news along the pike

DECEMBER 1998

CENTER FOR DRUG EVALUATION AND RESEARCH

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INSIDE . . .

PIKE'S CORNERS

20 Regulatory Science, Review Grants Funded

Research Coordinating Committee Makes Final Selection

BY JANET WOODCOCK, M.D.

In order to promote research within CDER, I recently put aside $250,000 to sponsor individual research projects under the Center's Regulatory Science and Review Enhancement Program.

The Center received 30 excellent applications. The Research Coordinating Committee took responsibility for review of these proposals and made the final recommendation on which proposals to fund. The committee established a subcommittee to review and rank the proposals. The following principal investigators and proposals were selected for funding in fiscal year 1999:

- **Mohamed Al-Osh, Ph.D.**—Evaluating the accuracy of a diagnostic test using imperfect references.
- **Paul Andrews, Ph.D.**—Analysis of the development toxicology of anti-cancer agents.
- **Dan Boring, Ph.D.**—Development of methods for assessing the cognitive toxicology of proposed drug names.
- **Badrul Chowdhury, M.D., Ph.D.**—Predictability of liver enzyme elevation during placebo treatment in clinical trials.
- **Diana Clark, Ph.D.**—Analysis of the predictive value of preclinical studies for anticancer agents.
- **Albinus M. D'Sa, Ph.D.,** and **Silvia Calderon, Ph.D.**—Proposal for acceptable chemical and biological standards for botanical marijuana.
- **Michael Fossler, Pharm.D., Ph.D.**—Gender-related differences in drug pharmacokinetics: Do they translate into clinical outcome?
- **Ji-Yang "Ted" Guo, Ph.D.**—Proof of concept: Intranet-aided medical and statistical

(Continued on page 12)

OCPB's 5th Science Day Highlights Research Projects

Peck Forecasts Productive Future for Clinical Pharmacology

BY LYDIA KIEFFER, LARRY LESKO AND VANITHA SEKAR

Former Center Director Carl Peck, M.D., predicted a productive future for clinical pharmacology in his keynote speech at the Office of Clinical Pharmacology and Biopharmaceutics's science day held Nov. 6. The meeting, the fifth in the series for OCPB reviewers, took place at the University of Maryland's Shady Grove annex.

Earlier use of clinical pharmacology holds the promise of cutting drug development times, from discovery to market, to five years or less, Dr. Peck maintained. He also predicted that success rates should rise and costs be reduced as a consequence of greater use of the discipline. He said clinical pharmacologists are playing a key role in the paradigm shift to a more scientific approach to drug development.

The new, rational drug development paradigm integrates sophisticated clinical-trial modeling technology into early clinical study designs, Peck said. The results of these studies will more effectively guide the design of the pivotal clinical trials that demonstrate efficacy and safety. Dr. Peck, CDER's director from 1987 to 1993, heads the Center for Drug Development Science at Georgetown Medical Center and is a professor of medicine and pharmacology at the university's medical school.

FDA scientists need to make regulatory decisions grounded in the best science, and need to stay current of new technology and regulatory issues in their field. With this in mind, OCPB organized its first science day in 1996 to promote intramural research and create an opportunity for its scientists to discuss cutting-edge regulatory science.

Shiew-Mei Huang, Ph.D., gave an update on OCPB's intramural and extramural research

(Continued on page 11)

JOE'S NOTEBOOK

Diversity Lessons Learned Firsthand

The *Pike* may be very focused in what it covers, but no one can say we're not trendy. I am writing this on the very day that I read about the Treasury revealing that the most popular choice for the new dollar coin is an image of Sacagawea, the young Native American woman who helped guide the Lewis and Clark expedition. Check out Gloria Marquez Sundaresan's EEO Corner (page 4) for this early example of the importance of diversity to our national life.

Earlier this month, I had a very personal and intense education in the virtues and importance of diversity to our country. I also learned the source of that time-worn alternative to making a mountain out of mole hill: "Don't make a Federal case out of it."

Like most of us, I've been called to report for jury duty many times. Every time I've been in the selection pool, however, I'm sure the defense attorneys have looked at me and said to themselves, "Not on my jury." Consequently, I've been sent on my way without getting the chance to serve.

Well, this time I was picked to be on a jury. My stern and unsympathetic appearance apparently was no bar to service. The jury at the U.S. District Court was certainly a cross-section of our local citizenry—hard-working souls and retired folks, black and white, young and old, men and women.

Over the course of our deliberations, all of us came to appreciate the lessons of consensus decision making:

- Everyone interprets the same events from his or her own unique perspective.
- No one's perspective is more important than another's.
- Each person's point of view is valuable, adds to the discussion and helps your own understanding.
- The process is time-consuming.
- At the end, each of us was convinced that we made the right collective decision.

Speaking of diversity, you'll have to look long and hard to find a more diverse group of people than those who have cranked up their word processors and contributed to the *Pike* this past year. Be sure to look for the names of your friends and colleagues here and give them an extra warm holiday greeting. Each one took time from a busy schedule and pressing duties to share his or her unique point of view with you.

Tanya Abbott, Wayne Amchin, Jerri Artis, Carol Assouad, Jackie Barber, Jim Baughman, Greg Brolund, Jonca Bull, Heather Chafin, Wendy Cheng, Charlene Cherry, Brownwyn Collier, Thomas Conrad, Joseph Contrera, Rose Cunningham, Maria deCarvalho and **John Emelio.**

Karl Flora, Elaine Frost, Charles Greishaber, Nancy Haggard, Anita Harrell, Steve Hayleck, Ajaz Hussain, Shelly Johnson, Lydia Kieffer, Carol Knoth, See Lam, Karen Lechter, Larry Lesko, Murray Lumpkin, Tim Mahoney, Sue Makoff, Fred Marsik, Cindy Marx and **Edwin Matthews.**

Melissa Maust, Judy McIntyre, Debbie McKemey, Edward Miracco, Jim Morrison, Janice Newcomb, Chris Nguyen, Robert O'Neill, Linda Papio, Carl Peck, Dee Rhodes, Kyati Roberts, Kathy Robie-Suh, C. Russ Rutledge, Nancy Sagar, Jamie Saunders, Lisa Schuyler, Vanitha Sekar, John Senior, Ted Sherwood, Harold Silver and **Nancy Smith.**

Gloria Marquez Sundaresan, Sarah Thomas, Vali Tschirgi, Jason Walther, Leslie Wheelock, Neil Wilcox, Roger Williams, Janet Woodcock, Jean Yager and **Robert Young.**

news along the pike

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

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OMBUDSMAN'S CORNER

Holidays Throw Spotlight on Patient Access Questions

BY JIM MORRISON

One of the toughest jobs any of us face is telling a dying patient or his family member why he can't have access to a drug he believes is his last, best chance for survival. Maybe the holiday season makes them more memorable, but lately it seems that I've received more patient-access questions.

