news along the pike

APRIL-MAY 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

VOLUME 6, ISSUES 4, 5

INSIDE . . .

PIKE'S CORNERS

'Love Bug' Repelled from CDER

Quick Response Isolates, Eradicates Destructive Virus

On May 4, the "IloveYou" virus spread worldwide from its origin in Manila, the Philippines. While millions of computers worldwide were severely hampered by the virus, CDER e-mail and its infrastructure systems were marginally affected. A quick response effectively isolated and eradicated any reported instances of the virus within CDER and prevented a potential electronic information catastrophe. Only a few Center employees received the e-mail virus attachment. Once opened, none of the attachments were able to infect CDER systems.

There are a growing number of variants of this "worm" virus being transmitted via e-mail attachments. They have different subject lines and attachment names than the original "IloveYou" subject.

This worm attempts to send copies of itself through address book entries and then tries to overwrite several types of files. This action can overload e-mail servers and corrupt files located within computer systems. One variant, "VBS/LoveLetter.worm," will attempt to download and install a file on your computer that will e-mail any stored passwords it finds to e-mail addresses outside of the Center. As a general rule, you should be wary of and avoid opening any e-mail you receive from an unknown or obscure source. Your safest choice would be to delete the e-mail without ever opening it.

(Continued on page 12)

CDER Labs Earn Accreditation for Animal Care

BY CELESTE BOVÉ

The Center's laboratories on March 8 received accreditation from an international association that promotes the humane treatment of animals in scientific research. Not only did CDER obtain accreditation, but did so with no deficiencies and only six suggestions for improvement—an almost unheard of achievement considering the intensive nature of the review.

CDER joins three other FDA centers—CBER, CVM and NCTR—and more than 600 research organizations throughout the world to earn accreditation from the Association for Assessment and Accreditation of Laboratory Animal Care International. The nonprofit organization operates a program of voluntary accreditation and peer-reviewed assessment programs. Attaining and maintaining the association's accreditation provides assurance of quality research programs involving animals, evidence of compliance with required regulations and conformance regarding recommended policies or guidelines.

Accreditation procedures are based on an in-house self-evaluation and description of the animal program followed by an on-site visit from a team that includes veterinarians specializing in laboratory animal medicine and researchers familiar with the care and use of animals.

The comprehensive evaluation incorporates professional judgment and performance-based criteria. The site visitors critically review and assess the overall animal care and use programs including institutional commitment and implementation for humane care. The accreditation is for a three-year period at which time the process is repeated to allow for program recertification.

The FDA's Institutional Animal Care and Use Committee began the process in 1992 that led to accreditation. The committee was motivated to bring Agency laboratories into compliance with the Animal Welfare Act and other regulations governing the use of animals in research. However, in order to obtain accreditation, the physical plant must be able to perform appropriately. Until some of the deficiencies in the building housing CDER labs were corrected, the Center didn't apply for accreditation. After plant improvements were made, CDER staff started in earnest in January 1999 preparing the application packet and confirming that

(Continued on page 12)

JOE'S NOTEBOOK

Office of Women's Health

Back in the dark ages when I took an introductory psychology course, I learned more than I cared to know about how rats press levers and run mazes. It turns out that I had learned even less than I thought I had learned and carried around a serious misconception for more than two decades. What I actually learned was how *male* rats press levers and run mazes.

At the time, one of the bright proto-feminists in my study group asked: "Why are all these experiments done with male rats?"

The graduate assistant imperiously told us: "Whenever we run an experiment, we try to control as many variable as we can. Because female hormones cycle, they add an uncontrolled variable."

I soon forgot most of what I learned in that course, but the message about male and female subjects in experiments lay undisturbed and unchallenged until I began working for HHS. The first scientist to disabuse me of my misconceptions was **Patricia Grady, R.N., Ph.D.,** now head of NIH's National Institute of Nursing Research. She explained how the past pervasiveness of those misconceptions had created large gaps in our knowledge about women's health and how to treat and prevent illness in half the population.

So, it was with the notion that I may have many misconceptions that need reappraisal that I accepted an invitation from **Jonca Bull, M.D.,** to learn more about the FDA's Office of Women's Health and share it with you. Dr. Bull, the acting director, explained OWH is more than a source of grants for Center scientists. Founded in 1994, the office is the focal point within the Agency for women's health issues in regulatory science and in the Agency's outreach to women consumers.

I learned that the office is much more than intramural research grants and has a great deal of experience in outreach to nontraditional stakeholders. **Marsha Henderson,** who is in charge of the outreach program, that in its three and a half years of operation the "Take Time to Care" campaign has reach 6.5 million women. The program has leveraged the resources of national non-profit organizations, business, associations and women's and ethnic groups to deliver an urgent message to women nationwide: "Use Medicines Wisely." The program makes use of a colorful and compact brochure with tips for taking medicines and a record card for tracking medicine use. The program recently received a prestigious HHS Secretary's Award.

The Gender Effects Scientific Council, co-chaired by Dr. Bull and CDER's **Sandy Kweder, M.D.,** addresses scientific and policy issues related to gender-specific responses to products. The council is responsible for policies regarding women in clinical trials, provides a forum for advocacy of women's health issues within the Agency and gives advice to conference and seminar organizers seeking FDA experts on women's health issues.

The scientific research program began in 1994 and is managed by **Margaret Miller, Ph.D.** The program funds intramural research projects aimed at improving the Agency's policies and decisions on women's health issues. Over the past six years, it was funded about 90 high-priority women's health projects with more than $8 million in grants.

Projects included basic and clinical research on autoimmune disease, cancer, cardiovascular disease, contraceptives, developmental and reproductive toxicology, gender differences, sexually transmitted infections, osteoporosis and pregnancy. The program has also funded several projects designed to examine gender differences in adverse events.

Other members of the office are **Kennerly Chapman,** project officer, and **Patti Bradfield** and **Deborah Douglas,** administrative staff. Take a moment to check out their newly redesigned Web site at http://www.fda.gov/womens.

news along the pike

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

http://www.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:

NEWS ALONG THE PIKE
CDER Office of Training
and Communications (HFD-200)
Parklawn Building, Room 12B-45

Editor: Norman "Joe" Oliver (OLIVERN)
Phone: (301) 827-1670
Fax: (301) 827-3055

OMBUDSMAN'S CORNER

'FDA Made Me Do It'

BY JIM MORRISON

In December and January, I focused on pet peeves about the industry from CDER reviewers. This time, I'd like to add one of my own. It seems that some people in drug company customer service departments and some pharmaceutical sales representatives have developed a new strategy. Whenever they get a complaint about their product, they just say that FDA made them do it. Over the years, I have received occasional questions from people who were told that FDA made a company do whatever was the subject of the complaint, but lately it has become a much more frequent occurrence.

