Based Non-Profit to Operate Under Purview of AAPS

The American Association of Pharmaceutical Scientists officially announced the formation of the Product Quality Research Institute during its annual meeting in New Orleans Nov. 14 to 18.

The goal of the collaborative effort among government, industry and academia is to produce scientific information to ensure that drug product quality is built-in without unnecessary testing. This information may then be used as a basis for recommendations to FDA for changes in current regulatory policies.

FDA Commissioner **Jane Henney, M.D.,** endorsed the institute in her keynote address at the AAPS annual meeting and emphasized the need to foster such collaborations to support FDA's science base.

The institute's recommendations are expected to improve the quality of drugs available to American consumers and reduce the industry's costs. The institute will bring together scientists from academia, industry and FDA. They will collaborate on research in the areas of drug chemistry, biopharmaceutics and science management.

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Fall Awards Emphasize Working Across Lines

BY JACKIE BARBER

The Center held its Fall Honor Awards Ceremony Nov. 19 at the Gaithersburg Marriott Washingtonian Center. "The Center's people continue to embrace the tremendous responsibility the American public has entrusted to us and meet this charge with distinction, ingenuity and a true spirit of cooperation," said Center Director **Janet Woodcock, M.D.** "Many of the awards we are presenting show a real commitment to work across organizational lines to do the very best job we can. Each discipline is well represented and serves as an inspiration to us all"

The Montgomery County Police Color Guard presented the colors, and **Kevin Barber** sang the National Anthem. **Ruth Clements** introduced each award, and office directors provided an explanation of individual or team achievements. The awards and those honored at the ceremony were:

FDA Commendable Service Award

Denise Rahmoeller Dorsie

Peter A. Dionne

CDER Year 2000 Working Group for Mission Critical Applications: **Melissa Chapman, Janet Gentry, Mark Gray, Gurminders**

(Continued on page 6)

OCPB's 7th Science Day Draws Record Number of Reviewers

BY EMMANUEL FADIRAN, MIKE FOSSLER AND LARRY LESKO

Scientists within the discipline of clinical pharmacology can have more influence on the drug development process, said Robert Powell, Pharm.D., vice president of pharmacokinetics, pharmacodynamics and drug metabolism at Parke-Davis/Warner-Lambert.

Dr. Powell was the keynote speaker at the seventh science day held by the Office of Clinical Pharmacology and Biopharmaceutics Oct. 29 at the University of Maryland Shady Grove annex. In a talk titled "The Ties that Bind Us," Dr. Powell gave examples of clinical pharmacology's positive impact on drug development and predicted a bright future for the discipline.

Larry Lesko, Ph.D., director OCPB, noted in opening remarks that a record number of reviewers within the office took part with nine podium presentations and 14 posters. He stressed that good science is the cornerstone of good reviews and that science days contribute to good science by giving reviewers a forum to

(Continued on page 8)

JOE'S NOTEBOOK

The Mike Mansfield Connection

One of the more newsworthy events that occurred during my service in Tokyo during the late 1970s and early '80s was the arrival of Mike Mansfield as U.S. envoy. For news junkies like myself and the rest of my co-workers on the Defense Departments' daily newspaper for U.S. forces in the Pacific, this was notable indeed. Mansfield, who began representing Montana in Congress in 1942 and the Senate in 1952, was elected majority leader of the Senate in 1961, a year before I graduated high school. He served in that position for 16 years—longer than anyone in U.S. history. He played leading roles in some of the important news events of my youth, including the 1964 Civil Rights Act and the Voting Rights Act of 1965. He was an early and principle supporter of lowering the voting age to 18. We were all surprised when, after retiring from the Senate at age 73, he agreed to serve as ambassador for President Carter in 1977 and again for President Reagan in 1981. He retired in January 1989 and now lives in D.C. with his wife, Maureen.

So I have an understandably personal interest in the Mike Mansfield fellowships that now engage two of the Center's scientists. Established by Congress, the fellowships each year enable six or seven federal employees to develop an in-depth understanding of the political, economic and strategic dimensions of the U.S.-Japan relationship. The two-year fellowships provide for a year of intensive, full-time Japanese language and area studies followed by a year of professional work in Japanese government offices.

In the September 1998 *Pike,* I introduced you to **Henry Malinowski, Ph.D.,** who is director of the Division of Pharmaceutical Evaluation I. In September 1999, he finished his language studies and began his professional work in Japan. "I periodically exchange e-mail with Hank," said CDER's latest Mansfield fellow, **Ken Kobayashi, M.D.** "He is doing well and has apparently been warmly received at the Ministry of Health and Welfare. He sounds like he is working quite hard."

Last month's *Pike* gave a brief notice of Dr. Kobayashi's selection. Kobayashi, a medical reviewer in the Division of Oncology Drug Products, has both family and professional ties to Japan. "The vast majority of my family, approximately 25 cousins and about 12 or so aunts and uncles, live in Japan, many in the Tokyo area," he said. His wife, Robynn, who accompanied him on a personal visit to Japan in 1992, will go with him next year.

Dr. Kobayashi's research interests include Phase I clinical trial designs in oncology, foreign drug approvals, clinical pharmacology of anticancer agents and population pharmacokinetics. His family has had one visiting Japanese physician as a house guest, and he has worked closely with two others on extended stays with the Agency. He maintains an active correspondence with officials in the Ministry of Health and Welfare and has hosted their visits to his division.

"Japan has several distinguished clinical investigators," he said, "and they are working very hard to develop new cancer treatments. The clinical trials and drug development system, as well as the drug regulatory system, are in the process of being harmonized in accordance with ICH guidances."

His most recent visit to Tokyo took place in February on a fellowship from Japan's Foundation for the Promotion of Cancer Research. During the visit, he spoke at the first U.S.-Japan Workshop on Clinical Trials for Further Development of Cancer Therapeutics and wrote the conference report, published in the *Japan Journal of Clinical Oncology.* He also made presentations to clinical investigators at the National Cancer Center and the National Cancer Center Hospital East.

