news along the pike

NOVEMBER 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

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INSIDE . . .

PIKE'S CORNERS

MedWatch's Couig Named PHS Chief Nurse

Surgeon General and Assistant Secretary for Health **David Satcher, M.D.,** announced on Nov. 30 that CDER's **CAPT Mary Pat Couig** from the MedWatch Staff in the Office of Training and Communications will serve a four-year appointment as the Public Health Service's chief nurse officer. With her appointment, she is promoted to the one-star rank of assistant surgeon general. She is the first chief nurse officer selected from FDA.

Couig will be nursing's voice to Dr. Satcher on health issues, professional practice, personnel concerns and advocacy to and for nurses and nursing. She will represent more than 6,000 nurses, including more than 1,000 members of the Commissioned Corps. She will continue to work with MedWatch as time allows.

She earned a bachelor's in nursing from Fitchburg State College in Massachusetts and a master's in public health from The Johns Hopkins University. She began her career in the Indian Health Service as a clinical nurse in Fort Defiance, Ariz. Her clinical experience includes, medical, surgical and emergency nursing as well as quality assurance and infection control. Her special assignments have included consulting to the Rwandan Ministry of Health, to the chief nurse scientist at the World Health Organization and to the National Committee for Quality Assurance.

Kelsey Inducted into National Women's Hall of Fame

SENECA FALLS, N.Y.—**Frances O. Kelsey, Ph.D., M.D.,** was inducted into the National Women's Hall of Fame on Oct. 7 in this historic birthplace of the American women's rights movement. Dr. Kelsey, a pharmacologist and physician, has long been honored for her role in blocking approval of the drug thalidomide in the l960s. Her refusal to approve thalidomide for use in the United States earned her national recognition and her work led to strengthened regulation of the pharmaceutical industry.

Dr. Kelsey, who was born in 1914, continues to work for FDA in medical and scientific affairs in the Center's Office of Compliance. She points out that thalidomide was the first drug application to which she was assigned after joining the Agency in 1960.

That thalidomide was not marketed at that time in the United States was largely due to her concerns about insufficient data in the thalidomide application. She withstood pressure to approve the drug quickly. As she raised questions, news of thalidomide-induced birth defects from European countries demonstrated dangers of its use during pregnancy. President Kennedy awarded Dr. Kelsey the President's

(Continued on page 12)

CDER Fall Ceremony Honors 60 Individuals, 40 Teams

BY JACKIE BARBER

The Center presented 60 individual and 40 group awards at its Fall Honor Awards Ceremony on Nov. 3 in Gaithersburg. The Montgomery County Police Color Guard presented colors, and Kevin Barber sang the National Anthem. Center Director **Janet Woodcock, M.D.,** gave opening remarks, and **Ruth Clements** introduced each award. The office directors along with other presenters provided an explanation of individual and team achievements.

At the ceremony CDER for the first time presented the FDA Quality of Work Life Award. Another special presentation was the FDA Outstanding Science Teaching Award to individuals in the Center. Dr. Woodcock thanked those who managed the awards program as well as the CDER Peer Honor Awards Committee. FDA Commissioner **Jane Henney, M.D.,** was in attendance as well.

The following awards were presented:

FDA Commendable Service Award

Renata Albrecht, M.D.

Betty L. Jones

Frederic J. Marsik, Ph.D.

(Continued on page 8)

JOE'S NOTEBOOK

Trailblazing Role Models

Frances O. Kelsey, Ph.D., M.D., has been recognized by the National Women's Hall of Fame as "both a woman of courage and one of reason—demanding of herself and others in her profession high standards of science and integrity." Dr. Kelsey herself says that one of her medical and scientific role models was fellow National Women's Hall of Fame member Virginia Apgar, M.D. (1909-1974). Dr. Apgar is best known for the Apgar score, a simple and physiologically sound numerical expression of a newborn infant's condition.

A significant portion of the program at Seneca Falls, N.Y., the site for Dr. Kelsey's induction ceremony, was a special half-day educational program for high school students called "Come Talk with Great Women." Dr. Kelsey was one of several of this year's inductees to address about 450 students. At the time Dr. Kelsey received her degrees, fewer than 10 percent of America's graduate and medical students were women.

With great role models like Dr. Kelsey, it's hardly surprising that hundreds of women are making significant contributions to the public health as they pursue scientifically and medically challenging careers at CDER. Indeed, women make up 55 percent of all Center employees. Of the 1,096 positions in CDER designated as "professional," 45 percent are held by women, according the Center's EEO Staff. The percentages of CDER women in several specific career fields tracked by EEO are:

- General biological scientist—29 percent.
- Microbiologist—41 percent.
- Pharmacist—33 percent.
- General health scientist—64 percent.
- Medical officer—39 percent.
- Consumer safety officer—59 percent.
- Chemist—31 percent.