For example, just recently I received several complaints alleging that drug company representatives said they couldn't change the size of the packaging, because FDA made them put the drug in that container size. Alternatively, one person was told that the company would have to redo all of its studies in order for FDA to allow a change in packaging. The implication was that they would have to retest the drug for safety and effectiveness, not just stability.

Another person was allegedly told that the same product was given two different names because FDA required it. Now, in rare instances FDA has asked companies to give a different name to a drug with a new indication, but only when safety issues were involved, such as special warnings, dosages and routes of administration. The complaint I'm concerned about involved a drug product that is sold under two different names purely for marketing reasons, a practice that FDA usually tries to discourage.

> "I don't think it's a conspiracy. It's more likely the result of misinformed employees."

This shifting of blame doesn't involve just one or two companies. It is such a common element in complaints about drugs made by different companies, that it appears to be a growing industry practice. I don't think it's a conspiracy. It's more likely the result of misinformed employees.

My appeal is to the folks at pharmaceutical companies who have opted to take this easy approach to dealing with complaints from consumers and health professionals. Every organization makes mistakes and unwise decisions. FDA certainly makes them, and when we do, it is difficult to explain to the public why they occurred. I certainly can empathize with customer service personnel, since a significant part of my job is handling complaints. But passing the buck eventually hurts the credibility of those who try to shift responsibility.

I am grateful to people who seek me out to confirm that FDA really did require that companies do these things. It gives me a chance to set the record straight. But I know that for every one of these questions I get, there are perhaps hundreds of people who don't bother to ask or who are all too willing to believe in the inherent stupidity of government agencies.

I also ask CDER staff to please let me know when they get a complaint from someone who was told by a drug company: "FDA made me do it." It will help me track this trend and try to find ways to address it.

Jim Morrison is the Center's ombudsman.

Employee Children Get Educational Look at Their Parents' Workday

BY SHELLEY JOHNSON AND LYNDA PAPIO

The Center held a fun and educational event for children ages 7 to 14 on April 27. At each location, CDER employees presented a morning program that pertained to the specific functions they performed at that site. At the Parklawn and Corporate buildings, activities included an overview of the drug review process.

At Woodmont II, the children discussed good drugs or medicines vs. bad or illegal drugs and the manufacture of safe drug products. They then broke into teams and developed their own "new medicine" complete with an ad campaign. Each team then presented a poster with information on their new drug, what it does, how it works, the underlying data, adverse reactions and a catchy name of the drug and their drug company. A few of imaginative examples were:

- "Can-be-gone," a chewing gum to cure cancer.
- "Go Gas Go," a treatment for stomach gas.
- "Sniff-not," a therapy for runny noses with the main side effect of a purple-striped nose.

After each presentation, the group voted to approve, make approvable or not approve each product. The junior CDER reviewers approved most of the drugs, but wanted Phase 4 studies to be conducted. Only one was sent to an advisory committee prior to approval.

The MPN I site activity entailed an overview of space allocation followed by a hands-on demonstration of developing floor plans. Each participant created and designed an office suite for a staff consisting of five employees. This involved building and replacing walls, placing electrical outlets and phone lines followed by selecting furniture and computer equipment. The children were very creative and presented a wide variety of stylish "executive" offices.

Several locations included games related to FDA responsibilities at the end of their programs such as "Who Wants to be a Millionaire at FDA" and word match games. During the afternoon children shadowed their parents to experience and learn about a typical workday at CDER.

Certificates, T-shirts and goody bags were presented to each child at the conclusion of the program.

Special thanks to the speakers and volunteers who helped make this event a success: **Mary Baucum, Tony Chite, Tricia DeSantis, Barbara Durst, Tom Hassall, Jamey Henneberger, Pat Gathers, Patty Littleton, Darek Maciasz, Julie Nguyen, Carol Norwood, Ellen Shapiro, Joanie Sitman,** and **Wendy Stanfield.**

Shelley Johnson and Lynda Papio are quality of work life coordinators and management analysts in the Office of Management.

Q&A Session with OIT Director

Editor's Note: This Q&A is with **Ralph Lillie,** Director of the Office of Information Technology. OIT is responsible for all information technology initiatives in CDER and is heavily involved in guiding the Center toward electronic submissions and a paperless review environment.

Until last year, Mr. Lillie served as the deputy director of the new Office of Post-Marketing Drug Risk Assessment, the organization charged with implementing the new Adverse Event Reporting System and administering the re-engineering of post-marketing drug safety.

Ralph Lillie is a 20-year FDA veteran with experience in new drug review divisions including antiviral drug products, oncology drug products and endocrine and metabolic drug products. Mr. Lillie is a pharmacist and has an master of public health in epidemiology.

Q: What type of work does OIT perform?

OIT is a large and complex organization consisting of an immediate office, three divisions and two staffs. The total size is around 120 persons with a large number of contractors. This may seem big; but, by industry standards, it is relatively small for the responsibilities we carry. For example desktop support in industry is usually at the level of 40 to 60 users per support person. CDER runs about one support person per 120 users. The principle components of OIT are:

- *The Immediate Office.* The director, deputy and associate directors, administration, procurement and project management.
- *Quality Assurance Staff.* Quality assurance, quality control, database management and quality guidance.
- *Technology Support Services Staff.* Computer training, Web design, procurements, security and electronic submissions.
- *Division of Infrastructure Management and Support.* Technical support from the desktop to the network and beyond, including the Help Desk.
- *Division of Application Development and Services.* Application development such as COMIS and Division Files System.
- *Division of Database Management and Services.* Electronic Document Room management, document room management and and Orange Book.

Q: Where is OIT?

OIT is not so much a physical place as a virtual concept, a state of mind if you will. Actually we are located in the Park Building, one of the buildings behind Parklawn Building north of the south parking lot. We moved in this new site in January from several locations in Parklawn and Nicholson Lane. The initial phases of the move are complete. The next phase, which will include additional equipment and a new training room, is in the planning stages. Rumors to the contrary, we haven't built a moat around the building.

In addition, we are in every CDER building. We have desktop support personnel positioned throughout the Center to provide onsite customer service.

Q: What are OIT's top projects?