Dr. Kobayashi is board certified in internal medicine, medical oncology and clinical pharmacology. Both he and Dr. Malinowski are maintaining their CDER e-mail accounts.

news along the pike

The Pike is published electronically on the X:drive in Cdernews and on the World Wide Web at:

http://vwww.fda.gov/cder/pike.htm

Photocopies are available in the Medical Library (Parklawn Room 11B-40) and its branches (Corporate Boulevard Room S-121 and Woodmont II Room 3001).

Have ideas, news or comments to contribute?
Please contact a member of the Editorial Board or:

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OMBUDSMAN'S CORNER

Say What You Mean

BY JIM MORRISON

Surprisingly, I get quite a number of complaints about how tactful people in CDER are. I don't mean courteous, which we should always be. The kind of tact I'm referring to is what my parents would have called "mealy mouthed" or "beating around the bush."

The complaints involve applicants being told in subtle, coded language that they have a problem with their application, compliance or other matters in dealing with the agency. Examples of phrases that convey a tentativeness—suggesting the speaker or writer is not sure of the validity of what he or she is saying—include:

- "Please review carefully your study size."
- "You may want to consider whether the Ames test alone is sufficient."
- "We cannot conclude that your product is exempt from the new drug provisions of the Act."

Let's face it, it's tough to come right out and say that if you conduct a study this way the Agency won't find the methodology wanting years down the road. So instead, we tend not to say anything that can come back to haunt us. The problem is, if we give advice in such a way that people in the future won't be able to pin down what we said, the people we are communicating with today won't understand it either.

Tact and circumspect language are absolutely essential if you are trying to tell someone you think they look older than their years. However, applicants and others whose livelihoods depend on how the Agency views their products want the straight, unvarnished truth. One can be direct without being discourteous, disrespectful or arrogant. If you know from experience that the proposed study is underpowered, tell the applicant that they need to design a larger study. Of course, you should always back up your statements with sound reasoning and data.

On the other hand, if you really feel reluctant to commit yourself to a piece of advice, you should reconsider giving it at all. No one expects you to be a universal expert. CDER is in a unique position to give advice on study design when we have seen similar studies conducted on the same class of drugs.

We also have expertise in what the law, regulations and guidances say. However, in less familiar territory, sometimes people who have a good background in designing studies, for example, know more than we do. In such cases, we can be most helpful by giving advice only in those areas we know best. If we are not sure of our statements, we should come right out and say so. No one will think less of you if you admit you are unsure. Although directness is appreciated, extraneous opinions and intemperate language are not. FDA regulation [10.70(c)(4)] directs Agency staff not to use "defamatory language, intemperate remarks, undocumented charges, or irrelevant matters (e.g., personnel complaints)" in Agency documents. The same caution should be used in meetings.

I would go further and add that even vague innuendoes of violative acts, such as references to filing false statements or doctoring data, should either be stated forthrightly in Agency regulatory actions or remain unuttered and deleted from documents. Besides causing everyone problems, such statements are just plain unprofessional. Purple prose and double entendres are best saved for moonlighting activities as a gothic romance novelist.

Jim Morrison is the Center's Ombudsman.

EEO CORNER

HHS Inducts Officers for 1st Asian Pacific American Employee Organization

BY GLORIA MARQUEZ SUNDARESAN

On Oct. 30, the HHS Asian Pacific American Network, the first Asian Pacific American employee organization in the Department of Health and Human Services, inducted three CDER employees among seven founding members at a ceremony held at the Parklawn Building.

The three CDER employees inducted among the group's officers are: **Gloria M. Sundaresan,** Chair; **Ken Kobayashi, M.D.,** Vice Chair (in absentia); and **Min Chen,** Treasurer. The other officers are **Dr. Hari Singh,** NIH, Vice Chair; **Astrid Szeto,** CBER, and **Kana Enomoto,** SAMHSA, secretaries; and **Yukiko Tani,** HRSA, auditor.

The employee organization will address issues that affect the Asian Pacific American employees in the Department and the community.

Speakers at the induction ceremony included Rep. Robert Underwood (D-Guam), Chairman of the Congressional Asian Pacific American Caucus; Irene Bueno, Special Assistant to the President on Domestic Affairs; Evelyn White, DHHS Deputy Assistant Secretary for Human Resources; Charmaine Manasala, Senior Policy Analyst, White House Asian American/Pacific Islander Initiative.

American Indian, Alaska Native Heritage Month

The Indian Health Service invited the Center to be a partner in the observance of the National American Indian and Alaska Native Heritage Month. CDER is one of the 35 members of the federal, state and local organizations invited to participate in organizing different activities for November's celebration.

CDER's contributions included:

- Preparing informative fact sheets on some of the IHS partners.
- Displaying "American Indian: Women of Hope" on a self-standing unit at the Parklawn Building's main entrance on the B-wing.
- Displaying "Code Talkers" at Woodmont II from Nov. 22 to 28.

The opening ceremonies at the Rockville Center on Hungerford Drive and the Humphrey Building in downtown Washington on Nov. 3 and 4 were both highly successful.

Gloria Marquez Sundaresan is an equal employment specialist on the EEO Staff.

REVIEWER AFFAIRS CORNER

RAC Intranet Site On Line; Impact of Union on Committee Debated

C. RUSS RUTLEDGE

The Reviewer Affairs Committee's intranet site (http://cdernet/rac/index.htm) is now up and running, thanks to RAC Vice Chairperson **Rob Shore, Jamie Metz, Jacqueline White** and the Training and Communication Subcommittee. You can access the site through the CDERnet homepage by clicking on Committees and Task Forces and then clicking on the "Reviewer Affairs Committee button.

This site provides links to RAC documents such as the bylaws, meeting minutes, RAC representative duties and the Reviewer's Handbook.

RAC, Union Future Considered

This is an interesting time in the history of the Reviewer Affairs Committee. Since the FDA workforce has voted to be represented by the National Treasury Employees Union, the question arose as to whether the RAC may continue in its function of voicing the concerns of reviewers to CDER management. This issue was addressed during the last month's quarterly meeting with the Senior Management Team. Various scenarios were discussed, some of which included:

- Reestablishing the RAC as a bargaining unit subcommittee.
- Disbanding the RAC.
- Having the RAC and its subcommittees remain as they are now but become a "sister" to the NTEU and provide assistance.