Thankfully, my job usually puts me in the positive position of trying to find a way to get needed drugs to patients rather than withholding them. When we are successful, the feeling of making a difference is terrific.

But often the problem is not simply one of access. Sometimes I know that a product is being promoted or used in a questionable manner, and an IND has been filed to lend an air of legitimacy. An IND also cloaks the product in secrecy, limiting what we can say about it.

One way out of this legal bind is used effectively by some project managers in CDER. They guide the inquirers by suggesting questions to ask of those who are promoting the fraudulent product:

- Where were the studies showing effectiveness of the product published?
- What are the credentials of those treating patients?
- Who is currently conducting studies of the drug?

Besides fraudulent products, there are other difficult issues relating to patient access. For example, a study may be on clinical hold—a procedure that prevents a sponsor from beginning a study because of unresolved issues related to patient safety or a lack of information. Such issues can't be discussed outside the Agency unless the sponsor chooses to make them public.

Sometimes the drug is approved in another country but not here. Since there are ways to import the product for one's own use if one has the resources or contacts with foreign physicians and pharmacists, difficult issues of equal access to such drugs arise.

Many of us in CDER deal with patient-access issues. Reviewing divisions, especially Oncology and Anti-Virals, and those who handle consumer questions and requests all face the issue often. Most people working in CDER will at some time be faced with questions about patient access. From my experience, CDER staff generally respond to such questions admirably, and patients and their families greatly appreciate a caring attitude from CDER staff.

At times, however, it is all too easy to merge into the gray fog of the organization, diluting responsibility for actions or policies. "After all," you may tell folks, "it is not I who took the action (or did not take an action), but the Center is bound by law and regulations to follow this path. If it were up to me, I would gladly do things differently."

For anyone tempted to use that old bureaucratic ploy, please remember CDER's mission to protect and enhance public health. We are all embarked on that mission, and we must all take ownership of it. If the mission statement is to be more than a facile sound bite, it must be translated into day-to-day, person-to-person interactions. It's very rare that laws or regulations mandate that we do things that, were we in our customer's shoes, would seem heartless and cruel. Laws and regulations generally have flexibility built into them.

Taking ownership does not mean shouldering the burden alone. Fortunately, there are excellent resources to help with patient access problems:

The FDA's Office of Special Health Issues is a source of information and help to patients with AIDS, cancer, Alzheimer's disease, chronic fatigue syndrome and other serious and life-threatening diseases and to their families. The staff does a terrific job, and they are advocates for patients, which is something we in CDER often don't have the time or mandate to do.

The OSHI staff can explain what it means to be in a clinical trial and can put patients in touch with NIH and other government and private sources of help. The Office of Special Health Issues can be reached at (301) 827-4460.

Within CDER, you can refer telephone inquiries to the Drug Information Branch and written or e-mail requests to the Executive Operations Staff. Both staffs can provide information on emergency INDs, personal importation and other issues related to experimental therapies, especially for disorders that OSHI doesn't handle.

Jim Morrison is the Center's Ombudsman.

PHS Launches Women's Health Information Center Web Site, Hotline

The Public Health Service last month launched the National Women's Health Information Center, a combination World Wide Web site and toll-free hotline that serves as a one-stop shopping resource for women's health information. NWHIC can be reached at http://www.4woman.gov or by calling 1-800-994-WOMAN.

"This information center represents the federal government's most comprehensive resource for women's health," said HHS Secretary Donna E. Shalala. "With a few strokes on a computer keyboard, or a toll-free call, women and their health care providers can open the door to a world of important medical information resources."

The Web site links to all federal agencies and publications on women's health, and to hundreds of government-screened private-sector organizations. NWHIC also provides frequently asked questions on top health issues of concern to American women. The toll-free number connects the caller to a health information specialist who will refer the caller to the right source of information. Women and their health care providers can also order fact sheets, brochures and other printed materials by phone.

NWHIC hyperlinks to more than 1,000 Web sites, including more than 300 federal sites, and to more than 2,700 federal documents on women's health, 1,800 of which are already online.

EEO CORNER:

Lewis, Clark Expedition Provides Lesson in Diversity

BY GLORIA MARQUEZ SUNDARESAN

November was National American Indian and Alaskan Native American Heritage Month. Our nation commemorated this with programs, activities and ceremonies that highlighted the countless contributions of Native Americans to the progress and greatness of our diverse country.

One of the most fascinating adventures in our history is the role and active participation of Native Americans during the trailblazing expedition of Capts. Meriwether Lewis and William Clark. American Indians served as interpreters, guides and cartographers. Friendly tribes also bartered horses in order to provide food for the explorers.

In 1803, President Jefferson ordered Lewis and Clark to find a Northwest route from Missouri to the Pacific Ocean. As part of this expedition, the president instructed them to make detailed observations of the climate, flora and fauna. They were also required to bring back samples, maps and an accurate record of Indian tribes, their number and way of life. If possible, diplomatic relations with the tribes were also encouraged. The team led by Lewis and Clark left St. Louis, Mo., on May 14, 1804, and returned on Sept. 23, 1806.

The delineation of the vast western land and other information that came out of the adventures of Lewis and Clark helped other explorations that followed and forever changed the nation's history. The team left a legacy of non-violent contact, respect and friendship toward the American Indians. The trail taken by Lewis and Clark still exists and is preserved for those who want to trace their footprints almost 200 years later.

The explorers made it all the way to the West Coast and back on foot, horses or canoes. The team survived inclement weather and endured thousands of miles of rugged terrain across mountains and rivers. A closer look at the group reveals that its members came from diverse backgrounds.

For instance, Lewis was botanist and a biologist and Clark was cartographer and a geographer. The remainder of the group consisted of York, a slave of Lewis; approximately 26 soldiers; and Scammon, a Newfoundland dog. A few months after the expedition began, a French trapper, Charbonneau and his pregnant Shoshoni wife, Sacagawea, also became a part of the team, serving as interpreters.

Sacagawea helped Lewis identify plants and animals. When she gave birth to a son, she also provided an important role in the safety of the team. Her presence as a mother with an infant projected the impression that the explorers could not have been warriors. Potentially hostile tribes became more friendly .

Pvt. Pierre Cruzatte, who was of French and Omaha Indian descent, also served as interpreter; but he was valued more for his talent as a violinist. His music provided fun and relaxation for everyone and fascinated the American Indians. The story of Lewis and Clark is incomplete without including the important role of Native Americans.

At present, we emphasize workforce diversity, but its value was demonstrated by the Lewis and Clark expedition. The survival of the explorers and the success of the mission depended on individuals who, with different backgrounds and experiences, were able to contribute their talents and skills.