Women make up 35 percent of the membership of CDER's advisory committees, according to the Advisors and Consultants Staff.

It might be tempting to think that CDER's 11 percent increase in 10 years in women employees is representative. There's progress elsewhere—but not as rapid—according the National Science Foundation in the 10th of its series of biennial reports on women and minorities in science and engineering.

Some of the findings in the first NSF report issued in 1982 still apply—the relatively small percentages of women earning science and engineering degrees and employed in science and engineering fields; the concentration of women in specific fields; higher rates of part-time employment for women; lower salaries for women; and lower percentages of women in full professorships even when adjusted for time since earning a doctorate.

There is, of course, progress. In education, there have been increases in both the numbers and percentages of women completing high school, enrolling in college and completing undergraduate and graduate degrees. In 1966, for example, women earned only 8 percent of the doctorates in science and engineering. By 1997, they were earning 33 percent, with the highest percentages in psychology (67 percent), the biological and agricultural sciences (41 percent) and the social sciences (39 percent).

Women represented 36 percent of those employed in the life and related sciences in 1997, according to the report. Women—especially younger women—are as likely as men to report management as their primary or secondary work activity. Among older age groups, however, women are less likely than men to report management as their primary or secondary work activity.

You can find the report, *Women, Minorities and Persons with Disabilities in Science and Engineering: 2000,* at http://www.nsf.gov/sbe/srs/stats.htm.

news along the pike

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Please contact a member of the Editorial Board or:

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OMBUDSMAN'S CORNER

Annual Report: Complaints About Processes Move to Top

BY JIM MORRISON

Two things you can count on at the end of a fiscal year are continuing resolutions to keep the Agency funded and my Ombudsman's annual report. The continuing resolutions are over, and here is my report. Complaints to the CDER Ombudsman are on a plateau, but there are a few worrisome trends that point to problems that need addressing.

As with last year, the number of cases stayed a little below 100, virtually all externally generated. I tabulated the complaints into the same classes that I did last year to make trends easy to spot. While unfairness of policies or decisions led the list last year, it dropped to second place, behind problems with processes or inadequate information about them. Specifically, there was a 20 percent decrease in unfairness complaints and a similar percentage rise in process problems.

The Center has spent a considerable effort to reduce inconsistencies among reviewing divisions, and I believe those efforts account for at least some of the drop in the unfairness complaints. I don't know why reported process problems rose, except that if one category drops others must rise, because reporting is on a percentage basis. However, many of the process-related complaints could have been avoided with additional clarity in our communications.

Untimeliness complaints continued to drop, a constant trend throughout the five years I have been ombudsman. The predictability of actions through user fee goals has made grumbling about new drug reviews virtually disappear.

Two trends are troubling, in that complaints about both difficulty in gaining access (mostly a lack of returned phone calls) and rude or unhelpful interactions rose, with the latter doubling from last year. It is difficult to pinpoint why this should be, but I would encourage CDER staff to reread my column in the June 1999 *News Along the Pike* (http://www.fda.gov/cder/pike/june99.pdf).

In December and January I devoted two columns to the results of a survey I did among CDER staff about their pet peeves regarding industry behavior. Those articles gained a lot of attention, demonstrating the wide readership of *News Along the Pike* outside the Agency. They resulted in a chapter in a Food and Drug Law Institute book about working with the FDA, and I heard from several companies that they were required reading in their regulatory affairs departments. The interest in the articles also shows that people are hungry for insights into the workings of the Center.

External Complaints	FY '99	FY '00
Process problems or inadequate information about them	36%	42%
Unfairness of a policy or decision	38%	30%
Untimeliness	15%	12%
Difficulty gaining access	5%	6%
Uncivil or unhelpful interactions	3%	6%
Miscellaneous	3%	4%

As I have said many times, most of the problems I see relate to miscommunications, a lack of communications and inappropriate communications. Despite the numerous guidances and procedures published by the Center, there is still a lot of mystery surrounding how CDER works and why we do what we do. The publication of standards and criteria is a good thing. But publishing *why* the Center is setting those particular standards and criteria is important as well.

People outside CDER will never fully understand what makes the Center tick unless they understand *why* we take the actions we do. Adding a few sentences in not approvable and clinical hold letters, for example, to explain why the actions are being taken, not just what needs to be done, will aid those receiving the letters immensely. We too often assume that the reasons for our actions are self-evident. But that assumption doesn't hold if you are addressing the letter to the person who put the application together and thought everything was fine.