In any event, there is a 120-day period to decide the issues. The RAC will continue as is through the end of the 120-day period that started with the implementation of the union contract on Oct. 1.

RAC accomplishes most of its work through its various subcommittees with members who are experienced in the current issues. See the RAC intranet site for a list of these and their chairpersons. The RAC subcommittees will continue working on projects already underway, but won't start any new projects until the above issues with the union are resolved.

Important subcommittee projects under way include:

- *Team Model.* A pilot workshop with **Jean Yager** and **Sousan Altaie** will be held in December to look at best team practices in the Center.
- *Guidance Process Improvement/Regulatory Changes Impact.* The subcommittee is working on conducting a survey on reviewer awareness of regulatory and guidance changes, if they have received training and how they are dealing with these changes.
- *CDER Reviewer Career Path Program.* The subcommittee is evaluating the Master Reviewer Pilot Program with **Nancy Smith, Ph.D.**
- *Training and Communication.* Improvements in the RAC intranet site to make it even more user friendly are on tap.
- *Comparable Pay.* The subcommittee is working on obtaining classification of the clinical pharmacologist/pharmacokineticist career series as one that allows for pay comparable with industry when the budget permits. RAC members of other disciplines are also working toward this same goal for their colleagues through the help of this subcommittee.

During the quarterly meeting, Center Director **Janet Woodcock, M.D.,** voiced her appreciation for the work the RAC has accomplished over the past several years and would like to see the RAC continue. NTEU's representative at this meeting, Chief Steward **Marilyn Wolf,** indicated NTEU supports the RAC and will recommend its continuation to NTEU headquarters.

However, the reviewers will need to vote on this. RAC Chair **Lydia Kieffer, Ph.D.,** proposed a task force to survey reviewers regarding RAC continuation. Dr. Woodcock stated that this should be a transparent process, in which the issues should be out in the open so that reviewers, NTEU and management are aware of the various options and their implications. Assuming that RAC members vote to continue the RAC, details will need to be worked out so that RAC's continuation is in full compliance with the FDA-NTEU agreement.

For instance, a question arose if there may be a change in core membership eligibility. Currently RAC membership eligibility is for non-management CDER staffers. With NTEU, eligibility might be redefined as dues-paying members.

At first this seems like a reasonable requirement, but it would exclude non-management PHS Commissioned Corps members, such as chair Lydia Kieffer. These types of issues present difficult decisions and will take time to resolve.

Both SMT and NTEU's representative are in agreement on the value of continuing the RAC. Once CDER reviewers are surveyed, the RAC will meet with the SMT and NTEU to discuss how best to proceed.

C. Russ Rutledge is a compliance officer in the CDER Office of Compliance's Division of Manufacturing and Product Quality.

Office of Generic Drugs Holds Workshop for Trade Associations

BY RITA HASSELL

On Oct. 18 and 19, the Office of Generic Drugs held a joint workshop with the three generic drug trade associations, the Generic Pharmaceutical Industry Association, the National Association of Pharmaceutical Manufacturers and the National Pharmaceutical Alliance. The goals for this workshop were to:

- Share with industry the status of key policies and issues under discussion.
- Help assure the review process is as "transparent" as possible to the industry.
- Provide a forum for FDA and industry to interact on a mutually beneficial basis.

Almost 200 representatives from generic manufacturing firms and industry consultants attended the third annual technical workshop, titled "The Generic Industry: Regulatory and Scientific Challenges." The FDA presentations provided information on the project manager role in OGD, updates and information on the use of electronic technology in the review process

(Continued on page 5)

Secure Electronic Mail System Now Available to 6 Drug Firms

The Center's secure electronic mail system is now available to send encrypted mail to participating pharmaceutical companies.

All e-mail into and out of the Center is routed through one of two mail servers. If encryption or decryption is needed, the server performs that task. CDER users don't need to do anything extra. Mail messages can include attachments. There is no known limitation on the kind of attachment that can be included in the message.

OIT's intranet has been updated to include the name and secure e-mail address of each participating pharmaceutical company so that you will know what messages will be encrypted. When you receive a message from a participating company, there will be an annotation in the message, verifying that it was received encrypted and that it was decrypted by the server.

There are six companies participating in the secure electronic mail program. The secure e-mail addresses for them can be found on the OIT intranet site (http://oitweb/) from the buttons for OIT Activities or Documentation or from the Notes section. The only requirements for a company to take part are a compatible mail system and a successful exchange of encryption and signature keys with CDER. Discussions and testing with several other companies are almost complete. These companies will be added to the intranet site as soon as testing is complete.

OIT points of contact are **Greg Brolund** (BROLUND) or **Wendy Bussey** (BUSSEYW).

QA Development

In October, OIT continued work on guidance documents in the improvement target area of project planning. It was determined that project plan samples should be developed incorporating elements from actual OIT projects. Meetings have been scheduled to gather sample data from each OIT division. Information about this project is located on the CDER intranet (http://oitweb/oit/) under the OIT Activities button.

The OIT point of contact is **Jerry Yokoyama** (YOKOYAMAJ).

PM Coordination

All 21 original OIT projects have undergone review by OIT senior managers. The review enables OIT senior managers to ask questions and provide input so that each manager agrees with the project intent, technical and management approach, and resource commitments.

The end result of the review is a documented and approved project baseline that serves as the basis for monthly status meetings with the PM Coordinator. Projects are prioritized in order to facilitate management decisions.

Two of the 21 projects have been approved. Six have been revised for approval, and the remaining projects are in varying stages of revision. Eleven new projects have been identified and are being scheduled for review.

Approved project descriptions are screened for confidential/proprietary information and posted on the CDER intranet (http://oitweb/oit/) under PM Coordination.

An individual is needed to serve as the permanent PM Coordinator for OIT. If you are interested in finding out more about this position, please contact **Vali Tschirgi** (TSCHIRGIV) or **Ralph Lillie** (LILLIE).

OIT point of contact is Vali Tschirgi.