Today, the relevance and importance of diversity is even more apparent in our everyday life—at work, schools, churches and communities all over the United States.

Until recently, not much attention was given to diversity. Now, however, it is discussed in academia, Congress and boardrooms all over the world. As the Lewis and Clark story illustrates, a focus on diversity will undoubtedly enhance our survival and success as a society and as a nation.

The source for this article was *Lewis and Clark Among the Indians* by James P. Ronda.

Gloria Marquez Sundaresan is an EEO Specialist.

MedDRA Maintenance, Support Services Organization Selected

GENEVA—The ICH Medical Dictionary for Regulatory Activities terminology in English and a Japanese translation will be available for licensing beginning March 1, according to a Nov. 24 announcement from the International Conference on Harmonization..

The new international medical terminology, developed by the International Conference on Harmonization, is designed to support the classification, retrieval, presentation and communication of medical information throughout the medical product regulatory cycle.

MedDRA will be particularly important in the electronic transmission of adverse event reporting, both in the pre- and post-marketing areas, as well as the coding of clinical trial data.

MedDRA is expected to become the accepted standard for all regulatory activities. The terminology serves a vital public health need: to facilitate the collection, presentation and analysis of regulatory information on medical products during clinical and scientific reviews and marketing.

BDM International has been selected as the maintenance and support services organization for MedDRA. A sublicense agreement names the Society of Japanese Pharmacopoeia as the Japanese management organization for MedDRA.

BDM will provide maintenance, distribution, implementation and ongoing development of the terminology to ensure that it continues to evolve in response to user needs.

The support services team will consist of a consortium of experienced international companies: BDM, Quintiles Transnational Corp., Stellar Business Systems and Cyntergy Corp. Ernst & Young will be retained to serve as knowledge management provider.

For information about subscribing to MedDRA, contact Kathryn Huntley at BDM by e-mail at khuntley@bdm.com.

WEB INSIGHTS

Development of CDER Kid's Page for Internet Needs Your Help

BY CAROL ASSOUAD

When we started our Web projects about three years ago, we thought: "What a marvelous way to exercise creativity, innovation, imagination, change and transition."

We saw the Web not only as a great way to store and deliver information but also as a great, new educational medium. We envisioned a simple organizational structure capped with innovative presentation techniques that would speedily deliver vast amounts of easily understood information. We saw a multitude of educational possibilities, from primary to post-graduate levels, as well as internal staff training.

To get moving on our educational efforts, we opted to begin with a CDER Kid's Page. That turns out to have been fortuitous, since an Executive Branch mandate earlier this year requires the inclusion of kids' pages on all agency Internet sites. We formed a team who took on the extra work of designing and creating a kid's page for elementary-school students. Led by **Karen Kapust,** the team currently consists of **Sonia Castillo, Wanda Clabaugh, Pam Fagelson, Brad Leissa, Dan Luckabaugh, Nancy Muir** and **Bill Woodard.**

After struggling with the objectives of the page for some time, the team decided that the Kid's Page should:

- Inspire an interest in science and statistics.
- Encourage kids to pursue a science career.
- Help them develop an understanding of the science behind what we do.
- Most importantly, teach them how medicines work and the importance of following directions.

The team wanted a Web site that would be fun, accurate, regularly updated and progressively challenging to young minds. We not only wanted repeat users, but we wanted teachers, parents and librarians using the page as a learning resource. For a team doing this on top of their regular jobs and other high-priority activities, getting these objectives down was a tough but essential step. Now they have a site ready for you to view on CDER's intranet at http://cdernet/kidsite/kidshome.htm.

What you'll find there is just the beginning—an adaptation for kids of the CDER handbook, interviews with people who work at CDER and a few graphics to give you some idea of the content that has to be developed.

We need more people to work on this site before it's ready to be published. We'll need even more to work on the other educational pages. We want to add instructional material and games on pharmacokinetics and bioavailability, clinical trials, statistics, advertising and health fraud. We will need to add a comments page and an area where users can submit contributions such as drawings, questions and puzzles.

To volunteer for this page, to submit your ideas and materials or simply to learn more about this opportunity, please contact either **Karen Kapust** or myself. We've also set up a forum to discuss these ideas and to work collaboratively. To use this, enter http://cdsmlweb1/forums/Index.cfm?CFApp=60& and join in any of the ongoing conversational threads or establish a new one. Instructions on using forums are at http://cdsmlweb1/forums/cder_doc.html.

We can provide administrative, graphics and training support. We really do want your contribution to this effort, so please think seriously about this call for help and ideas.

Carol Assouad is Division Director, Medical Library and Program Manager, CDER Web Sites.

Huque to Head Statistical Support at Corporate Boulevard for ODES IV, V

BY ROBERT T. O'NEILL, PH.D.

Dr. Mohammed Huque, Ph.D., is the new Director of the Division of Biometrics III, which provides statistical support to the Corporate Boulevard complex, including the medical review divisions in the Offices of Drug Evaluation IV and V.

Dr. Huque brings a wealth of experience and science-based expertise to this position. When he joined FDA in 1986 as a mathematical and statistical reviewer, he brought extensive industry and academic experience in biostatistics and clinical trials. He has served in progressively more responsible positions since then. Most recently, he served as the Acting Director of the Division of Biometrics IV in the former Office of Epidemiology and Biostatistics. Before that, he was a team leader and a group leader responsible for supporting the Division of Gastrointestinal and Coagulation Drug Products.

He has provided substantial support to reviews of investigational drugs, new drugs, over-the-counter drugs and generic drugs. He has made contributions to post-marketing surveillance and analysis of carcinogenicity and stability testing. Dr. Huque has implemented new review policies, significantly improving the quality and timeliness of the reviews, enhancing interaction and communication between statistical reviewers and among all disciplines supported.

Prior to joining FDA, Dr. Huque held senior statistical positions in the pharmaceutical industry. He taught for several years in the Department of Psychiatry at New York Medical College as an assistant professor. While at FDA, he has been an adjunct professor at George Washington University and an instructor at NIH's Foundation for Advanced Education in the Sciences. He has also been very active in supporting OTCOM's Division of Training and Development, having developed and presented several courses and specific lectures.

Dr. Huque received his master's and doctorate degrees in statistics from the University of Missouri and has undergraduate and graduate degrees from Bihar and Bhagalpur universities in India. He has authored numerous articles, many on methodological topics derived from his experience in the CDER drug review process.

Robert T. O'Neill is Director, Office of Biostatistics.

UNION CORNER

Right to Official Time for Union Activities Comes in Two Flavors

BY ROBERT YOUNG

"Official time" designates time on the clock or duty status used by unionized Federal employees to meet their representational responsibilities. Federal unions rely exclusively on the voluntary efforts of their members to support chapter activities. The national union has officers and employees supported by dues and operates as a coordinating and cooperative service organization for the local chapters.