We have many projects in the mill and many more coming down the pike. Some of the priority projects we are currently involved in include:

- *Electronic Charge and History Card Rewrite Project*, needed for version 2.0 of DFS.
- *DFS Version 2.0*, which will supply electronic signature capability, paper copies and update databases, all critical to moving forward on Electronic Regulatory Submission and Review and meeting our paperless goals for 2002.
- *International Conference on Harmonization M-2.* Establishing and maintaining electronic standards for pre- and post-marketing adverse event electronic submissions and the common technical document.
- *Adverse Event Reporting System.* AERS including electronic submissions of adverse drug reports, the E-Prompt project for paperless expedited reports and the ADR Datamart to be used by the new drug reviewing divisions.
- *FACTS/EES.* ORA and CDER integration for inspection information.
- *E-Doc Query Project.* Ultimately, this will be a single, seamless query tool for CDER users to access all document types, images, data and documents.

We are also heavily involved in the Oracle and OpenVMS upgrade; an OIT process improvement; the corporate database redesign project; our MS Exchange implementation project; the Dark Fiber Project to increase bandwidth and

(Continued on page 5)

June IT Training

Monday	Tuesday	Wednesday	Thursday	Friday
			1	2
5 **CDER Standard Letters System 5.0** 9:00-11:00	6	7 **Intro. Word 97** 9:00-12:00 **Word 97 Formatting** 1:00-4:00	8 **Word 97 Tables** 9:00-12:00 **Intro. PowerPoint** 1:00-4:00	9 **PowerPoint Charts** 9:00-12:00
12	13	14 **NEST** 9:00-12:00 **DFS** 1:00-4:00	15 **Intro. Access** 9:00-12:00 **Access Queries** 1:00-4:00	16 **Access Form Design** 9:00-12:00 **Access Report Design** 1:00-4:00
19 **MS Project for CDER PMs** 9:00-12:00 **Creating PDF Documents** 1:00-4:00	20	21 **NEDAT** 9:00-12:00 **DFS** 1:00-4:00	22 **CDER Standard Letters System 5.0** 9:00-11:00	23 **Intro. TeamLinks** 9:00-12:00 **TeamLinks Attachments** 1:00-4:00
26	27	28	29	30

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

OIT Posts Sample Format for Patent Submissions on WWW

In an effort to expedite publication in the Orange Book of patent information for recently approved new drug applications, OIT's Division of Data Management and Services has posted a patent submission sample format on the CDER Internet site.

The sample format is available in both HTML and PDF formats and can be found at:

- http://www.fda.gov/cder/orange/patdecl.htm.
- http://www.fda.gov/cder/orange/patdecl.pdf.

Previously, drug companies had to rely solely upon the Code of Federal Regulations (21 CFR 314.53) to determine information to be submitted to the Agency regarding their patents.

Although the regulation indicates the data elements needed, no format was included for the submitting data. This resulted in incomplete submissions. Timeliness of patent submissions is a critical factor in the generic drug approval process.

A PDF document containing information from CDER's patent and exclusivity database is posted on the CDER Website under regulatory information and contains the most current patent and exclusivity information.

This information is also available in a drilldown from any of the search categories of the Electronic Orange Book. In addition, the data files used to create the patent and exclusivity information for the Electronic Orange Book are available on the Internet as part of the Electronic Orange Book data set.

The OIT point of contact is **Mary Ann Holovac, R.Ph.** (HOLOVACM).

Lillie Outlines Priorities, Projects for Information Technology Support

(Continued from page 4)

performance for all CDER functions and applications; a remote connectivity project review at home project; secure electronic e-mail; and an enterprise computing architecture project. As you can see, in addition to all of the work on Electronic Regulatory Submission and Review, we have a lot on our plate, with more to come. You can find copies of our approved project descriptions and the current list of our priority projects on the OIT Web site (http://oitweb).

Q: What kinds of support can we expect from OIT? Desktop? Electronic Submissions?

OIT is highly aware that end user computer support is critical to the Center and its mission. We are in the process of a desktop support initiative that will increase our ability to provide support with more efficient contract support, identified building leads, standard operating procedures on process and implementation of user feedback and appeals. We are also in the midst of a Web redesign project that will provide increased, user-friendly information to users inside and outside of CDER. We are re-engineering our procurement process in service contracting and physical handling of hardware.

In the area of electronic submissions, we will continue to offer and expand our ERSR training curriculum that includes instruction on desktop as well as customized applications used directly in the electronic review process. We are also exploring other mechanisms (FTEs, contract employees or details) of IT savvy trainer and support personnel who will work directly in the office with reviewers working on electronic submissions and application or data problems. These initiatives do not stand alone, and the achievement of each is vital to OIT's success in providing support to our end user communities.

Q: When can we expect Microsoft Outlook and Exchange in the Center?

As of now, the assessment of the migration to Microsoft Exchange Service is ongoing, and we plan to initiate a large pilot in the Center this fiscal year with the potential to expand to full production if no major problems are encountered. Many new issues are being generated by this process regarding how the Center uses e-mail, including storage capacity, types and sizes of attachments and so forth which will be addressed in a MaPP currently being drafted for comment.

Q: When can we expect Windows 2000?

Windows 2000 and Windows NT are now accepted as desktop and server standards for the Agency. There are advantages to these newer operating systems including distribution of upgrades, faster processing and increased hardware capabilities; but, as with any newer investments, we have to consider all of the variables in the cost-benefit equation. A small but critical piece is not getting too far out of sync with other Agency components and creating incompatibilities. Currently these products are part of our larger software and hardware strategic planning for central purchasing but are not in the immediate future.

Q: When can we expect everyone in the Center to start using the Division Files System?

We are currently scheduled for version 2 of DFS to be in production by midsummer. With this version, the system can then be used primarily to create, store and track review documents. We are making all efforts to meet this window and chances of success look good.

Q: How does OIT work with other FDA centers, industry and the public to provide IT support?

We interact with our sister centers on electronic submission and review projects including CBER, ORA and the Office of Information Resources Management at the FDA level. Industry interactions include a variety of activities under the PhRMA umbrella in the user fee area and electronic policy and guidance directions.

In addition, we are active in the international areas in the electronic transport areas. Another major collaborative IT area is the variety of Web sites in OTCOM that provide guidance on electronic policy and actual data along with data available through the National Technical Information Service.

EEO CORNER

Asian Pacific American Heritage Month Observed in CDER

BY GLORIA MARQUEZ SUNDARESAN

May, designated as Asian Pacific American Heritage Month, once again brings attention to the annual presidential proclamation that recognizes Asian Pacific American contributions to this country.

In the late 19th century immigrants from China began arriving to this country. They were later followed by the Japanese, Filipinos, Koreans, Asian Indians and other Asian groups. In the past, Asians provided labor and support to the growing railway and agricultural industries. The Chinese provided intensive labor in the completion of the western half of the first transcontinental railway, a badly needed link to the Pacific. The Japanese and Filipinos provided labor in pineapple farms in California and Hawaii.