Overall, the actions CDER takes are well-reasoned and valid. We can reduce the complaints about processes if we take the time to explain the actions we take to those we regulate and to those we serve.

If you have a complaint or suggested solution to a problem, please give me a call (301-594-5443) or send me an e-mail (morrisonj@cder.fda.gov).

Jim Morrison is the Center's ombudsman.

Pike's Puzzler: Anatomy, Medicine, Chemistry or Geography?

BY TONY CHITE

1. The median nerve which supplies feeling to thumb, index, middle and ring fingers runs through a passageway called the:

a. circumflex humoral; b. zygomatic arch; c. bulbocavernous venter; d. carpal tunnel

2. A smooth, slightly elevated area on the body surface, which is redder or paler than the surrounding skin and is often attended with severe itching, is also known as a:

a. hive; b. wheal; c. welt; d. all of these; e. a and c only

3. A benign, soft, rubbery, encapsulated tumor of adipose tissue, usually composed of mature fat cells and generally occurring as a solitary lesion in the subcutaneous tissue of the trunk or forearms, is a:

a. lipoma; b. wart; c. bunion; d. nodule

4. Which of these elements is not a halogen:

a. bromine; b. chlorine; c. sodium; d. iodine

5. If you located the Circle of Willis you would be in:

a. Chevy Chase, Md.
b. The Tropic of Capricorn
c. The human brain
d. The left ventricle of the heart
e. The retina of the eye

Answer key: 1d, 2d, 3a, 4c, 5c

Tony Chite is a pharmacist and CSO in the Center's Division of Freedom of Information.

INFORMATION TECHNOLOGY CORNER

Helpful Answers on DFS; E-Records Guidance Available

Q: My DFS password does not work. What can I do?

A: DFS passwords are case sensitive. After you have double-checked to make sure that your DFS password is entered correctly, try typing the password in a different case. Hold the shift key down while typing in your password. If this still does not work, contact the help desk (HELP) for additional password support.

Q: I checked a document into DFS that needs to be edited. Is there any way to stop the routing process and delete the document so I can edit and start again?

A: Yes! You can search for all your documents in progress from the new search features in DFS 2.0. To search for documents in progress:

- On the DFS menu bar, click Search|Standard
- From the menu, select Author Revise/ Reassign Documents Search. A list of all the documents you've authored is displayed.
- Click on the file to delete.
- Click on the Revise button. The document will be sent back to your inbox.
- Click the Yes button. The routing process is permanently stopped for this document. You can delete the document from your DFS inbox and start again.

If the document does not appear in the list, it may be in final form. Contact the Help Desk (HELP) for additional support.

Guidance Available on E-Records

The Government Paperwork Elimination Act mandates that, when practicable, by 2003 federal agencies use electronic forms, electronic filing and electronic signatures to conduct official business with the public. Many of these documents have enduring long-term legal, fiscal or operational value that may last beyond the functional life of the software and hardware used to create them. How to preserve such records is a major challenge facing IT personnel and records managers alike.

The National Archives and Records Administration has issued a guidance on the management of electronically signed records. This document is a primer that frames the issues involved, discusses the records management principles applicable to e-signatures and suggests possible methods for their long-term maintenance. The guidance's key points are:

- Signatures are an integral part of the record whose trustworthiness must be preserved.
- The characteristics of a trustworthy record are reliability, authenticity, integrity and usability.
- To demonstrate trustworthiness, the record's content, context and (sometimes) structure must be preserved.
- Suggested approaches for ensuring trustworthiness are keeping the documentation of the record's validity or maintaining the ability to revalidate the signature.
- Also outlined are the components of a non-repudiation service, the elements of an e-signature record, which must be maintained if separate from the document itself, and an explanation of risk analysis.

The guidance can be found at http://www.nara.gov/records/policy/gpea.html. Scott Zeiss (ZEISSS) is the point of contact.

Process Improvement Project

The second round of training on Capability Maturity Model processes began Oct. 31 in OIT. The training is part of OIT's effort to achieve CMM Level 2. As of Sept. 19, all prioritized projects in OIT had to meet a minimum requirement toward CMM Level 2.

A policy document and 14 guidance documents have been written outlining the new CMM Level 2 activities, which include formal project planning, project tracking and oversight, configuration management and quality management. The training provides an in-depth overview of each of these areas. Approximately 60 OIT staff members completed the first round of training and are now ready to begin implementing the new processes. **Vali Tschirgi** (TSCHIRGIV) is the point of contact.