The law provides two kinds of official time: time to negotiate a collective bargaining agreement, which is guaranteed in the law, and time for all other activities, which is contained in the labor-management negotiated agreement.

Official time to negotiate a collective bargaining agreement. Official time to negotiate of a collective bargaining agreement is granted employees representing an exclusive representative as a statutory right. The number union employees cannot exceed the number of individuals designated to management in the contract negotiations. The term negotiations includes not only that time spent sitting at the bargaining table but also covers related activities, such as attendance at impasse proceedings.

The National Treasury Employees Union and FDA will be negotiating the nationwide collective bargaining agreement early next year. The contract will be effective for three years. Negotiations will be held during three two-week sessions in January, February and March. Six rank-and-file FDA employees will sit at the bargaining table with six FDA employees representing management. The contract will govern all aspects of the FDA work environment and bind all rank-and-file employees. The union's proposed contract is more than 100 pages long. A professional negotiator from NTEU National will lead the union team.

Official time for all other representational activities. The law specifically excludes from official time any activity related to the internal business of the union, such as electing officers or collecting dues. Otherwise any employee representing the union or any employee engaged in any activity covered by the statute must be granted official time to engage in such activity to the extent that the union and agency agree that the use of official time is reasonable, necessary, and in the public interest.

Official time is not a benefit or privilege conferred upon employees by the agency, but is mandated by the statute. Employees engaged in covered activities have a right to official time.

The amount of official time to be allocated is negotiable. All bargaining unit employees, not only union members, officers and stewards, are covered.

The negotiation of official time for labor-management relation activities is affirmed. The union and management may agree to permit official time in circumstances unrelated to labor-management relation activities, provided that the activities are consistent with the law.

A variety of activities have been found to be appropriate, including attendance at Equal Employment Opportunity Commission hearings; responding to discovery requests made in Merit Systems Protection Board hearings; attendance at meetings with management; attendance at third-party proceedings where the employee is the affected employee or a witness in a grievance or appeal proceeding; preparing a grievance; responding to inquiries from the media and public about issues affecting the terms and conditions of employment within the unit; visiting, phoning and writing to elected representatives in support or opposition to pending legislation which would impact employee working conditions.

The union is obligated to make a reasonable effort to schedule the use of official time to avoid absences from agency duties. The use of official time can be suspended only when the absence would cause substantial adverse effects on the work product of the employee's group and an alternative time is provided.

An agency's ordinary workloads are insufficient to suspend the use of official time, just as they are insufficient to justify restored leave.

Official time is time on the clock or duty time. It is not time shifting—merely shifting the time when regular work is done. The activity for which official time is granted is assigned work, in most position descriptions to be found as "other duties as assigned." It is not an additional duty to be added on or superimposed upon the employee's regular work increasing an employee's total workload.

The crunch usually comes when an employee's regular work fills nearly 100 percent of his or her duty time, and then he or she engages in official time activities. Since the regular work day is limited by law to eight hours and the work week to 40 hours, something has to give. It should not be the employee.

Ordinarily, official time activities replace regular agency work. When this would result in an immediate, substantial adverse effect on the work group's work product, time to make the necessary adjustments and accommodations is proper.

Controlling the above results are three key concepts:

- Employees are to chose their own representatives.
- There should be a balance between management representatives and employee representatives.
- Official time is a "carve-out" exception to management's general right to direct employees and assign work.

The union is sympathetic to the plight of first-level supervisors. They have work to complete and, generally, a staff insufficient for the task. When some of their staff use official time, there is a real reduction in the staff available to them. If a single member of a small group goes on official time 100 percent, a very substantial reduction in available workers may result. Only supervisors higher up have the resources to make the required adjustments. There is nothing inherently unfair about this. It is precisely these kinds of problems they sought and were chosen to solve.

Robert Young, M.D., Ph.D., is interim president of Chapter 282, National Treasury Employees Union.

ANATOMY OF A HAMMER

Russ Goes on Road to Promote New Guidance, Wins Gore's Award

BY C. RUSS RUTLEDGE

As everyone on the planet must know, the Government Performance and Results Act requires us to reevaluate how we do business and identify areas in which we be more effective and efficient. One strategy FDA uses is pursuing opportunities to work with industry and gain the benefit of their insights. Naturally, it's a two-way street, and industry sometimes needs guidance from the Agency.

About two years ago, the Division of Field Sciences in FDA's Office of Regulatory Affairs sponsored an open meeting with the pharmaceutical industry. About 200 laboratory managers and quality assurance and control professionals met with representatives from various FDA components. The focus was for the regulated industry to identify those areas in laboratory operations that they felt were most in need of guidance or clarification from FDA. Presentations on the top two selections would then be given in a series of nationwide meetings.

During the course of the meeting, dozens of possible topics were identified, discussed. The relative importance of topics was discussed, and the list narrowed. At the end of the meeting, the audience voted that the top two were how to handle:

- Out-of-specification laboratory results
- Adjustments to parameters in validated methods—how much could an analytical method's parameters be adjusted before the method itself would be changed.

The task of finishing the out-of-specification guidance was one of the reasons I accepted a position within the Office of Compliance. I knew it was an important topic, but was surprised that it was voted as the topic most in need of guidance. This gave me additional incentive to finish the document and obtain clearance using good guidance practices.

I wrote a speech, made slides and overheads and prepared myself for the rigors of public speaking. For the road show, **Tom Layloff** and **Bill Furman** delivered the adjustments talk, and I gave the out-of-specification one.

In June 1997, I gave the first in a series of presentations on the upcoming out-of-specification guidance. This was to an enthusiastic audience of about 400 in Puerto Rico. The feedback was almost all positive; although, one person commented that the presentation needed examples. I responded by including examples of successful out-of-specification investigations in subsequent talks. While in Puerto Rico, I also gave the presentation to the district office.

Three months later, I gave a videoconference presentation to all district offices from the Philadelphia Regional Office. This was video taped, and the tape distributed to the District Offices for their training library. Later that afternoon I gave the presentation to industry. Two speeches per day both in Puerto Rico and Philadelphia were hard but very satisfying work. Tom and Bill had the opposite schedule: they presented to industry in the morning, and did the videoconference for the districts in the afternoon. Thus, neither of us saw the other's presentation.

In late September DFS took the road show to a professional society's annual meeting of about 400 people in Bethesda. By this time I was getting fairly comfortable with the talk, and the event was very successful. Tom and Bill gave their presentation in the adjacent room giving the audience their choice of topics.

These talks were given on the East Coast. To keep our promise of presenting the topics nationwide, last month we took the road show to the West Coast for one week—Seattle, Wash., and Irvine and Oakland, Calif. It was grueling, a speech and questions one day, travel the next.