Today, the contributions of Asian Americans are felt in all aspects of American life, including health care, national defense, academia, public service, education, sports, Congress, finance, arts, information technology and space exploration.

For years the sons and daughters of immigrants from Asia shared their creative talents, skills and dedication to make this country great. In science, David Ho stands out as *Time* magazine's 1996 man of the year for his research on the AIDS virus that gained international recognition. For skating enthusiasts, there is the sheer joy of watching Michelle Kwan and Kristi Yamaguchi twirl and momentarily suspended in space. Both have dominated the Olympic figure skating competition.

On the golf course, we have Tiger Woods and Vijay Singh. In public service we have seven Asian Pacific Americans in Congress; Gary Locke, governor of Washington State and the first Asian American elected to head a mainland U.S. state; and Yvonne Lee, one of eight commissioners of U.S. Commission on Civil Rights.

The Boston Symphony Orchestra has two renowned Asian members: its director, Seiji Ozawa and cellist, Yo-Yo Ma. NASA employee Kalpana Chawla holds a doctorate in aerospace engineering and is a member of the Columbia Space Shuttle. Not to be forgotten are Asian Pacific American soldiers who fought in the different wars that this country was involved in defending freedom all over the world. In business, more and more Asian Pacific Americans are joining the list of CEOs including Thinh Tran, Charles Wang and Yahoo! co-founder Jerry Yang.

Today, HHS has an APA group working to implement the White House Asian American and Pacific Islander Initiative, which was signed by President Clinton in June 1999. Members of this group include **Shamina Singh** who is the executive director and her staff: **Ruby Lam, Charmaine Manansala, Lisa Hasegawa, Christie Onoda, Neolani Kayetani** and **Angie Comeau.** This group works hard to improve the participation of Asian Pacific Americans in federal programs as well as their quality of life in the federal sector and the community.

To observe the APA Heritage Month, CDER set up a display, "APA Women of Hope," honoring Asian Pacific American women who have made a significant contribution to this country. In addition, the Center participated in a one-day APA Heritage Month program and leadership training conference held May 25 in Parklawn.

At present, Asian Pacific Americans make up about 3.8 percent of the U.S. population. By 2050, one in 10 Americans can be expected to trace their heritage to Asian Pacific Americans.

Gloria Marquez Sundaresan is a member of the Center's EEO Staff

REVIEWER AFFAIRS CORNER

Vote of 177-23 Favors Continuation

The Reviewer Affairs Committee received 200 responses to its survey on the status of the group. There were 177 votes in favor of continuing the RAC and 23 votes for disbanding it. Many of those voting to continue the committee expressed a desire that it function in its traditional way.

The Center would like to honor reviewers' preferences; however, discussions with the NTEU have to take place before a final decision can be made. CDER management, RAC leadership and the NTEU are engaging in discussions on how best to proceed.

On March 29, the Design Team and Best Practices Subcommittee held its second workshop. Individuals responsible for the success of this event were co-chairs **Jean Yager** and RAC representative **Sousan Altaie** along with workshop facilitators **Deborah Kallgren, Fred Marsik, Lana Pauls, Luqi Pei** and **Mary Jane Walling.**

This group has identified the qualities of successful and unsuccessful multidisciplinary review team. Some of the topics discussed included preparedness of the team, mutual respect between disciplines, proper documentation of meetings, decision-making skills, communication and the influence that leadership has on the team. Additional details will be provided in the near future.

The Comparable Pay Subcommittee would like to remind the disciplines to contact their RAC representatives or send an e-mail to the RAC account to obtain information on how to approach the possible implementation of comparable pay within a discipline.

Tuegel Earns 1st Award For Excellence in Support

CDER celebrated support staff excellence March 8 when **Patricia Tuegel** was presented with the first Quarterly Support Staff Award. Members of the Support Staff Coordinating Committee surprised Patricia at work with balloons, a plaque and a time-off award.

Patricia's supervisor, **Peter Cooney, Ph.D.,** associate director for microbiology in the Office of New Drug Chemistry, said of her in his award recommendation: "Her performance in this position has exceeded the highest standards of leadership, innovation and professionalism."

The Quarterly Support Staff Award is part of committee's ongoing mission to recognize and reward outstanding performance by Center staff.

COMPLEX DRUG SUBSTANCES COORDINATING COMMITTEE

Large Molecules Present Scientific, Regulatory Challenges

BY MEI-LING CHEN, PH.D., AND YUAN-YUAN CHIU, PH.D.

In June 1998, CDER established the Complex Drug Substances Coordinating Committee as the primary body to coordinate scientific and technical issues related to complex substances that are contained in drugs or used to manufacture drugs and are regulated by the Center.

The committee defines complex drug substances as:

- Macromolecules, which are very large molecules such as proteins.
- Mixtures of many macromolecules.
- Mixtures of macromolecules and small molecules.
- Mixtures of many small molecules.
- Substances produced by the use of complex biological systems.

Many of these complex drug substances are natural products extracted from plants or from organs, tissues or the body fluids of animals or humans (except human blood).

Unlike drugs that are made of purified, small molecules, complex drug substances are difficult to characterize chemically. In certain cases, a product is defined by its manufacturing process, and a product can be process specific. For these reasons, it is challenging both scientifically and regulatorially to determine if complex drug substances are comparable before and after manufacturing changes or to decide if they are therapeutically equivalent when they are made by different firms.

It is equally challenging to determine the "sameness" of two complex drug substances under the orphan drug regulation for establishing exclusivity.

Furthermore, unlike other drugs that are synthesized chemically, many complex substances require documentation and validation studies on the biological identity and purity of the naturally occurring or genetically engineered source materials. Manufacturers must show the absence of contamination by viruses and other human pathogens including the bovine spongiform encephalopathy agent.

In order to address all the issues surrounding complex drug substances, the committee has been formed with multidisciplinary members from the different centers in FDA. The committee also provides oversight for CDER members serving on the intercenter working groups for transgenic plants and the International Conference on Harmonization document on biotechnology products. There are three technical subcommittees and seven working groups involved with guidances, issues and topics concerning complex drug substances, excipients and reagents.

The technical subcommittees deal with proteins used as active ingredients and reagents, excipients (liposomes and cyclodextrins) and synthetic peptides. The working groups handle cell metabolites derived from genetically engineered cells, natural and synthetic conjugated estrogens, botanical drugs, bovine spongiform encephalopathy, antibiotic fermentation, synthetic oligonucleotides and comparability protocols.