December IT Training

Monday	Tuesday	Wednesday	Thursday	Friday
				1
4 **CDER Standard Letters System** 9:00-12:00	**5** **JMP Session 1** 1:00-4:00	**6**	**7** **Access 97 Intro & Tables** 9:00-12:00 **Access 97 Queries & Reports** 1:00-4:00	**8** **Access 97 Form Design** 9:00-12:00 **Access 97 Report Design** 1:00-4:00
11 **Creating PDF Review Documents** 1:00-4:00	**12** **JMP Session 2** 1:00-4:00	**13**	**14**	**15**
18	**19** **JMP Session 3** 1:00-4:00	**20** **E-Doc Query** 9:00-12:00 **E-Doc Query** 1:00-4:00	**21** **E-Doc Query** 9:00-12:00 **E-Doc Query** 1:00-4:00	**22**
25	**26**	**27**	**28**	**29**

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

CDER CFC Campaign

Nearly 100 CDER employees have decided to contribute not only their money but also their time, talent and energy to the CFC campaign as office captains and keyworkers in this year's effort to raise $189,000 within CDER.

"CFC gives all of us the opportunity to show our gratitude for our good fortune by sharing with those in need, said Center CFC Coordinator **John Friel,** deputy director of the Office of Training and Communications. "None of us knows when he or she may be in need of a hand or when the CFC 2000 slogan will ring even more true: 'It All Comes Back to You.'"

OPS Leverages with USP for Financial Support of St. Louis Labs

By John A. Spencer, Ph.D.

ST. LOUIS—A recent leveraging agreement between FDA and U.S. Pharmacopeia will provide the Agency $1.1 million over three years to support the characterization of the U.S. Pharmacopoeia Reference Standards at the Division of Pharmaceutical Analysis, part of the Office of Testing and Research in the Office of Pharmaceutical Science.

The agreement, signed in August, calls for USP to provide financial support to FDA to purchase new and service existing equipment, to maintain an inventory of laboratory supplies and to hire sufficient personnel to keep up with the demand.

USP will provide approximately $300,000 per year to cover personnel and supplies. In addition, the first year includes a sum of $200,000 to purchase state-of-the-art laboratory equipment to support this scientific collaboration.

FDA will take primary responsibility for management of the terms of the agreement. DPA will continue to provide laboratory space, equipment, supplies, personnel and expertise in support of maintaining the quality and availability of USP's Reference Standards.

One of the keys to accurate chemical analysis of pharmaceuticals is the use of certified reference standard materials. Most pharmaceutical analyses rely on a quantitative comparison of an instrument response to the active ingredient in the drug product being tested and the response to a reference standard of the active ingredient.

For many of the common prescription drugs in commerce the reference standards issued by USP are used. In the United States, they are the legal references prescribed by Congress. Also, many countries around the world recognize USP standards for their tests of purity and long-term, lot-to-lot consistency. That consistency is due, largely, to a rigorous program of verification and testing involving both USP and DPA laboratories.

Various drug manufacturers typically produce these reference materials in large batch quantities for USP. This can involve direct chemical synthesis or extraction and purification from natural sources. In many cases, important impurities such as potentially toxic degradation products must also be measured, so USP maintains references for these as well. In addition, 80 or more candidates for new standards must be screened every year.

Before any of these standards can be used for regulatory analysis, they must be carefully tested to establish that they are of high chemical purity and have the correct properties to be used in the prescribed assay method.

Industry and FDA each have an important stake in maintaining the availability of USP's reference materials to assure the quality and safety of pharmaceuticals. Without a steady and reliable supply of USP Reference Standards both the manufacture and the regulation of many prescription drugs would become impossible.

Faced with level budgets—decreasing in real terms in non-user fee areas—and the important mission of acting as a collaborating partner in certifying the purity of USP Reference Standards, DPA and OPS began exploring the possibility of a cooperative research and development agreement.

Preliminary discussions in June 1999 gained the support of USP's board of trustees. John Fowler, USP's chief operating officer and several of USP's legal, financial and scientific staff negotiated with FDA. **Moheb Nasr, Ph.D.,** DPA Director, **Helen Winkle,** OPS Acting Director, and **Beatrice Droke,** FDA's Office of Facilities, Acquisitions and Central Services joined in the deliberations for FDA.

The agreement formalizes the partnership by spelling out FDA's and USP's commitments to the USP Reference Standards Collaboration.

John Spencer is a chemist in the Division of Pharmaceutical Analysis.

Leveraging Teleconference Highlights Need, Unveils Guidance Handbook

Leveraging—or the creation of collaborative relationships and formal agreements with others outside FDA in ways that will help the Agency meet its public health responsibilities—was the subject of a teleconference held in November.