Even though we were only scheduled to speak for an hour and address questions for another, we represented the FDA the whole time we were at the event. We realized we needed to act professionally and treat people with courtesy at all times. This may have been their only exposure to FDA, and we wanted them to remember us with positive thoughts.

These events show how a group in the Agency recognized a deficiency, met with industry to get its input and identify specifics and then responded in a positive manner. For these efforts, the team involved was selected to receive Vice President Gore's Hammer Award. These recipients were Tom Layloff, Bill Furman and myself from CDER and **Richard Baldwin, Len Valenti** and **Elise Murphy** from DFS.

The item after lunch in Oakland was a short ceremony in which we were each presented with the hammer lapel pin and certificate signed by Vice President Al Gore. To receive the Hammer Award was extra special. I can look back on my FDA career and identify maybe a half dozen high points—events which really stand out. Friday, Nov. 20, was one of those.

Russ Rutledge is a compliance officer in OC's Division of Manufacturing and Product Quality.

Leber to Leave Division of Neuropharmacological Drug Products

Paul Leber, M.D., will leave FDA service Jan. 2. Dr. Leber has served the FDA and the public for more than two decades, for the last decade and a half as the Director of the Division of Neuropharmacologic Drug Products.

He has helped guide the development of an explosion of drugs that has changed the face of therapy for such disorders as obsessive compulsive disease, depression and dementia.

He has overseen the development of new classes of drugs offering important advances such as the selective serotonin reuptake inhibitors and other new antidepressants, the "triptan" antimigraine drugs as well as new drugs for epilepsy and Parkinson's disease.

Dr. Leber has made critical contributions to FDA thinking about active control equivalence trials, criteria for antidementia claims and interpretations of results in clinical trial settings with very high drop-out rates.

Russell Katz, M.D., will be acting director of the division once Dr. Leber departs.

Update Continues; Spring Course Schedule Announced

BY JUDY MCINTYRE

This continues the updates on OIT's activities begun in the November issue.

Corporate Database Redesign: In December, the redesign development team began conducting workshops, interviewing users and attending meetings that have a direct impact on the requirements phase of the project. This first phase of the redesign is scheduled to end in May. The contact is **Mark Gray** (GRAYM).

Year 2000 Renovations: OIT is working on the Agency's formal year 2000 independent validation and verification program for systems identified as mission critical.

Thus far, Y2K renovation has been completed for all 16 systems identified by CDER as mission-critical. Compliance packages for two of these systems have been completed. This consisted of identifying critical dates in each system and performing a series of tests to ensure the system can correctly accept, process, manipulate and return dates before and after Jan. 1, 2000. Work also continues on infrastructure components such as PCs, servers and telecommunications systems to ensure Y2K compatibility. More information about CDER and FDA's year 2000 activities can be found on the Web at http://www.fda.gov. The contact is **Judy McIntyre** (MCINTYREJU)

VMS/ORACLE Upgrade: A general description of the upgrade project was in November's Pike. The upgrade working group is preparing a final plan for the upgrade and conducting preliminary tests to determine the most effective migration strategy. The test results, plans and supporting documentation will be placed on the OIT Web page in late and will be updated as this project continues. The contact is **Greg Brolund** (BROLUND).

Development Project for QA: The Quality Assurance Development Project completed its assessment of OIT's software engineering and service on Nov. 19. OIT was rated at CMM Level 1, the initial maturity level according to the Software Engineering Institute's Capability Maturity Model (http://www.sei.cmu.edu). The QA Development Project is part of a continuous improvement effort in OIT. The initial goal of the QA Development Project is to reach CMM Level 2. According to the SEI, the median time for an organization to move from Level 1 to Level 2 is 26 months. OIT will focus first on high-priority activities that achieve the greatest benefit. The results of the assessment are available on the CDERnet (http://oitweb/oit/) under OIT Activities. The improvement plan will also be posted on the Intranet when it is finalized. The contact is **Vali Tschirgi** (TSCHIRGIV).

Excalibur EFS Replacement: Several CDER components have been using Excalibur's Electronic File System since 1993 to search and display documents that have been scanned and stored electronically. Adverse experience reports, approved label package inserts, drug master files and reviews and biopharmaceutic reviews are examples of documents that are available through EFS.

EFS will no longer be supported by the vendor and will not be compatible with OIT's planned upgrade to the operating system and database (see the VMS/Oracle upgrade section of this article). OIT is evaluating Excalibur's replacement software and other products to find the most effective replacement and most efficient migration path for CDER's EFS file rooms. A test of replacement products is planned by May. The contact is **Linda Sigg** (SIGGL)

ERSR Training and Core Software Courses: In addition to core Center software training, OIT offers the following three courses to help meet CDER's Electronic Regulatory Submission and Review 2002 goals:

- *MS Project98 for Project Managers:* Jan. 6, Feb. 26, March 18, 1 p.m. to 4 p.m. Learn how to reach review objectives by using the software to define tasks, assign and manage task duration times, mark milestones, assign and manage resources and print management reports for single and multiple drug review projects.
- *NDA Electronic Submissions Training:* Jan. 27, Feb, 24, March 17, 9 a.m. to noon. Learn to search for a specific NDA via the electronic document room. Use Adobe Acrobat Exchange to open, navigate, view, follow links, create electronic notes and copy and paste text and graphics.
- *NDA Electronic Data Analysis Training:* Feb. 28, March 26, 9 a.m. to noon, and Feb, 28 and March 17, 1 p.m. to 4 p.m. Use several software packages to open NDA data files via a Windows interface, convert and analyze data to formats compatible with Center software applications, such as Excel and Access.

The schedule for other courses is:

- *Access:* Introduction and Tables, Jan. 21, Feb. 19, March 25, 9 a.m. to 11:30 a.m.; Queries and Reports, Jan. 21, Feb. 19, March 25, 1 p.m. to 3:30 p.m.; Report Design, Jan. 22, March 26, 9 a.m. to 11:30 a.m.; Form Design, Jan. 22, March 26, 1 p.m. to 3:30 p.m.
- *Acrobat:* Introduction, Feb. 1, 9 a.m. to 11:30 a.m.
- *Division Files System:* Jan. 27, Feb. 25, March 19, 1 p.m. to 4 p.m.
- Excel: Introduction, Jan. 8, 9 a.m. to 11:30 a.m.
- *Local Area Network:* Feb. 1, 1 p.m. to 3:30 p.m.
- *PowerPoint:* Introduction, Jan. 7, March 5, 9 a.m. to 11:30 a.m., and Feb. 16, 1 p.m. to 3:30 p.m.; Charts and Templates, Jan. 7, March 5, 1 p.m. to 3:30 p.m.
- *Windows:* Introduction, Jan. 5, March 1, 9 a.m. to 11:30 a.m.
- *Word:* Introduction, Jan. 5, Feb. 2, Feb. 17, March 1, 1 p.m. to 3:30 p.m.; Formatting, Jan. 6, Feb. 3, March 2, 9 a.m. to 11:30 a.m., and Feb. 17, 1 p.m. to 3:30 p.m.; Tables, Jan. 6, Feb. 3, Feb. 18, March 2, 1 p.m. to 3:30 p.m.