December IT Training

Monday	Tuesday	Wednesday	Thursday	Friday
		1 **Intro Word** 9-12 **Word Formatting** 1-4	**2**	**3**
6 **DFS** 9-12 **NEDAT** 1-4	**7** **Intro Access** 9-12 **Access Queries** 1-4	**8** **Access Forms** 9-12 **Access Reports** 1-4	**9**	**10**
13 **Standard Letters System** 9-12 **Creating PDF Documents** 1-4	**14**	**15** **NEST** 9-12 **Project for CDER PMs** 1-4	**16**	**17**
20	**21**	**22**	**23**	**24**
27	**28**	**29**	**30**	**31**

The catalog, training materials, schedule and online registration can be found at http://oitweb/.

Demonstration of Electronic Submissions Proves Big Hit at Workshop

(Continued from page 4)

and updates on various guidances coming from OGD and OPS coordinating committees.

The trade associations had volunteers from their membership who provided the industry viewpoint on some of the topics.

Concurrent with the workshop sessions, OGD's information technology specialists had a booth where they demonstrated the mechanism for submitting generic drug applications electronically. They were able to answer many questions, and the display was a big hit at the workshop.

In the plenary sessions, there were lively discussions and those who attended found that the information provided was beneficial.

Several OPS and OGD staff members made presentations, including **Richard Adams, Mark Anderson, Pat Beers Block, Joseph Buccine, Gary Buehler, Dale Conner, Pharm.D., Barbara Davit, Ph.D, Dave Gill, Ph.D., John Grace, Frank Holcombe, Yana Mille, Cecelia Parise, Peter Rickman, Susan Rosencrance, Nancy Sager, Lizzie Sanchez, Eric Sheinin, Ph.D., Richard Sponaugle, Douglas Sporn, Robert Trimmer, Ruth Warzala, Ph.D., Robert West** and **Roger Williams, M.D.**

Rita Hassell is special assistant to the OGD Director.

Working Across Organizational Lines Emphasized in Awards

(Continued from page 1)

Khalsa, Victoria Levi, Paul Loebach, Heather Pierce, Sally Newman and **Carolyn Yancey.** *PHS Unit Commendation:* **CDR John Quinn.**

DQRS Team: **Roger Gregorio** and **Ralph J. Schmid.**

Pediatric Pharmacokinetic Guidance Working Group: **Leanne Cusumano, J.D., Michael J. Fossler, Pharm.D., Ph.D., Mohammad Hossain, Ph.D., Janeth R. Rouzer Kammeyer, M.D., John A. Lazor, Pharm.D., Samuel D. Maldonado, M.D., Saul N. Malozowski, M.D., Ph.D., Rosemary Roberts, M.D.,** and **Barbara J. Townsend.** *PHS Unit Commendation:* **LT Kimberly Struble.**

Safety Evaluators of the Division of Drug Risk Evaluation I and II: **Janos Bacsanyi, M.D., Katherine Bennett, Pharm.D., Renan A. Bonnel, Pharm.D., Debra Boxwell, Pharm.D., Min Chen, Ann Corken, Evelyn Farinas, Charlene M. Flowers, Lanh Green, Toni Piazza-Hepp, Pharm.D., Claudia B. Karwoski, Pharm.D., Susan Lu, Mary Mease, Kathleen M. Phelan, Sarah J. Singer** and **Ronald Wassel, Pharm.D.** *PHS Unit Commendation:* **CAPT Michael F. Johnston.**

FDA Outstanding Achievement Award

Shukal Bala, Ph.D.

Rachel Behrman, M.D.

Leanne Cusumano, J.D.

Michael J. Fossler, Pharm.D., Ph.D.

Hebert Gerstenzang

Ronald Honchel, Ph.D.

Gabriel Robbie, Ph.D.

Barry A. Rosenweig

Sandra Van Buskirk

Zakaria Z. Wahba, Ph.D.

FDA Group Recognition Award

Competency Program Group: **Tanya L. Abbott, Funmilayo O. Ajayi, Ph.D., Aisar H. Atrakchi, Ph.D., Dorothy C. Ballmann, Paula G. Bourkland, Heidi N. Burch, Sonia C. Castillo, Ph.D., Aloka G. Chakravarty, Ph.D., Tien-Mien Chen, Ph.D., Ling Chin, M.D., Sandra L. Coffin, Philip M. Colangelo, Pharm.D., Ph.D., Eldridge F. Coles, Thomas A. Cunningham, Velma L. Cunningham, Joseph J. DeGeorge, Ph.D., Kuldeep R. Dhariwal, Ph.D., Angelica Dorantes, Ph.D., Patricia L. Downs, Amy L. Ellis, Ph.D., John L. Emelio, Jr., Emmanuel O. Fadiran, Ph.D., James G. Farrelly, Ph.D., Glenna G. Fitzgerald, Ph.D., Noreen A. Gomez, Alice L. Gray, Kenneth L. Hastings, Dr. P.H., Carol H. Hall, Anita G. Harrell, Devota D. Herbert, Karen M. Higgins, Sc.D., Robin A. Huff, Ph.D., Patricia F. Hughes, Ph.D., Patricia A. Johnson, Barbara M. Jones, Joyce Ann Korvick, M.D., E. Douglas Kramer, M.D., Kofi A. Kumi, Ph.D., See-Yan Lam, Pharm.D., Ph.D., Sheryl L. Lard-Whiteford, Ph.D., Sue-Chih Lee, Ph.D., Sally J. Lewis, Kooros Mahjoob, Ph.D., Iftekhar Mahmood, Ph.D., Maureen D Majors, Frederic J. Marsik, Ph.D., Patrick J. Marroum, Ph.D., Jamie M. Metz, Veronica E. Milstead, Rebecca E. Nalley, Shriniwas G. Nerurkar, Ph.D., Janice L. Newcomb, Peggy A. Noland, Carol T. Norwood, Susan H. O'Malley, William W. Oswald, Larry A. Ouderkirk, Dawn M. Reid, Charles A. Resnick, Ph.D., Delores A. Rhodes, Laura E. Riddle, Kathy A. Rios, Lawrence F. Sancilio, Ph.D., Wendelyn J. Schmidt, Ph.D., John R. Senior, M.D., Daniel A. Shames, M.D., Janice M. Sheehy, Barbara E. Shekitka, Albert T. Sheldon, Ph.D., Robert M. Shore, Pharm.D., Ronald W. Steigerwalt, Ph.D., He Sun, Ph.D., Vijaya K. Tammara, Ph.D., Sandra Van Buskirk, Victor H. Vail, Richard T. Vengazo, Vera K. Viehmann, Zakaria Wahba, Ph.D., Michelle L. Walling, Juandy S. Walston, Dan Wang, Ph.D., Andrea B. Weir, Ph.D., Karen R. Weller, Laura M. West, Leslie DeLaPena Wheelock , Grant A. Williams, M.D., Rosa L. Williams, Tonya R. Wise** and **Matthew A. Zell.** *PHS Unit Commendation:* **CDR Nanette S. McAtee, CAPT Frank D. Sistare** and **CAPT Ching-Long J. Sun.**