"Because of the extent of our mandate, we sometimes feel we have the weight of the world on us. Leveraging is a chance to share the burden," said FDA Commissioner **Jane Henney, M.D.** "Think of leveraging as a first opportunity—not a last resort. It's permission not just to think, but to do."

While leveraging has been going on at FDA for years, it has been getting greater emphasis in the last year, according to Senior Associate Commissioner **Linda Suydam.**

Suydam highlighted the new *Leveraging Handbook,* which provides guidance and describes various leveraging mechanisms.

The handbook, other information, speeches and talking points can be found on FDA's leveraging intranet site at http://intranet.fda.gov/oc/oea/opa/lever-aging.

Representatives from various FDA centers presented their successful leveraging programs, including **Helen Winkle,** Acting Director, Office of Pharmaceutical Sciences, who spoke about the Product Quality Research Institute *(Pike,* November 1999).

Every center has a leveraging point of contact, and **Paula Bourkland** (BOURKLAND, 4-6741) is CDER's contact. According to Bourkland, several members of the Center's senior management team are looking at other possible leveraging projects. She encouraged those with ideas regarding leveraging to discuss them with their supervisors and to contact her if they have any questions.

—Patrick Clarke

2001 FDA Science Forum

The 2001 FDA Science Forum,, "Science Across the Boundaries," will be held Feb. 15 and 16 at the Washington Convention Center and is free to all FDA employees. Session topics will include privacy and confidentiality; modeling and simulation; and unique partnerships outside the Agency.

Awards will be given for excellence in analytical science, laboratory science and review science as well as for outstanding intercenter scientific collaboration.

Ground Broken for White Oak; 1st CDER Units Eye 2002 Move

By Patrick E. Clarke

FDA and the General Services Administration held a groundbreaking ceremony for the combined FDA facilities at White Oak on Oct. 10. Dignitaries in attendance included Secretary of Health and Human Services **Donna E. Shalala,** FDA Commissioner **Jane E. Henney, M.D.,** members of the Maryland congressional delegation and other local elected officials.

The first building, expected to open in November 2002, will hold the Office of Compliance and laboratories for the Office of Testing and Research. Buildings for the rest of CDER are slated for completion between 2002 and 2004, and the entire FDA consolidation is targeted for the end of 2007. The project's 14 interconnected buildings, placed in a campus-like setting, will replace FDA's 48 leased buildings.

"The 100th anniversary of FDA is in 2006, so if you could hurry up we could have a real birthday party," Dr. Henney said. "The road that led to today's groundbreaking has been somewhat long and rocky, but certainly worth it."

Dr. Henney praised the efforts of LABQUEST, the community group officially coordinating the redevelopment of the former Naval Surface Warfare Center. "Never doubt that a small group of thoughtful citizens can change the world," said Henney, quoting anthropologist Margaret Mead. "We were always confident that the community would be supportive of the important work we do."

Betsy Bretz, LABQUEST chairperson, explained that her group focused on getting FDA to White Oak because FDA "is the only federal agency involved in all our lives every day."

Montgomery County Executive Douglas M. Duncan gave Dr. Henney the key to White Oak. "This key is heavier than the building we're going to break ground for," Duncan said.

Bob Beck, GSA's public building commissioner, presented Dr. Henney with the Maryland flag.

"Today is not just about breaking ground, it's about gaining ground," Shalala said, noting that the new facilities will enable better research and oversight.

Shalala praised both Dr. Henney and other FDA officials for their efforts in helping the facility become a reality. "She wanted facilities as good as her employees and she's getting them," Shalala said. "Under Dr. Henney, the FDA continues to set the highest standards for safety."

At the end of the ceremony, the VIPs each shoveled a small amount of dirt on a prepared portion of ground.

More information is on FDA's intranet site at http://intranet.fda.gov/ofacs/white_oak/gb2000.htm and the National Treasury Employee Union Chapter 282's Web site at http://www.nteu282.org/.

Patrick Clarke is a public affairs specialist in OTCOM.

EEO Corner

National American Indian and Alaska Native Heritage Month Celebrated

By Gloria Marquez Sundaresan

"Celebrating Our Strengths" was the theme for November's activities to support American Indian and Alaska Native Heritage Month. Strengths come from the estimated 2.4 million native Americans in 556 federally recognized American Indian and Alaska Native tribal entities. The Indian Health Service, with the strong support from the HHS Office of the Secretary, took the lead in organizing celebrations, especially the program held in Rockville on Nov. 1 and the opening ceremony for the Department held the following day at the Humphrey Building.