Training manuals and the calendar are available on CDERnet (http://oitweb/oit/) under the Training button. The contact is Lana Kostecka (KOSTECKAL).

Judy McIntyre is a supervisory computer specialist on OIT's QA Staff.

ADMINISTRATIVE MANAGEMENT CORNER

Center Phases In Automated System to Support Administration

BY JERRI ARTIS, JANIE SAUNDERS AND LISA SCHUYLER

An automated system to expedite the processing of administrative functions, known as the Enterprise Administrative Support Environment or EASE for short, is being introduced to CDER. Created by an FDA contractor, it contains six different modules: core, time and attendance, travel, personnel, procurement and training. Currently, the time and attendance and core are the only functioning modules.

The time and attendance module eliminates paper time cards and manual processing, reduces the amount of time spent processing time and attendance, cuts down on payroll errors and corrections and allows easier and faster access to more accurate and timely data for reporting purposes. The core module stores employees' official information.

The associate director for administrative services in the Office of Management has the task of rolling out EASE in the Center. The implementation team consists of **Banks Johnson,** the associate director for administrative services, **Janie Saunders, Lisa Schuyler** and **Jerri Artis** in the Office of Management and **Lana Kostecka, Peggy Goebel** and **Wil Brooks** in the Office of Information Technology.

The team has trained out about 370 employees,starting this July with the Office of Drug Evaluation II's Division of Pulmonary Drug Products as the pilot group. More than 100 employees in ODE II have completed training and are now being paid through EASE. In mid-November, the team trained about 125 employees supervisors and timekeepers in ODE I, the Office of Center Director and the Office of Pharmaceutical Science. The training schedule for 1999 is:

- January: ODE III.
- February: Office of Review Management, Office of Clinical Pharmacology and Biopharmaceutics and ODE IV.
- April: Office of Management, Office of Biostatistics, Office of Post-Marketing Drug Risk and Assessment and ODE V.
- June: Office of New Drug Chemistry and Office of Information Technology.
- August: Office of Training and Communication and Office of Testing and Research.
- October: Office of Compliance and Office of Generic Drugs.

The team looks forward to training and working with CDER staff and having the entire Center use this automated system by next fall when we will have trained almost 1,700 CDER employees.EASE was was created and introduced to FDA by Booze Allen and Hamilton.

Jerri Artis, Janie Saunders and Lisa Schuyler are program analysts in the Office of the Associate Director for Administrative Services, Office of Management.

REVIEWER'S AFFAIR CORNER

Henney to Address CDER Reviewers at RAC's Networking Event Jan. 25

BY LYDIA KIEFFER

Commissioner **Jane E. Henney, M.D.,** will address CDER's reviewers for the first time Jan. 25 at the Reviewer's Affair Committee's third annual networking event to be held at Parklawn from 11 a.m. to 1 p.m. in Conference Rooms D and E.

The primary goal of the RAC is to improve the reviewer's personal work environment and provide a sense of appreciation for the work the primary reviewer accomplishes. In this manner, we can all provide CDER customers with quality reviews in a timely fashion.

The RAC provides a forum for all CDER primary reviewers to express their ideas and concerns about CDER, the work they do and their work environment directly to the Office of the Center Director.

The networking event is a great opportunity for you to find out more about RAC and how you can help the RAC grow in its influence. Information about the RAC and about its many activities will be available at the meeting. We welcome new members and ideas.

Come join us to find out more about RAC and mingle with other reviewers in a congenial atmosphere.

Lydia Kieffer, Pharm.D., is an OCPB reviewer

Modernization Act's Nov. 21 Anniversary Sees FDA on Track for Deadlines

On the first anniversary of the FDA Modernization Act, the Agency met nearly all the law's deadlines. In many cases the Agency was able to finish projects ahead of schedule.

The law required FDA to complete 17 regulations, 11 guidance documents, six regulatory notices, nine reports and at least 18 other tasks. The Agency found scores of other regulatory measures were needed to meet the law's objectives.

So far, FDA has issued 16 final rules, nine proposed rules, 36 guidance documents, 11 regulatory notices and one report. Completed Modernization Act initiatives include:

- A final rule establishing parameters for distributing sound and balanced information about off-label uses for marketed drugs, biologics and medical devices.
- A guidance on FDA's fast track programs, which are designed to facilitate the development and evaluation of new drugs and biologics designed to treat serious and life-threatening illnesses.
- An agency plan for statutory compliance with Modernization Act developed through "stakeholder" meetings.

For more information on FDA's Modernization Act-related activities, visit FDA's Modernization Act Website at http://www.fda.gov/opacom/7modact.html. The CDER-specific site is at http://www.fda.gov/cder/fdama/.

New HIV Therapy; Hepatitis C Treatment Approved for Wider Use

In recent drug news, abacavir received accelerated approval for the treatment of HIV-1 in adults and children, a combination product for treating hepatitis C received an expanded indication, and labeling for sildenafil was updated.

On Dec. 18, FDA approved abacavir. The oral medication, taken twice daily, is one of a class of medicines called nucleoside analogue reverse transcriptase inhibitors and is taken in combination with other anti-HIV medications. The combination of medicines helps to lower the amount of HIV found in the blood.

Abacavir offers another choice for the treatment of HIV. Abacavir, available in tablet and liquid form is approved for adults and pediatric patients older than 3 months.

A potentially fatal hypersensitivity has been associated with the abacavir in at least 5 percent of patients. Symptoms of this reaction may include skin rash, fever, nausea, abdominal pain and severe tiredness.

A written list of the hypersensitivity symptoms is printed on a warning card and is provided along with a medication guide to patients by pharmacists. Anyone who experiences a hypersensitivity reaction must stop taking the medicine and call their health care provider immediately. Abacavir should not be taken again after a reaction occurs because more severe symptoms will arise within hours and may include life-threatening low blood pressure or death.

An abacavir hypersensitivity reaction registry has been established. Physicians should register patients developing symptoms of hypersensitivity by calling 1-800-270-0425.

All nucleoside analogue reverse transcriptase inhibitors can cause lactic acidosis—a fatal metabolic disturbance that causes an abnormal buildup of lactic acid. Symptoms may include an enlarged liver.