Many documents for policies and scientific standards have been drafted or are under development by the technical subcommittees and working groups. Conjugated estrogen products provide an excellent example to illustrate the complicated issues facing the committee and its accomplishments.

The committee has drafted and forwarded to the U.S. Pharmacopoeia for its review and adoption monographs on natural conjugated estrogen drug substance, synthetic conjugated estrogen drug substances and synthetic conjugated estrogen drug products.

The committee recently issued a draft guidance for industry on a method suitable for characterizing the more than 100 components present in natural conjugated estrogens. Another draft guidance on chemical characterization, documentation of pharmaceutical equivalence, bioavailability and bioequivalence of natural conjugated estrogen is close to being finalized.

These three different documents for natural conjugated estrogen have been written partially based on the analytical method developed by CDER's laboratory and the results of their analytical studies performed on Premarin.

Availability of generic products containing synthetic conjugated estrogens and, more importantly, natural conjugated estrogens will be possible when the monographs and guidances are finalized and followed by drug sponsors and applicants.

Mei-Ling Chen and Yuan-yuan Chiu are co-chairs of the CDSCC.

Examples of Complex Drug Substances

Some typical examples of complex drug substances are:

- Human insulin and thyroid hormone derived from genetically engineered cells.
- Menotropins, containing follicle-stimulating hormone and leutenizing hormone, extracted from the urine of postmenopausal women.
- Alglucerase extracted from human placentas.
- Heparin extracted from porcine intestines.
- Beractant extracted from bovine lungs.
- Conjugated estrogens extracted from pregnant mare urine
- Many crude plant extracts.

Complex drug substances such as peptides and oligonulceotides are chemically synthesized. Synthetic oligonucleotides used in human gene therapy are regulated as drugs by CDER.

Many excipients such as liposomes and cyclodextrins contained in a drug product are complex substances.

Many reagents such as monoclonal antibodies, enzymes and bovine serum used in the manufacture of a drug are also complex substances.

Chemically, these complex substances can be peptides, proteins, oligonucleotides, oligo- and polysaccharides, lipids and phospholipids and conjugates of conventional drugs with macromolecules such as monoclonal antibodies.

They can also be mixtures of naturally derived small molecules such as steroids and plant sterols.

Finally, they can be cell metabolites such as antibiotics, amino acids and vitamins produced by recombinant DNA technology.

Keynote Speaker Discusses Usefulness of PK/PD Models

BY KOFI KUMI, PH.D., EMMANUEL FADIRAN, PH.D., LYDIA KIEFFER, PHARM.D., AND LARRY LESKO, PH.D.

Regulatory scientists within the Office of Clinical Pharmacology and Biopharmaceutics held their eighth science day March 13. The keynote speaker was William J. Jusko, Ph.D., professor of pharmaceutics, State University of New York at Buffalo. Dr. Jusko is a world-renowned scientist who specializes in clinical, basic and theoretical pharmacokinetics and pharmacodynamics of diverse drugs, particularly corticosteroids and immunosuppressants.

Dr Jusko's presentation was entitled "The Role of PK/PD Modeling in Drug Development." Dr. Jusko discussed the purpose of PK/PD modeling and the components of models. He gave examples of models and used a case study to illustrate the utility of modeling in drug development. The goals of modeling, he said, are to codify current facts, test competing hypotheses, predict system response under new conditions and estimate inaccessible system variables.

- Pharmacokinetics (PK) describes the action of drugs in the body over a period of time, including their absorption, distribution, localization in tissues, biotransformation and excretion.
- Pharmacodynamics (PD) is the study of the biochemical and physiological effects of drugs and the mechanisms of their actions.

He used an information flow diagram to illustrate how PK/PD affects drug discover, preclinical studies, clinical trials and regulatory decision making. He illustrated how PK/PD was involved in the development of a benzodiazepine antianxiety agent and the immunosuppressant drug tacrolimus.

Dr. Jusko concluded by noting that diverse mechanisms and processes control drug effects. There are a variety of mechanism-based models available for handling experimental data. PK/PD models allow rational use and coupling of *in vitro*, animal and human data for quantification and prediction of drug responses.

Intramural Presentations

Brian Booth, Ph.D., started the day's podium presentations with an update on a proposed guidance on analytical methods validation. Technical progress within the past decade has required additions to the proposed guidance, first issued as a report in 1992. He provided an update on a January workshop held to develop a consensus statement regarding bioanalytical method validation. The workshop was co-sponsored by the Association for the Advancement of Pharmaceutical Science and FDA. The consensus statement from the meeting is expected to assist in the preparation of the final version of the guidance.

Joette Meyer, Pharm.D., was the initial speaker in a series of presentations on PK/PD relationships in drug development. Dr. Meyer's presentation, "A comparative analysis of the concentration-effect relationship for two antibiotics in establishing cardiac safety," discussed a new antibiotic submitted for approval that was found to prolong the QT-interval of the electrocardiogram during development and another drug of same class also known to prolong the QT-interval.

The use of QT-interval data can establish a concentration-effect relationship for a drug and can be useful in comparing the safety of two related antibiotics. Since the concentration-effect response was similar for both drugs, Dr. Meyer concluded that data from the time of the new drug's actual maximum concentration demonstrated an improved correlation with effect compared to an analysis using a fixed time point.

Sam Haidar, Ph.D., pointed out some important shortcomings discovered in recent submissions in his talk, "Factors to consider in the design of PK/PD studies using QTc prolongation as a PD endpoint."

Some of the shortcomings involved using incorrect subjects and giving doses lower than the marketed doses, which resulted in erroneous conclusions between QTc prolongation and dose or drug concentration. Other studies failed to appropriately characterize baseline values of the QTc interval.

Elena Mishina, Ph.D., presented a talk entitled "Population PK/PD model for nitroglycerin as a supportive evidence in the approval of a new formulation." The objective of the talk was to establish a PK/PD model for comparing the pharmacodynamic effects of a newly developed nitroglycerin product and the marketed formulation.

The PD end-points were real time systolic-diastolic blood pressure ratio and the ratio of the pulse pressure value to the diastolic portion of the blood pressure waveform value. The results showed that the newly developed compressed tablets and the currently marketed reference tablet produced similar effects on peripheral vasodilatation when measured in the finger.

Dr. Mishina concluded that although the new formulation has not met the bioequivalence criteria with respect to Cmax of nitorglycerin, this inequivalence in plasma concentration did not seem to result in clinically significant differences in the PD effect.