The opening ceremony was well attended by federal employees, representatives from local governments and out-of-state Indian tribes. The entire program presented a mixture of cultural and educational information including the traditional blessing by Clayton Old Elk, a Crow; music from flute, drums and songs; hoop and eagle dances. Lillian Azalea Sparks Rosebud, a Sioux, presented the "Story of Four Directions Told to a Child." Sparks is Ms. Indian World, and she was chosen to be the model for Sacagawea that appears on the new dollar coin. Sacagawea was a member of the successful Lewis and Clark expedition to the West in 1804. She played a very important role as translator contributed enormously to the survival of the team during the entire journey.

In welcoming remarks, HHS Secretary **Donna Shalala** who said that, despite her departure this coming January, the work started under her watch to improve health services for the American Indians must continue to improve.

Michael Trujillo, M.D., Director of Indian Health Service, spoke of the diversity among the many Indian tribes and the American Indian influence of spirituality, tolerance and respect, which are interwoven into American society. He also pointed out the American Indian names given to streets, bridges, rivers, lakes and towns. Dr. Trujillo received an award for dedication and outstanding service as head of the Agency. Assistant Secretary for Health and Surgeon General **David Satcher, M.D.,** presented the award to Dr. Trujillo.

Other speakers included Malcolm Bowekaty, governor, Zuni Pueblo; and Michael Masetky, Comanche tribe of Oklahoma, and Director, Legislative Affairs, Indian Health Service.

Amos Goodfox, Osage/Pawnee, Department of Education, gave the closing benediction. The Veterans' Color Guard accompanied by the Little River Drummers and Singers retired the colors. James Greely played the flute at the end of the program.

Including FDA and CDER, participation in and support of the activities came from 24 different departments, agencies and organizations such as the Billings Gazette, Billings, Mont.; City of Rockville; Montgomery County Offices of the County Executive; HHS APAnet (Asian Pacific American Network); National Institutes of Health; and Department of Interior.

Gloria Marquez Sundaresan is an equal employment specialist in the Center's EEO Staff.

REVIEWER'S CORNER

Plant Orientation Site Visits by Chemists Benefit CDER, Industry

BY RAJENDRA UPPOOR, PH.D., R.PH.

Today's pharmaceutical industry uses new and ever-changing manufacturing and testing technologies to produce modern medicines. In the context of CDER's mission to assure the availability of safe and effective drugs of high quality to the American people, the Center encourages industry's use of scientifically developed, robust manufacturing technologies.

Review chemists must have a good understanding of the latest technologies used in the pharmaceutical industry. The plant orientation site visit program is one of the methods the Center uses to provide its review chemists with direct exposure to on-going research, manufacturing techniques and quality control procedures.

During visits, review chemists can observe current technologies, equipment and facilities used in developing, testing, manufacturing, packaging, storing and distributing drug substances, drug products and investigational clinical supplies.

The visits also offer reviewers a platform to meet and interact with industry's scientists, management and other personnel to exchange professional and scientific knowledge, experience, views and opinions outside the context of specific and routine regulatory submissions to the Agency.

Through these interactions, review chemists can develop a better understanding of state-of-the-art instruments, equipment and processes. Some of the general manufacturing and regulatory issues that arise in the various phases of new drug product development are also discussed at the host's facilities in an informal setting. These discussions promote mutual understanding of the roles and responsibilities of all scientific, technical and regulatory personnel involved in the systematic processes of new drug discovery, development, manufacturing and testing by industry and review at CDER.

During the recently concluded fiscal year 2000, the Office of New Drug Chemistry paid for several plant orientation visits by its review teams to enhance CDER's science-based review approach.

The following chemists may be consulted about their observations at these sites:

- Abbott Laboratories, Automatic Liquid Packaging and Baxter Healthcare, located in Illinois—**Vispi Bhavnagri, Ph.D., Bart Ho, Ph.D., Sue-Ching Lin, M.S., R.Ph., Rao Puttagunta, Ph.D.,** and **Mona Zarifa, Ph.D.,** from the anti-inflammatory, analgesic and OTC drug products review group.
- Gilead Sciences, Genentech, Alza Corp., Allergan Inc. and FDA Los Angeles District Offices located on the West Coast—**Hossein "Shawn" Khorshidi, Ph.D., Lucious Lim, M.D., Yong-de Lu, Ph.D., Linda Ng, Ph.D., Lebaniel Rodriguez, Ph.D.,** and **Su Tso, Ph.D.,** of the ophthalmic drug products review team.
- Baxter manufacturing facilities located in Marion, N.C.—**Peter Cooney, Ph.D., Paul DeLeo, Ph.D., David Hussong, Ph.D., Steve Langille, Ph.D., Nrapendra Nath, Ph.D., Vinayak Pawar, Ph.D., Brian Riley, Ph.D., Marla Riley, Ph.D., Paul Stinavage, Ph.D., Neal Sweeney, Ph.D., Patricia Tuegel** and **Carol Vincent, Ph.D.,** of the ONDC and OGD microbiology review group.
- Astra-Zeneca and DuPont manufacturing facilities located in the Wilmington, Del., area—**Donald N. Klein, Ph.D.,** and **Ali Al-Hakim, Ph.D.**
- Merck's fermentation, natural product isolation and analytical characterization facilities located in Rahway, N.J.—**Susan Rosencrance, Maria Shih, M.S., Jim Timper, Ph.D., Joel Unowsky, M.D., Sylvester West, Ph. D.,** and **Andrew Yu, Ph.D.,** of CDER's antibiotic working group.
- Agouron, La Jolla Pharmaceuticals and Bachem California manufacturing and research facilities located in the San Diego and Torrance, Calif., areas—**Tiffany Archer, Xiao-Hong Chen, Ph.D., Kathleen Jongedyk, M.S., Shanell Owens, Hasmukh Patel, Ph.D.,** (Deputy Director, DNDC I), **Kasturi Srinivasachar, Ph.D., Rajendra Uppoor, Ph.D., R.Ph,** and **Stuart Zimmerman, Ph.D.,** from the oncology and cardio-renal drug products review teams.
- A Schering Plough manufacturing facility located in Manati, Puerto Rico—**Charlotte Yaciw** of the OTC drug products review team.

In every instance, the industry personnel always expressed their appreciation for the very diverse scientific interactions that occurred during plant orientation visits. It is our experience as well, that site visits do benefit CDER reviewers and the industry.

Rajendra Uppoor is a review chemist in the Division of New Drug Chemistry I.

FDA Science Board Meets to Discuss FDA Challenges, Priorities

The bi-annual meeting of the FDA Science Advisory Board was held in November. The function of the board is, primarily, to provide advice to the commissioner, deputy commissioner and the senior advisor for science on specific, complex, technical issues and emerging developments within the scientific community in industry and academia.

"This agency needs your help more than ever," said FDA Commissioner **Jane E. Henney, M.D.** She referred to a Pew Research Center Study showing the strong consumer confidence held in the FDA and how that must continue.

Each center outlined its priorities.

"The last four decades have been devoted to whether drugs work or not. Safety and predicting toxicity will be the endeavor of the next decade," CDER Director **Janet Woodcock, M.D.,** said.

"We need better-predictive preclinical models for toxicity."

Dr. Woodcock spoke of the need not just for scientific understanding, "but how can we ensure that both the clinical community and consumers will use the drugs properly." She said her second priority was knowledge management.

—Patrick E. Clarke

Buehler, Lewis Earn First FDA Quality of Worklife Award

(Continued from page 1)

Terry S. Peters, D.V.M.

Terri F. Rumble

Kimberly L. Topper

Tiratricol Compliance Team: **A. Joel Aronson, Lois Duval, Edward Miracco** and **Mary E. Thompson;** PHS Unit Commendation: **LCDR Jan Davis.**

Financial Disclosure Rule Team: **Linda S. Carter** and **Mary C. Gross.**

Dissolution Equivalence Assessment Methods Development Team: **Pradeep M. Sathe, Ph.D., Vinod P. Shah, Ph.D.**, and **Yi Tsong, Ph.D.**

Lotronex Risk Management Working Group: **Steven A. Aurecchia, M.D., Jason D. Brodsky, Bronwyn E. Collier, Ann Corken, R.Ph., Mary J. Dempsey, Hugo Gallo-Torres, M.D., Florence Houn, M.D., M.P.H., Zei-Pao Huang, Kati A. Johnson, Scheldon Kress, M.D., Randy C. Olmstead, Nancy M. Ostrove, Ph.D., Toni D. Piazza-Hepp, Pharm.D., Victor F. Raczkowski, M.D., Patricia Kuker Staub, R.Ph., Lilia Talarico, M. D., Russell M. Williams, Jr.,** and **Crystal L. Wyand;** PHS Unit Commendation: **LT Jennifer Agyepong** and **CAPT Thomas H. Perez.**