Accelerated approval of abacavir was based on analyses of surrogate markers in three controlled studies of up to 24 weeks in duration. At present there are no results from controlled trials with abacavir evaluating long-term suppression of HIV infection or AIDS. Abacavir is manufactured and marketed under the trade name Ziagen by GlaxoWellcome Inc. of Research Triangle Park, N.C.

On Dec. 9, FDA expanded the indication of a drug/biologic product to include chronic hepatitis C patients who have not been treated with alpha interferon therapy. The product, ribavirin capsules and interferon alfa-2B recombinant for injection, was previously approved only for patients who had relapsed following treatment with interferon alone.

The combination product is not a cure for chronic hepatitis C, and it is unknown if this treatment will delay liver disease progression. Ribavirin alone is not effective for the treatment of chronic hepatitis C. It also is unknown how the two agents work together against the hepatitis C virus, but the combination appears to suppress blood levels of the hepatitis C virus better than treatment with interferon alone.

Clinical studies of treatment with the ribaviron-interferon alfa-2B combination over a course of 24 or 48 weeks resulted in higher virologic responses compared to interferon alfa-2B treatment alone. However, the same studies found that patients who had not responded to the combination by week 24 were unlikely to benefit from further treatment.

Due to the adverse reactions that can accompany the use of this combined therapy, it is important that the duration of its use be individually tailored to patient's baseline characteristics, virologic response at week 24, and tolerablility of the regimen.

Signs of serious side effects should be closely monitored by physicians. Both ribaviron and interferon alfa-2B have been found to cause significant adverse reproductive effects, including fetal death or structural malformations, in the developing fetus in several animal species. Female patients and female partners of male patients must not become pregnant while receiving this therapy and for six months after completing therapy.

Ribavarin causes anemia, which can be serious especially in patients with underlying cardiovascular disease. Interferon alfa-2B has been associated with psychiatric disorders, including depression and suicidal behavior (suicidal thoughts, suicide attempts and completed suicides). Depression, suicidal ideation and suicides occurred in patients treated with the combination. Lastly, most patients who receive interferon alfa-2B therapy complain of "flu-like" symptoms, fevers, chills and body aches. These symptoms are often relieved with nonprescription medicines such as acetaminophen or ibuprofen.

Schering Corporation of Kenilworth, N.J., markets the product as Rebetron Combination Therapy and includes detailed patient information with each dispensed package. FDA's approval of the Rebetron Combination Therapy package in no way restricts or precludes a request by the manufacturer to sell ribavirin (Rebetol) or its interferon (Intron A) separately. The decision to market them in a strictly combined form rests with the company.

FDA and Pfizer Inc. advised doctors Nov. 24 about new warnings and information in the product labeling for sildenafil in response to postmarketing reports of serious adverse events. The new information augments the original drug labeling which warned against the concomitant use of sildenafil and nitrates.

Revised in consultation with FDA, the new labeling is intended to help make sure that consumers and doctors are fully informed about the benefits and risks of using sildenafil, know that consideration must be given to the cardiovascular status of patients prior to prescribing sildenafil , and know how to safely use the drug.

Health care professionals are encouraged to report any unexpected adverse or serious events associated with the use of sildenafil (Viagra) directly to Pfizer Inc. at 1-800-438-1985 or to FDA's MedWatch program at 1-800-FDA-1088, by fax at 1-800-FDA-0178 or by mail (MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20857).

FDA talk papers and news releases.

OCPB's 5th Science Day Highlights Research Projects

(Continued from page 1)

projects. In collaboration with the Universities of North Carolina, Pittsburgh and Colorado, OCPB is conducting a series of integrated extramural research projects to support policy development in clinical pharmacology.

- The North Carolina program is exploring optimal study conditions to validate an *in vitro* human hepatocyte model that would evaluate the enzyme induction potential of new molecular entities.
- One Pittsburgh project, "*In vitro* models for predicting clinically relevant interactions for drugs metabolized by CYP2C9: an *in vitro–in vivo* correlation," is investigating the enzyme's inhibition and activation properties.
- Another OCPB and Pittsburgh research project being conducted through FDA's Office of Women's Health and the NIH is investigating gender differences in P-450 enzyme activities and their implications for *in vivo* drug-drug interactions.
- The University of Colorado is developing a P-450 drug metabolism and drug-drug interaction electronic database. The evaluation of available commercial software is under way.

OCPB has also requested research funding for intramural projects through FDA's Office of Science, CDER's Regulatory Science and Review Enhancement program and the OWH.

Traditionally OCPB's science days are held in November before the American Association for Pharmaceutical Sciences annual meeting and in March before the American Society of Clinical Pharmacology and Therapeutics annual meeting. Reviewers scheduled to present at these professional meetings have an opportunity to give a dry run at the science day and benefit from peer review before giving their presentations at these major meetings. Science days also provide a forum for reviewers to present their professional development work as interim research reports.

One of OCPB's newest colleagues, **Soraya Madani, Ph.D.,** presented her podium presentation from AAPS 1997 entitled: "*In vitro* comparison of CYP2D6 content and catalytic activity between human liver and intestinal mucosal microsomes: prediction of metoprolol first-pass metabolism." Dr. Madani was the recipient of OCPB's science day first-prize award for podium speakers.

OCPB's second-place recipient was **He Sun, Ph.D.,** who presented a study on optimizing sampling times and their application to designing population pharmacokinetic studies. Through simulation, Dr. Sun was able to demonstrate that robust estimates of clearance were obtained regardless of the level of inter-subject variability investigated.

Ameeta Parekh, Ph.D., presented results of a survey that addressed the prioritization of the review load for investigational new drugs in the Division of Cardio-Renal Drug Products. The study is timely in light of the shrinkage of review time relative to the number of submissions. Results indicated that about 10 percent to 15 percent of the 700 INDs screened in a four-month period could benefit from a clinical pharmacology and biopharmaceutics review. Subsequent reviewer effort could be maximized by providing input to sponsors on study design of future clinical pharmacology and biopharmaceutics studies.

Kofi Kumi, Ph.D., previewed his AAPS podium presentation, which focused on the development of OCPB's draft recommendations for studies that may be necessary to fulfill the requirements for the human pharmacokinetics and bioavailability section of a NDA for liposomal and lipid complex drug products.

A presentation by **Arzu Selen, Ph.D.,** addressed the optimization of innovation and predictability in drug development. Perspectives addressing the role of the scientist, regulatory agencies, industry and academia in shaping drug development in the next century were presented for discussion.