Trovan Postmarketing Safety Evaluation Team: **Regina Alivisatos, Norman Drezin, Mark J. Goldberger, M.D., David J. Graham, Brad G. Leissa, Lorene M. Kimzey, Dianne Murphy, M.D., Murray Lumpkin, M.D., Leah M. Palmer, Toni D. Piazza-Hepp, Pharm.D., Sarah J. Singer, Ellen Shapiro** and **Crystal L. Wyand.** *PHS Unit Commendation:* **CDR Sandra L. Kweder, CDR Evelyn M. Rodriguez** and **CDR Jo Ann Spearmon.**

OPS Vioxx Review Team: **Sue-Chih Lee, Ph.D., Veneeta Tandon, Ph.D.,** and **Dan Wang, Ph.D.** *PHS Unit Commendation:* **CDR Edward Bashaw.**

PHS Commendation Medal

CDR Robin E. Anderson

CDR Terrie L. Crescenzi

CDR John J. Feeney, III

CAPT Thomas H. Hassall

LCDR Lydia V. Kieffer

CDR Nanette S. McAtee

CDR Evelyn M. Rodriquez

CDER Special Recognition Award

Sousan S. Altaie, Ph.D.

Charlotte Brunner

Philip Colangelo, Pharm.D., Ph.D.

Lawrence Goldkind, M.D.

John R. Senior, M.D.

Veneeta Tandon, Ph.D.

Randall L. Woods

Materiality Committee Group: **Richard C. Adams, Brenda T. Arnwine, James M. Fan, Frank O. Holcombe, Jr., Ph.D., Andrew J. Langowski, Albert J. Mueller, William P. Rickman** and **Stephen Sherken.**

PAHO Initiatives Support Team: **CAPT Justina Molzon, Edwin Ramos** and **Alfredo Sancho, Ph.D.**

Pulmonary Drug Delivery Systems Chemistry Review Team: **Craig Bertha, Ph.D.,** and **Dale Koble, Ph.D.**

Zanamivir Review Team: **Girish Aras, Ph.D., Narayana Battula, Ph.D., Debra Birnkrant, M.D., Daniel Boring, Ph.D., Michael Elashoff, Ph.D., James G. Farrelly, Ph.D., Paul Flyer, Ph.D., Brad**

(Continued on page 7)

51 Individuals, 30 Teams Receive Awards at Fall Ceremony

(Continued from page 6)

Gillespie, Ph.D., John Jenkins, M.D., Heidi Jolson, M.D., Dale Koble, Ph.D., Stanka Kukich, M.D., Kuei-Meng Wu, Ph.D., Robert J. Meyer, M.D., Stephen Miller, Ph.D., Kellie S. Reynolds, Pharm.D., and **Barbara Styrt, M.D.** *PHS Unit Commendation:* **CDR Sylvia Lynche.**

CDER Administrative/Program Management Excellence Award

Cathie Chaplin

Laura M. West

CDER Excellence in Communication Award

Edwin Melendez

Barry Rothman

CDER Information Technology Excellence Award

Janet Gentry

Ruth Warzala

CDER Year 2000 Working Group for Technical Infrastructure: **Janice Ausby, Naresh Bhanot, John Brinsko, Gregory Brolund, Margaret Cates, Anthony Chuo, Patrick David, Fred Goetze, Richard Johnson, Paul McCarthy, Nancy Shermer, Scott Shippey** and **Jerry Yokoyama.**

Office of Information Technology Support Services Staff: **Kathleen A. Bright, Heather A. Chafin, Ken Edmunds, Lana Kostecka, Mark A. Magee, Timothy M. Mahoney, David M. Moss, Raye P. Parker** and **Paul M. Seckler.**

OPS Laboratory Research Y2K Team: **Prince Bosley, Celeste F. Bové, Alan S. Carlin, Jonathan D. Cook, Christopher D. Ellison, David Holovac, Everett H. Jefferson, Apspandiar G. Katki, Agnes NguyenPho, Robert J. Parker** and **P. Scott Pine.**

CDER Leadership Excellence Award

Patricia M. Beers-Block

Bronwyn Collier

Peter H. Cooney, Ph.D.

Judith M. McIntyre

Victor Raczkowski, M.D.

John M. Strong, Ph.D.

Helen N. Winkle

CDER Excellence in Mentoring Award

Ajaz Hussain, Ph.D.

Kati Johnson

Richard Kolinski

Division of Reproductive and Urologic Mentoring Working Group: **Susan S. Allen, M.D., Kim Colangelo, Karen Davis-Bruno, Ph.D., Jeri El Hage, Ph.D., Mark Hirsch, M.D., Venkat Jarugula, Ph.D., David Lin, Ph.D., Kate Meaker, Ph.D., Diane Moore** and **Terri Rumble.**

CDER Project Management Excellence Award

CAPT Mark D. Anderson

Kim Colangelo

Patricia Long-Bradley

Maria R. Walsh

Co-Project Managers of the OIT Process Improvement Project Team: **Shelia K. Andrew** and **Jerry Yokoyama.**

CDER Support Staff Excellence Award

Shawnte L. Adams

Renee V. Redd

Rose M. Smith

Patricia Tuegel

Nadine Warren

DTAAD Administrative Staff: **Tedera Miliken** and **Loretta Saey.**

CDER Team Excellence Award

Amprenavir Review Team: **Therese Cvetkovich, John Martin, M.D., Narayana Battula, Ph.D., Lalji Mishra, Ph.D., James G. Farrelly, Ph.D., Paul Flyer, Ph.D., Owen G. McMaster, Stephen Miller, Ph.D., George Lunn, Ph.D., Guoxing Soon, Kellie S. Reynolds, Pharm.D., Prabhu Rajagopalan, Ph.D., Sherrie Shade** and **Melissa Truffa.**