Joga Gobburu, Ph.D., gave a presentation entitled "Chrono-Pharmacological Modeling of Ambulatory Blood Pressure Monitoring Data." The objective of Dr. Gobburu's work was to develop a nonlinear, mixed-effect model that describes the treatment effects of placebo and the antihypertensive drug diltiazem in patients with moderate to severe hypertension. The observed plasma concentrations were correlated with blood pressure measurements using a dual-cosine function for the placebo effect and a linear model for the treatment effect. Nonlinear, mixed-effects modeling was performed.

The contribution of age, body weight, race and gender in explaining the inter-individual variability was tested. The modeling exercise indicated that the asymmetric pattern in the circadian rhythm in blood pressure could be modeled using the sum of two cosine functions. None of the covariates tested showed significant influence on the model parameters.

Dr. Gobburu concluded that a correlation between diltiazem concentration and blood pressure was established. This relationship helped to better appreciate the

(Continued on page 9)

PIKE'S PUZZLER

Test Your Medical Spelling Skills

BY TONY CHITE

1. Excessive growth of the male breast is:
a. gynocomastia b. gynecomastia c. gynecomostia d. gynecomastio

2. A doctor trained in the diseases and other disorders of domestic animals is a:
a. veterinarian b. vetrinarian c. vetrenarian d. veteranarian

3. When one drug is joined with another in therapy it is said to be:
a. concommitant b. concomittant c. concommittant d. concomitant

4. A space devoid of air or other gases is a:
a. vaccuum b. vaccum c. vacuum d. vaccume

5. An abnormal frequency and liquidity of fecal discharges is:
a. diarrhea b. diarhhea c. diarrhhea d. diaorhhea

6. A place for serving meals to the public is a:
a. resteraunt b. restaurant c. restaraunt d. restoraunt

7. To disable or to deprive of strength or ability is to:
a. incapacitate b. incopacitate c. incapacotate d. incapasitate

8. That which is absolutely required is:
a. nesessary b. necessary c. nessecary d. neccessary

9. An exact copy as of a document is a:
a. fascimile b. facisimile c. facsimile d. facsemile

10. A form of dislocation in which there is separation of two bones normally attached to each other without the existence of a true joint is:
a. diastasis b. diasstasis c. diastassis d. diastisis

Answers to the spelling quiz:
1b; 2a; 3d; 4c; 5a; 6b; 7a; 8b; 9c; 10a

Tony Chite is a consumer safety officer in CDER's Freedom of Information Division.

PK/PD Contributions to Regulatory Decision-Making Highlighted

(Continued from page 8)

effect of biorhythm on blood pressure and the shallow nature of the effect.

In "PK/PD modeling as a legal aid: Diltiazem's twin-peak citizen's petition," **Patrick Marroum, Ph.D.** illustrated how PK/PD was used to support a regulatory decision regarding a citizen's petition requesting that a generic version of diltiazem not be approved because it failed to exhibit the same concentration and dissolution profile as the original product with regard to a second peak in plasma.

The relationship between plasma diltiazem concentration and blood pressure could be explained by a linear pharmacodynamic model. The concentration-effect, based on the model, appears to be shallow. Large changes in concentration elicit small changes in pharmacodynamics.

Dr. Marroum concluded that based on the predictions of the model, the Agency was able to argue that a second peak in plasma concentration, when present, is not clinically necessary for maintaining adequate blood pressure lowering effect over the dosing interval and is not controllable in terms of the formulation's delivery of drug to the plasma.

Posters

The 14 poster presentations, including one from the Office of Generic Drugs by **Pradeep Sathe, Ph.D.,** were:

- PK/PD modeling of QT prolongation, **Suliman Al-Fayoumi, Ph.D.**
- Narrow therapeutic index drugs: Preliminary definition and criteria, **Sayed Al-Habet, Ph.D.,** and others.
- Role of exposure-response relationship in drug development: Case studies, **Dhruba Chatterjee, Ph.D.,** and others.
- Reversal of P-glycoprotein-mediated multidrug resistance *in vitro* by antihistamines and diuretics, **Adorjan Aszalos, Ph.D., Safaa Ibrahim, Ph.D.,** and others.
- Current approaches: Evolution of pediatric exclusivity efforts in OCPB, **Suresh Doddapaneni, Ph.D.,** and others.
- Modulation of the function of P-glycoprotein in NIH3T3 and human capillary endothelial cells by Ca2+ channel blockers, Dr. Ibrahim and others.
- Non-parametric modeling to evaluate combined drug action, **Kooros Mahjoob, Ph.D., Joga Gobburu Ph.D.,** and others.
- Steps for development of a dissolution test for sparingly water-soluble drug products, **Carol Noory, M.S.,** and others.
- Population pharmacokinetics of Drug X, **Prabhu Rajagopalan, Ph.D.**
- Effect of pancreatico-billiary secretions on ranitidine absorption in humans, **Kellie Reynolds, Pharm.D.,** and others.
- Delivery-agent-facilitated pulmonary insulin absorption: Pharmacokinetics and pharmacodynamics in rats, **Sandra Suarez, Ph.D.,** and others.
- The use of bootstrap resampling method with model stability check in pediatric population pharmacokinetic studies, **He Sun, Ph.D.,** and others.
- Comparison of artificial neural network and multiple linear regression as dissolution predictors, Dr. Sathe, and others.
- Application of modeling and simulation to compare two dosage regimens of Drug X to treat intra-abdominal infection, **Jenny Zheng, Ph.D.,** and others.

Prizes

The top three podium prizes went to Drs Gobburu, Marroum and Haidar in order. Drs Ibrahim and Zheng shared the first and second poster presentation prizes, and the third prize went to Drs. Reynolds and Chatterjee.

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

Abstracts are available on OCPB's intranet site at http://cdernet/ocpb/PRESMAIN.HTM.

All the authors are members of OCPB, and Dr. Lesko is OCPB Director.

Reviewer Education Team Manages Four Broad Programs

The Division of Training and Development's Reviewer Education Team develops and coordinates a broad range of educational programs for CDER's staff. The team's overall goal is to provide all employees involved in the drug review process with the tools they need to perform quality and timely reviews, ensuring the approval of safe and effective medicines for the American public.

These tools range from basic information about drug regulations, ethics rules, freedom of information and protecting proprietary data to advanced information needed for complex regulatory issues.

The team has developed and currently manages four broad training programs to meet the educational needs of CDER's review staff, non-review staff and support staff. These four programs focus on general training, reviewers education and training, interpersonal skills for individuals and leadership and management development.

The General Training Program is offered to all CDER staff. New employees should take advantage of these programs within the first three months of joining the Center. Offerings include an orientation for new employees, time management and basic concepts in the drug review process for the non-reviewer.