OCPB science day poster presentations included:

- "Calcitonin gene-related peptide release from rat aorta by select nitric oxide donors: A nitroxyl anion-dependent process," **Brian Booth, Ph.D.,** and colleagues.
- "Application of PK/PD modeling in the drug development process." **Elena Mishina, Ph.D.,** and **Raymond Miller, Ph.D.**
- "Effect of renal disease on the disposition of highly metabolized oral drugs," **Sayed Al-Habet, Ph.D.,** and colleagues.
- "A novel pharmacokinetic-pharmacodynamic model which describes the indirect, irreversible and saturable effect of finasteride on circulating dihydrotestoterone levels in the plasma," **Sam Haidar, Ph.D.,** and colleagues. Dr. Haidar received OCPB's second prize for best poster presentation.
- "Modeling the pharmacodynamics of a unique oral hypoglycemic agent using neural networks," **Michael Fossler, Pharm.D., Ph.D.,** and colleagues. Dr. Fossler won OCPB's first prize for best poster presentation.
- "Assessment of the quality of the 'Hepatic Impairment' studies in recent NDAs," **Mehul Mehta, Ph.D.,** and colleagues.
- "Pharmacokinetic/pharmacodynamic evaluation for mycophenolate mofetil using logistic regression," **Chandra Sahajwalla, Ph.D.,** and colleagues.
- "Poor and unusually prolonged oral absorption of amphotericin B in rats," **Gabriel Robbie, Ph.D.,** and **Win Chiou, Ph.D.**
- "Data imbalance and parameter estimation in longitudinal pharmacokinetic studies," **He Sun, Ph,D. Dr.** Sun won second prize for best podium presentation.

Some directions for future science days include a debate format because differences of opinion among scientists really do exist, opening attendance to the Office of Generic Drugs and others as well as developing a historical database of SD through OCPB's Web site.

The fifth science day was an excellent professional development exercise, an intellectual learning experience and an opportunity to discuss science one-on-one with colleagues.

Lydia Kieffer, Pharm.D., is an OCPB reviewer; Larry Lesko, Ph.D., is OCPB Director and Vanitha Sekar, Ph.D., is an OCPB reviewer.

Final Rule Requires Labeling for Drugs Important in Treating Kids

FDA announced on Nov. 27 final regulations to require labeling information for the safe pediatric use of new drugs and biologics that are therapeutically important for children or will be commonly used in children.

Every year more than half of the newly approved drugs and biologics that are likely to be used in children lack information to permit safe and effective use. Without adequate information, physicians may be reluctant to prescribe certain drugs for their pediatric patients, or they may prescribe them inappropriately. The new rule makes it more likely that children will receive improved treatment because doctors will have more complete information on how drugs affect children and what age-appropriate doses are needed.

The rule also allows FDA to require pediatric testing of already-marketed products in certain compelling circumstances such as when a drug is commonly prescribed for use in children but the absence of adequate labeling could pose significant risks.

FDA issued a regulation in 1994 simplifying the type of information needed to demonstrate the safety and effectiveness of drugs in children to encourage drug manufacturers to submit pediatric data voluntarily for review. While these voluntary efforts were helpful, there are still a large number of drugs and products without adequate pediatric labeling.

The final rule allows pediatric data to be submitted after a drug has already been approved if FDA has safety concerns about testing the drug in children before testing it in adults is finished. FDA, however, will not delay the approval of a drug for adults if the pediatric studies are not yet completed. Even if the drug is one that is commonly used in children or will be therapeutically important for children, the pediatric study requirement can be waived entirely if:

- FDA finds that the product is likely to be unsafe or ineffective in pediatric patients.
- Pediatric studies are impossible or highly impractical.
- Reasonable efforts to develop a pediatric formulation have failed.

FDA's Scientific Awards Ceremony Honors 10 Center Scientists

Ten CDER scientists were honored at the 1998 FDA Scientific Achievement Awards ceremony held Dec. 9 as part of the Agency's Science Forum held at the Washington Convention Center.

- **Frank. D. Sistare, Ph.D., Karol L. Thompson, Ph.D.,** and **Barry A. Rosenzweig** received a Center-level Excellence in Laboratory Science Award for identifying genetic instability in a transgenic mouse carcinogenicity model and for discovering a genetic marker to identify, explain and eliminate the nonresponder phenotype.
- **Abdul J. Sankoh, Ph.D.** and **Mohammad F. Huque, Ph.D.,** received a Center-level Excellence in Review Science Award for outstanding contribution to the statistical review process through innovative research about the effects of multiplicity on design and analysis of clinical trials
- **Robert C. Nelson, Ph.D., David J. Graham, M.D.,** and **Susan L. Lu, R.Ph.,** were CDER members of the Pharmacovigilance Project Advisory Group nominated for the Outstanding Intercenter Scientific Collaboration Award for the development of improved pharmacovigilance structure and functions within the new Adverse Event Reporting System consistent with sound epidemiological principles.
- **Yuan-Yuan Chiu, Ph.D.,** and **Carol Keller Vincent, M.S.,** were Center members of the Transmissible Spongiform Encephalopathy Working Group, nominated for the Outstanding Intercenter Scientific Collaboration Award for outstanding scientific leadership in analyzing risks of TSE transmission via regulated products and issuing regulations and guidances to industry to safeguard public health.

20 Regulatory Science, Review Grants Receive Funding for FY 1999

(Continued from page 1)

review of NDAs.

- **H.M. James Hung, Ph.D.**—Adaptation of design/analysis and strength of evidence in clinical trials.
- **Kun Jin, Ph.D.**—Clinical decision rule and statistical support structure: An innovative way to handle the multiple endpoints problem.
- **Ken Kobayashi, M.D.**—Comparative review of oncology Phase I dose escalation designs.
- **Karl Lin, Ph.D.**—The establishment of a CDER/FDA carcinogenesis bioassay database.
- **Chandra Sahajwalla, Ph.D.**—Mechanistic basis for age dependent differences in pharmacokinetics.
- **Surendra Shirvastava, Ph.D.,** and **Don Hare**—Application of DPK Approach in drug bioequivalency determination.
- **Ana Szarfman, Ph.D.,** and **Joyce Korvick, M.D.**—Improvement of the analytical processes involved in reviewing the safety data of an NDA.
- **Ana Szarfman, Ph.D.**—Uncovering potential serious adverse drug events in pediatric and geriatric subpopulations using data mining techniques.
- **Vijaya Tammara, Ph.D.**—Application of novel pattern recognition tools to predict the impact of formulation and manufacturing variables on product quality.
- **Yi Tsong, Ph.D.**—Equivalence assessment with multivariate or multiple endpoint data.
- **Rae Yuan, Ph.D.**—Standardization of *in vitro* methodology used to determine CYP metabolic activity.
- **Jenny Zheng, Ph.D.**—Simulation approach for optimal dose selection in clinical trial.

I want to thank everyone for their interest in this program and especially those who took the time to submit an application as well as all who participated in the review of the projects. Congratulations to all principal investigators.

Janet Woodcock is Center Director