CDER Executive Secretariat Team: **Celia Delawter, Diana Hernandez, Vikki Kinsey, Coralee Lemley, Terry Martin** and **Liz Ortuzar.**

Denavir Rx-to-OTC Switch Review Team: **Nilambar Biswal, Ph.D., Marina Chang, Paul Flyer, Ph.D., Zi Qiang-Gu, Ph.D., Linda Hu, M.D., Linda Katz, M.D., Christine Kelley, Karen J. Lechter, J.D., Ph.D., Laura Lu, Ph.D., Babette Merritt, Stephen Miller, Ph.D., Jeffrey Murray, M.D., Joanne Rhoads, M.D.,** and **Joseph Toerner, M.D.** *PHS Unit Commendation:* **CAPT Teresa Wu.**

DPE III Team: **Funmilayo Ajayi, Ph.D., Philip Colangelo, Pharm.D., Ph.D., Kofi Kumi, Ph.D.,** and **Joette Meyer, Pharm.D.** *PHS Unit Commendation:* **CDR Houda Mahayni.**

DTAAD Conjugated Estrogens Team: **James Brower, William Doub, Ph.D., John Reepmeyer, Ph.D., Larry Revelle, Ph.D.,** and **Benjamin Westenberger.**

DTAAD New Drug Application Methods Validation Team: **Harry Coffman, Donald Cox, Mary Ann Kreienbaum** and **Duckhee Toler.**

Major/Minor Guidance Team: **Patricia M. Beers-Block, CAPT Rita R. Hassall, Frank O. Holcombe, Jr., Ph.D., Allen Rudman, Ph.D., LCDR Aida L. Sanchez, Edward M. Sherwood , Michael J. Smela, Jr.,** and **CAPT Robert L. West.**

OCPB Science Day Committee: **Emmanuel Fadiran, Ph.D., Michael Fossler, Ph.D., CDR Lydia Kieffer, Lillian Riley**, **Vanitha Sekar, Ph.D.,** and **Helen White.**

Office of Compliance Postmarket Surveillance Team: **Roger Gregorio, Nancy Haggard, Andrea Schaub, Ralph J. Schmid, Donna Stewart** and **Puri Subramaniam.**

Office of Pharmaceutical Science Microbiology Team: **Peter H. Cooney, Ph.D., Lynne Ensor, Ph.D., Vivian Greenman, Andrea S. High, Ph.D., Patricia Hughes, Ph.D., CAPT David Hussong, Bryan S. Riley, Ph.D., Paul Stinvage, Ph.D., Neal J. Sweeney, Ph.D., Brenda Uratani, Ph.D.,** and **Carol K. Vincent.**

Ophthalmic Chemistry, Manufacturing and Controls Review Team: **Allan Fenselau, Ph.D., Sue C. Tso, Ph.D.,** and **Rajendra Uppoor, Ph.D.**

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OCPB's 7th Science Day Draws Record Number of Reviewers

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present to and receive feedback from their peers. Retention of good scientists is also a key to good reviews, and science days contribute to retention as well.

Usually, science days are held twice a year, in October before the American Association of Pharmaceutical Scientists annual meeting, and in March before the American Society of Clinical Pharmacology and Therapeutics annual meeting. Reviewers scheduled to present at these meetings have an opportunity to present at science days and receive peer review prior to their public presentations. Science days are also a forum for reviewers to present interim reports on their professional development projects. Also invited to attend the meeting are reviewers from the Office of Generic Drugs and post-doctoral fellows from the Center for Drug Development Science at Georgetown University.

Brian Booth, Ph.D., presented a report from an OCPB quality assurance and quality control working group titled "What have we learned from the recent market withdrawal of terfenadine, mibefradil and astemizole?" The conclusions of the study were that industry and regulatory authorities must work together to assign a relative level of risk to drug-drug interactions in the product label, use prominent warnings in the initial product label for serious drug-drug interactions and develop effective ways to communicate key information in product labels to prescribers and patients.

Soroya Madani, Ph.D., in her talk, "Terfenadine metabolite formation kinetics in human liver and intestinal microsomes," demonstrated the importance of determining accurate kinetic parameters in ***in vitro*** drug metabolism studies in order to make accurate predictions of what will occur clinically. Dr. Madani won first prize at Science Day for her presentation.

Gabriel Robbie, Ph.D., presented results of simulations of bioequivalence studies to identify factors which affect parent and metabolite concentrations under various scenarios: pre-systemic metabolism, post absorption metabolism and rate limitations on dissolution, absorption and elimination at different levels of interindividual variability. Through simulation, Dr. Robbie showed that there are cases that would require measurement of parent and/or active metabolite to avoid false positive or false negative bioequivalence results. Dr Robbie won second prize for his presentation.

Rae Yuan, Ph.D., presented a paper titled "Effect of chronic renal failure on the disposition of a highly hepatically metabolized drug." She concluded that chronic renal disease should not be considered as an isolated event that affects only renally excreted drugs. Uremia may also modify the disposition of a highly metabolized drug by changes in plasma protein binding and/or hepatic metabolism.

"Population PK/PD of rivastigmine, a cholinesterase inhibitor, in patients with Alzheimer's disease: a dose–plasma/csf concentration–acetylcholine-esterase (ache) activity–computerized neuropsychological test battery score relationship" was the title of the presentation by **Joga Gobburu, Ph.D.** The population PK/PD model adequately characterized the dose-plasma-biophase-biomarker-clinical endpoint relationship for rivastigmine.

One of OCPB's newest colleagues, **Sandra Suarez, Ph.D.,** presented a paper titled "The effect of dose and rate release on pulmonary targeting of glucocorticoids using liposomes as a model dosage form." The results of her studies showed that pulmonary targeting can be optimized by modulating drug release rate and dose. Dr. Suarez won third prize for her podium presentation.

Jenny Zheng, Ph.D., presented a paper on "Can we choose an optimum dose for clinical trials using preclinical and Phase I data?" She concluded that data obtained from early drug development could provide very useful information on dose selection in Phase II and III studies.