The FDA Modernization Act mandated that each FDA center conduct training and education programs related to the regulatory responsibilities of new employees. Included in this general mandate is a specific reference to reviewer training, both basic and advanced.

The Reviewer Education Training Program provides reviewers with the skills needed to perform professional and timely drug reviews. Courses include workshops on issues for new reviewers, risk management, regulatory science, basic drug law and the regulatory review of investigational new drug applications.

In addition to critical scientific skills, our employees must communicate effectively with each other and their colleagues throughout FDA and with advisory committee members, industry representatives and with other external stakeholders.

The Interpersonal Skills Program provides training in basic presentation skills, conducting successful meetings and producing effective minutes.

In addition to technical skills, CDER's employees need to adapt to change through strong leadership and management skills. The Leadership and Management Development Program develops the Center's managers and team leaders. The courses offered are an eclectic mix of internal and external development opportunities and include the essentials of team leadership, an introduction to supervision and the CDER Leadership Development Program.

The team also coordinates and schedules the Technical Writing Program, a comprehensive series of courses designed to improve the overall capabilities of CDER staff in grammar, organization and basic writing style.

Additional courses provide instruction in managing the writing of others and in preparing to publish in a scientific or technical journal. Special sessions can be organized for senior CDER managers and personnel with individual writing challenges

The team manages a two-day training course to improve the communication skills of reviewers who present at advisory committee meetings.

The Reviewer Education Team's members are **Janice Newcomb** (acting team leader), **Sonya Armstrong, Dee Rhodes, Charlotte Henning, Debra Rose, Cheryl Kaiser, Noreen Gomez** and **Jim Mintner.**

If you have questions about the reviewer education programs, contact Janice Newcomb (NEWCOMBJ, 7-4580).

Review Science Research Grants Featured in Scientific Rounds

Scientific Rounds in February, March and April featured presentations of investigations performed by Center scientists. The individual research projects were funded under the Center's Regulatory Science and Review Enhancement Program. The investigators and their projects were:

- **Paul Andrews, Ph.D.,** Analysis of the developmental toxicity of anticancer agents.
- **Sandip Roy, Ph.D.,** Analysis of predictive value of preclinical studies for anticancer agents.
- **Karl Lin, Ph.D.,** The establishment of a CDER/FDA carcinogenesis bioassay database.
- **James Hung, Ph.D.,** Adaptive design/ analysis and strength of evidence in clinical trials.
- **Mohamed Al-Osh,** Evaluating the accuracy of diagnostic tests using the results of imperfect references.
- **Ana Szarfman, M.D.,** Improvement of the analytical processes involved in reviewing safety data of an NDA: Application of preprogrammed interactive graphical tools.
- **Steven Hirschfeld, M.D.,** Comparative review of oncology Phase I dose escalation designs.
- **Ajaz Hussain, Ph.D.** (for **Vijaya Tammara**), Application of novel pattern recognition tools to predict the impact of formulation and manufacturing variables on product quality.
- **Surenddra Shrivastava, Ph.D.,** Application of DPK Approach in drug bioequivalency determination.
- **Jenny Zheng, Ph.D.,** Simulation approach for optimal dose selection in clinical trials.
- **Soraya Madani, Ph.D.,** Evaluation of *in vitro* selectivity of cytochrome P450 substrates.
- **Chandra Sahajwalla, Ph.D.,** Mechanistic basis for age dependent differences in pharmacokinetics.
- **Mei-Ling Chen, Ph.D.,** Gender-related differences in drug pharmacokinetics: Do they translate in clinical outcome.
- **Badrul Chowdhury, M.D., Ph.D.,** Predictability of liver enzyme elevation during placebo treatment in clinical trials.
- **Albinus D'Sa, Ph.D.,** and **Silvia Calderon, Ph.D.,** Proposal for acceptable chemical and biological standards for botanical marijuana.

STUDENT PERSPECTIVE

Freedom to Choose Found Worth Confronting Anxiety of Change

BY DAREK MACIASZ

As a student in pharmacy school I had spent several years pounding out exam after exam, not realizing that I would soon have to pick out my three "practice sites." Practice sites provide different settings for students to apply what they have learned. At my school, for example, we are required to choose a hospital and a retail setting, as well as an elective, which can be almost anything.

At first, I was overwhelmed by the number of practice sites available. Then, years of negative feedback in from individuals who tried to make me believe that, after I graduated from pharmacy school I would have limited career opportunities. Being born and raised in Chicago, I was neither timid nor easily dissuaded.

With the deadline for picking practice sites approaching fast, I had chosen my hospital and retail sites. I had picked a clinical site for my elective, but I felt that my choices were too limited. To find more opportunities, I approached the dean of my college and the director of student practice sites. During a discussion I asked if they knew of a practice site that was different.

After brainstorming the idea for several months, the government came into focus. To my great surprise, I wasn't at all discouraged from pursuing this idea. In fact, it became a challenge for the three of us to locate a government rotation site. After seemingly endless phone calls and submissions of paperwork between the Agency and the school, I was fortunate enough to get accepted for a site with CDER's Drug Information Branch. At that moment, I felt proud to be an American because I would be helping my country to the best of my ability.

After the initial shock of the announcement set in, my immediate family and I faced a big reality check. What was I getting myself involved in? How expensive would it be. Would I survive the drive and being 13 hours away from the comforts of home. What would it be like to be part of an government institution that helps the whole U.S. population?

As many of these thoughts were at first overwhelming, others added to my anxiety by sharing their supposed insights on how the federal government worked. This constant badgering began to cloud my perspective. The mental strain that began to develop as time wore closer to my arrival at the FDA was nerve-racking. I began to think: Would I be able to fit in? Could I be successful in my rotation? Would I be able to learn all that there is to be offered by the government? Is it seriously true what people have said?

A lot of individuals back home had told me the people I would meet would be very snobbish and that if you don't fit in with the crowd I would be outcast. Well, don't believe everything people tell you.

I arrived in Maryland on Saturday, April 15, to begin my rotation on Monday. Great, I had two days to relax and familiarize myself with the area. On Sunday, I practiced the drive from where I was staying to FDA. Let me tell you, driving Interstate 495 is no problem on a Sunday. Driving on Monday morning was a nightmare. I thought the Kennedy in Chicago was bad, but this was just crazy. People have to drive 495 every day. No wonder they go crazy!

When I entered the Parklawn Building that first day, I was impressed and felt timid. All the governmental employees I met were sincere and willing to help. I was amazed at the people that work here. People back home had told me that I would just be a workhorse and that I wouldn't see or meet anybody since I'd be stuck working behind a desk all day. They were wrong.