Dan Wang, Ph.D., presented a paper titled "Enhance population pharmacokinetic knowledge for a sparsely sampled population by borrowing strength of information from different populations." The results of her study showed that by appropriately pooling information from a different population, PPK parameter estimates of the sparsely sampled population can be greatly enhanced.

A presentation by **He Sun, Ph.D.,** on "The reliability of population pharmacokinetic approach in pediatric exclusivity claims" showed that PPK offers the opportunity to easily predict individual clearance, explain covariance effects more easily and that covariance misspecification can be reduced by using partial resampling and bootstrapping model stability checks.

Poster presentations included:

- "Cardiovascular pharmacodynamics of calcitonin gene-related peptide (cgrp) in rats," **Brian P. Booth, Ph.D.,** and **Ho-Leung Fung, Ph.D.**
- "Tamoxifen bioequivalence study: an example of BE studies for drugs with long half-life and active metabolite," **Zongyi J. Duan, Ph.D.**
- **"**Pharmacokinetic/pharmacodynamic modeling of ritepace: example of PK/PD modeling as an aid for efficient and successful drug development," **Gabriel Robbie, Ph.D., Jogarao Gobburu, Ph.D.,** and **Patrick Marroum, Ph.D.**
- **"**Population pharmacokinetics and pharmacodynamics of Drug X, an irreversible aromatase inhibitor," **Jogarao Gobburu, Ph.D., Zongyi J. Duan, Ph.D.,** and **Emmanuel Fadiran, Ph.D.**
- "Is metabolism-based drug interaction a serious concern for safe use of Drug

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Fall Ceremony Honors 51 Individuals, 30 Teams

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Research Subcommittee of the Pharmacology/Toxicology Coordinating Committee: **Paul A. Andrews, Ph.D., Adorjan Aszalos, Ph.D., Celeste F. Bové, Joseph F. Contrera, Ph.D., Joseph J. DeGeorge, Ph.D., Joseph P. Hanig, Ph.D., Eugene H. Herman, Ph.D., John K. Leighton, Ph.D., Asoke Mukherjee, Ph.D., Robert E. Osterberg, Ph.D., Nakissa Sadrieh, Ph.D., CAPT Frank D. Sistare** and **Karol L. Thompson, Ph.D.**

Scientific Investigations Team: **Jacqueline O'Shaughnessy, Ph.D., C.T. Viswanathan, Ph.D.,** and **Martin K. Yau, Ph.D.**

Jackie Barber is CDER's incentive awards officer.

Science Education Team to Develop Self-Learning Modules

BY JACK MORIN

The Science Education Team in OTCOM's Division of Training and Development works with the Center's biomedical and scientific staff and the Committee for Advanced Scientific Education to identify, plan and deliver CDER's Science Education Program.

This program includes all educational activities such as courses, seminars, workshops and conferences that address CDER's need for basic and advanced science education.

Because CDER's scientists and reviewers are unable to attend as many CDER Seminars as they would like, the Science Education Team is developing self-learning modules based on the seminars.

The first self-learning modules are expected to be ready by late spring and will be based on the series of clinical pharmacology seminars. This first self-learning module's contents will include antibiotic resistance, drug interactions and molecular genetics.

The modules will be delivered through various media, such as CD ROMs and videotape with accompanying self-study guides. Continuing educational credit for the modules will be based on whether credit was provided for the original seminar.

In addition, the division has established the Academics to CDER Program and is developing relationships with academic institutions that will address present and future educational needs. These relationships will increase the depth and breadth of CDER's scientific education. Topics for the program will be evaluated and selected based on:

- Relevance to CDER's mission.
- Reviewers' core competencies.
- Reviewers' discipline specific core competencies
- Advancement of CDER's science base.

Members of the team are **Sonya Armstrong, See Yan Lam, Nanette McAtee, Sakti Mukherjee, Chris Nguyen and Dale Wilcox.** Please contact acting team leader Dale Wilcox (WILCOX, 7-3498) if you have questions or would like to discuss science education programs.

Jack Morrin is a writer/editor in DTD.

Center's CFC Intranet Site Provides Links to Contests, Catalog of Caring

BY TIM MAHONEY

You can find information about the Center's Combined Federal Campaign quickly and easily on the CDERnet at http://cdernet/cfc. The site provides information on upcoming CDER CFC events, contests, keyworker contacts, pledging instructions, links to other CFC sites and Center campaign goal updates.

CDER's CFC site also provides fun and a chance to win weekly prizes. All you need is your *Catalog of Caring* (a link to the online version is available) and a little detective work to be eligible to win one of the weekly prizes donated by local merchants. Just go to the Events/Contest page to enter or review the question.

In addition, remember to enter the various CFC raffles held throughout the rest of the campaign. Each ticket is only $1 and enters you in the weekly drawing for multiple prizes like lunch or dinner at your favorite local restaurant, free wheel alignments and antiques. Tickets can be purchased between 11 a.m. and 1 p.m. daily at the CFC tables in the Parklawn cafeteria. Tickets are also sold on Monday, Wednesday and Friday from 11 a.m. and 1 p.m. at the 5th floor B-wing entrance. If you are in another building, look for a list on contacts on the CDER CFC site.

Tim Mahoney is CFC coordinator for the Office of the Center Director.

Clinical Pharmacologists, Biopharmaceuticists Rehearse Presentations

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A?" **Rae Yuan, Ph.D.,** and **Joga Gobburu. Ph.D.**

- **"**P-glycoprotein is not involved in changes in dofetilide human pharmacokinetics caused by verapamil," **Emmanuel Fadiran, Ph.D., S. Ibrahim, Ph.D., A. Parekh, Ph.D., A. Knapton, T. Licht** and **A. Aszalos, Ph.D.**
- "Feasibility of predicting drug dissolution from multisource tablet formulations," **Vijay K. Tammara, Ph.D., Alan Carlin, Mehul Mehta, Ph.D.,** and **Ajaz S. Hussain, Ph.D.**
- "Early exposure in bioequivalence: evaluation of statistical criteria using clinical trial simulation," **Michael J. Fossler, Pharm.D., Ph.D.,** and **Mei-Ling Chen, Ph.D.**
- "Applying neural network analysis for the evaluation of drug-drug interaction studies," **Steven B. Johnson, Pharm.D.** and **Sam H. Haidar, Ph.D.**
- "Individual precision threshold in the design of population trials," **Dan Wang, Ph.D., Guangrui R. Zhu Ph.D., and Thomas M. Ludden, Ph.D.**
- "Treatment of pulmonary tuberculosis in a low-dose inoculum aerosol infection guinea pig model: efficacy of single and multiple doses of aerosolized rifampicin-loaded poly(lactide-co-glycolide) microspheres," **Sandra Suarez, Ph.D., Patrick O'Hara, Ph.D., Christian E. Newcomer, Ph.D., Roy Hopfer, Ph.D., David N. McMurray, Ph.D., and Anthony J. Hickey, Ph.D.**
- "The Office of Pharmaceutical Science: *in vitro* research and method development program," **Carol Noory, Vinod P.Shah, Ph.D., Larry A. Ouderkirk, Ph.D.,** and **Nhan Tran, Ph.D.**

The poster prize award winners were: Dr. Robbie, first prize; Dr. Fadiran, second prize; and Dr. Gobburu; third prize

Finally, **Roger Williams, M.D.,** Deputy Center Director (Pharmaceutical Science) shared his thoughts on where OCPB has been, where it is going and areas that need further work.

Abstracts of the podium and poster presentations can be found by selecting the Presentations button on OCPB's CDERnet site at http://cdernet/ocpb/index.html.

The next science day in March will feature regulatory scientists invited from Canada, Europe, Japan and Mexico.

Product Quality Research Institute Creates Collaborative Structure

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The institute's goal is to identify better test methods for assessing the quality of drugs and improved manufacturing and management processes. The institute will make non-binding recommendations about its findings to the FDA.

PQRI won't test specific drugs, said Larry Augsburger, Ph.D., AAPS President. "We are testing processes and procedures that will be used to help verify pharmaceutical properties and their effectiveness."

PQRI is a nonprofit, non-stock and tax-exempt Virginia-based corporation. Under the purview of AAPS, PQRI will consist of a board of directors, a steering committee and technical committees. The structure is modeled after that used by the International Conference on Harmonization.

"PQRI represents a unique collaboration between FDA, industry and academia to determine the optimum type of information to be included in a regulatory submission to document product quality attributes," said **Roger Williams, M.D.,** Deputy Center Director (Pharmaceutical Science). "It provides a 'win-win-win' opportunity for the industry, CDER and, most importantly, the public."

In addition to the Center and AAPS, the founding organizational members of PQRI include six trade associations: Consumer Healthcare Products Association, Generic Pharmaceutical Industry Association, National Association of Pharmaceutical Manufacturers, National Pharmaceutical Alliance, Parental Drug Association, Pharmaceutical Research and Manufacturers of American.

No member or representative will be compensated in any way for participating in PQRI. In an effort to reach the scientific community worldwide with its findings, PQRI has established a Website at http://www.pqri.org where all recommendations will be published.

PQRI's five-member board of directors is charged with the administrative management and operations of the institute. The board has authority over the collection and disbursement of funds and the administrative procedures that will guarantee effective operations. Three of the board members are appointed by the AAPS executive council and two are recommended by the Institute's steering committee.

Each of the eight founding member organizations will appoint a formal representative to the steering committee. The committee will develop specific missions for the institute, set priorities for research projects, mange the review of research results and recommend how institute funds will be spent on scientific activities and research.

Technical committees, formed by the steering committee, will develop research programs and projects. The technical committees will oversee the direction for research projects, form appropriate working groups and monitor projects and supporting research data. The technical committees will also outline the potential impact of the research projects on the public health and product quality and describe the potential impact of research outcomes on the pharmaceutical industry.

Currently, there are four operating technical committees for drug substance, drug product, biopharmaceutics and science management.

Under the direction of the technical committees, working groups will further develop and execute specific research proposals. Their goal will be to develop scientific knowledge that will result in appropriate changes to regulatory policies that will, in most cases, be less burdensome. Working group members will be subject matter experts who will meet at least quarterly, participate in monthly electronic communications and, in some cases, conduct research in their own institutions.

Once a working group finishes a project, the technical committee will present the results to the steering committee. If a steering committee vote is required, the Center's representative will abstain. Following approval, the steering committee will send its non-binding policy recommendations and related research data to FDA.

Working groups in the following areas are planned:

- Specifications and BACPAC.
- Methods for determining physical attributes starting with particle size.
- Impurities and how best to detect, identify and quantify impurities.
- Blend uniformity testing—necessity and test methods.
- Preapproval and postapproval manufacturing changes.
- Reliance on product specifications.
- Qualifying changes to container and closure systems—solid oral dosage forms.
- Waiver of in vivo bioequivalence testing for immediate release solid oral dosage forms.
- In-vitro methods to assess bioavailability and bioequivalence of topical products.
- In-vitro methods to assess bioavailability and bioequivalence of nasal and inhalation drug products.
- Process mapping—CMC and biopharmaceutics review.
- Crisis and risk management.
- New models for product updating.

Performance of the institute's research programs will rely on contributions from the pharmaceutical industry. Companies that would like to contribute research funds to improve on product quality in relation to efficiency and consistency in regulatory processes should contact David C. Pang, Ph.D. at pang@aaps.org for more details.

FDA staff who want additional information on PQRI should contact **Ajaz Hussain, Ph.D.,** (HUSSAINA).

Three from ODE III Witness 1999's Total Eclipse

By Nelson Arnstein, M.D.

For 1999, the astronomical event of the year would have to be the Great European Eclipse of Aug. 11. As nature's grandest spectacle, the sky show was also seen in Turkey, Iraq, Iran, Pakistan and India as well as southwestern England. As the lunar shadow swept across the Black Sea and Turkey, the event was experienced by three of us from ODE III: **John Senior, M.D., Lilia Talarico, M.D.,** and myself.

Three photographs of the eclipse can be viewed by clicking here.

Nelson Arnstein, an avid amateur astronomer, is a medical officer in the Division of Medical Imaging and Radiopharmaceutical Drug Products.