My preceptors at the Drug Information Branch helped me really get a better understanding of the structure of FDA. They showed me how the drug approval process works from the inside and didn't just provide a textbook overview. They helped me in addressing issues when answering questions from members of the public by returning e-mails and phone calls. Yes, I did have to work, but I learned. It was easy to overlook the inconvenience of getting to work, because this was such a great opportunity. It was a great place to meet future healthcare professionals and people who will have a great impact on the public health of all Americans.

It was a feeling of freedom to have an opportunity to learn how I can be a part of and help my fellow Americans. We have the freedom to pursue what we want in life. If there is a barrier in the road you are traveling, find a different path, go around it, fly over it or dig a tunnel underneath it. I am grateful that my *alma mater*, the Chicago College of Pharmacy is open-minded and a true creator of freedom.

Darek Maciasz participated in the month-long pharmacy student mentoring program operated by the Drug Information Branch. The program enhances the Center's consumer education efforts. For more information, contact Barry Poole (7-3454, POOLEB).

CDER, Industry Confer on Creating New Knowledge

(Continued from page 12)

that tremendous progress had been made since the 1970s when there were explicit policies to keep contacts between industry and FDA to a minimum. At that time, he said, there was no progress because of a lack of constructive dialogue.

"Industry has shown that where there is a spirit of communication, real progress can be made," he said. As examples, he cited legislation in the 1980s and 1990s for orphan drugs, generic drug competition and user fees. He predicted a future enabled by electronic submissions in which industry and FDA can analyze and process data simultaneously.

The addresses were followed by panel discussions and questions and answers from the approximately 350 attendees.

Other Center speakers at the conference and their topics were:

- **David Lepay, M.D., Ph.D.,** clinical research quality and integrity.
- **Murray Lumpkin, M.D.,** fast track drug development; FDA integration with non-U.S. agencies and mutual recognition agreements.
- **Randy Levin, M.D.,** electronic submissions for NDAs, INDs and safety information.
- **Linda Carter,** financial disclosure: recent FDA guidances.

OIT's Quick Response Isolates, Eradicates 'Love Bug'

(Continued from page 1)

In order to ensure that CDER computers remain protected from this latest and any similar outbreaks the Center's Office of Information Technology took the following actions:

- During the crisis, CDER worked with the other centers to restrict access to Agency e-mail systems and computers. Access to the Web was blocked by the Agency's firewall while centers upgraded their virus protection software.
- OIT technicians updated McAfee, our desktop virus protection software, to the newest release. While this is routinely done, an immediate mandatory update was necessary due to the seriousness of this crisis.
- All incoming and outgoing e-mail is continuously scanned for any messages containing the 'IloveYou' subject line (or variants of this), along with checking all script attachments that may contain the virus code. Any messages that are infected are immediately deleted from our mail system.
- OIT is also implementing new software, to be activated at login time, that will automatically detect any files on your desktop that may have been infected by this new virus.
- OIT created an install from the OIT Website that will automatically copy McAfee to diskettes on your desktop. You can then take these home and upgrade your CDER loaned PC.

You should be aware that, even though all the other Centers have cleaned their databases, you might still receive e-mail with the 'IloveYou' virus. If you should receive this e-mail, please delete it at once and empty your wastebasket.

In some cases you may receive a warning e-mail from others with the subject: "The VBS/LoveLetter virus was found in e-mail." Please delete this message if you receive it.

Please contact the OIT Help Desk (HELP, 7-0911) if you suspect a virus has infected your computer or for more general information on computer virus protection.

CDER Labs Earn Prestigious International Accreditation for Animal Care

(Continued from page 1)

its program met the requirements of the regulations in order to meet an August deadline for submitting the application packet submission.

Many individuals contributed to the successful accreditation application:

- **Patricia E. Long-Bradley,** the primary contributor and coordinator, provided the major effort for the application process and was commended in the evaluation report.
- **Gene New, DVM, M.S.,** the contract CDER attending veterinarian, provided excellent fine tuning after a simulated site visit performed by several veterinarians from centers already accredited. Dr. New is a diplomate of the American College of Laboratory Animal Medicine, a difficult-to-obtain certification.
- **CAPT Ed Radden,** CDER safety officer, provided important information about occupational safety and health.
- **Robbe Lyon, Ph.D.,** chair of the Institutional Animal Care and Use Committee, and past committee chair **Donna Volpe,** past chairperson, provided input for program improvements and general support. The other CDER members of the IACUC—**Neil Hartman, Ph.D.,** and **Hirsch Davis, Ph.D.**—lent their support. Don Niebuhr, the non-affiliated member of the committee, was commended during the site visit for his involvement and enthusiasm.
- **Jim MacGregor, Ph.D.,** Director of Office of Testing and Research, provided very important administration support, described in the program evaluation as commendable.
- **CAPT Frank Sistare,** Director, Division of Applied Pharmacology Research, provided support throughout the process.

CDER assisted CDRH and CFSAN in their application process by inviting them to attend the site visit and providing CDER's application package and evaluation report to help with their application packets and program reviews. The assistance provided to those Centers by CDER was much appreciated and acknowledged at the FDA Research Animal Council.

Additional information about the Association for Assessment and Accreditation of Laboratory Animal Care International may be obtained through its Web site at http://www.aaalac.org.

Celeste Bové is a health scientist administrator in the OTR.

CDER, Industry Exchange Held at Temple University

PHILADELPHIA—"Industry and FDA share a common goal to get useful and helpful drugs on the market to help patients," said Center Director **Janet Woodcock, M.D.,** during the FDA keynote address at conference sponsored by the Temple University School of Pharmacy graduate program in quality assurance and regulatory affairs.

"It is essential for FDA and industry to work together and to have frank and open communication and share knowledge," she said. "We need to recognize that there are other parties. Standard setting activities are only credible if they include all parties, including the public. This is often hard to do because our scientists and industry's are the technical experts and want to move ahead. In the heat of scientific exchange, it's important to keep in mind that other parts of the public need to be included and their participation may be harder to obtain."

She used changes to standards as an example. It is relatively easy to obtain industry and FDA agreement on technical issues, she said. Although some patient groups have become very educated, many patients groups and most consumer groups worry that a standard change represents a diminution of consumer protections.

David W Blois, Ph.D., vice president for worldwide regulatory affairs at Merck Research Laboratories presented the industry keynote address at the April 4 conference called "Creating New Knowledge: FDA and Industry in Dialogue." He noted

(Continued on page 11)