The Linezolid Team: **John J. Alexander, M.D., Erica H. Brittain, Ph.D., Elizabeth A. Duvall-Miller, Qihao Jiang, Ph.D., David B. Katague, Ph.D., Joyce A. Korvick, M.D., Daphne L. Lin, Ph.D., Frederic J. Marsik, Ph.D., Robert E. Osterberg, Ph.D., Francis R. Pelsor, Ph.D., David B. Ross, M.D., Ph. D., Kenneth A. Seethaler, Ph.D., Albert T. Sheldon, Ph.D., Janice M. Soreth, M. D., Ana Szarfman, M.D., Mathew T. Thomas, M.D., James M. Timper, Jr.,** and **Jenny J. Zheng, Ph.D.**

FDA Outstanding Achievement Award

Kathleen R. Anderson
Nancy E. Derr
Kim E. Dettelbach
Mary F. Goodson
Daphne Lin, Ph.D.
Andrea C. Masciale
Leslie De Le Pena Wheelock
Lawrence X. Yu, Ph.D.
Hong Zhao, Ph.D.

FDA Group Recognition Award

MPCC Policy Drafting Subcommittee Adverse Reaction Working Group: **Rachel E. Behrman, M.D., Joy L. Bennett, Joseph P. Griffin, Thomas P. Laughren, M.D., Nancy M. Ostrove, Ph.D., Toni D. Piazza-Hepp, Pharm.D.,** and **Toni M. Stifano.**

OGD Regulatory Support Branch; **Margo L. Bennett-Bartle, Norma Jean Grimes, Marilyn J. Leach, Saundra T. Middleton;** PHS Unit Commendation: **LT Gregory S. Davis, CDR Harvey A. Greenberg, LT Nasser Mahmud, LTJG Paras M. Patel** and **LTJG Emily S. Thomas.**

Cisapride Working Group: **Suliman I. Al-Fayoumi, Ph.D., Steven A. Aurecchia, M.D., Mark I. Avigan, M.D., Jason D. Brodsky, Ann Corken, R.Ph., Mary J. Dempsey, Suresh Doddapaneni, Ph.D., Hugo E. Gallo-Torres, M.D., Katrina Garry, David Graham, M.D., Sam H. Haidar, Ph.D., Florence Houn, M.D., M.P.H. , Shiew-Mei Huang, Ph.D., Zei-Pao Huang, Ruth Carolyn Jones, Bonnie M. Justice, John E. Koerner, Ph.D., Melodi McNeil, R.Ph., Cathy Miller, Toni D. Piazza-Hepp, Pharm.D., Victor F. Raczkowski, M.D., Karen M. Templeton Somers, Ph.D., Patricia Kuker Staub, R.Ph., Lilia Talarico, M.D., John M. Treacy, Diane K. Wysowski, Ph.D.;** PHS Unit Commendation: **LT Jennifer L. Agyepong, CAPT George D. Armstrong, Jr., CAPT Thomas H. Perez** and **CDR Kathleen Uhl.**

PHS Commendation Medal

LCDR Terrie L. Crescenzi
LT Nasser Mahmud
CDR Susan E. Molchan
LCDR William A. Russell, Jr.
CDR Denise P. Toyer
LCDR Jacqueline H. Ware

FDA Quality of Work Life Award

Gary J. Buehler
Sally J. Lewis

FDA Outstanding Science Teaching Award

Jerry Collins, Ph.D.
Karen Higgins, Ph.D.

Center Director's Special Citation

Reviewer's Affairs Committee: **Tanya L. Abbott, Ali H. Al-Hakim, Ph.D., Sousan S. Altaie, Ph.D., Indra Antonipillai, Ph.D., Karen A. Bernard, Ph.D., Roy A. Blay, Ph.D., Allen D. Brinker, Zhou Chen, Ph.D., Jean-Ah Choi, Pharm.D., Jacqueline D. Council, Pharm.D., Russell D. Fleischer, Mamata S. Gokhale, Ph.D., Linda S. Hu, M.D., Venkateswar R. Jarugula, Ph. D., Kathleen E. Jongedyk, Jahnavi Kharidia, Ph.D., Lydia Velazquez Kieffer, Pharm.D., Margaret M. Kober, R.Ph., Marie Kowblansky, Ph.D., Indira Kumar, Steven C. Kunder, Adebayo A. Laniyonu, Ph.D., Sue-Chih H. Lee, Ph.D., Houda Mahayni, R. Ph., Ph.D., Norman S. Marks, M.D., Katherine B. Meaker, Diane Moore, James J. O'Leary, M.D., Ali Olu, Philip N. Orticke, Jr., Robert J. Parker, Ph.D., Luqi Pei, Ph.D., Andrea M. Powell, Ph.D., Paul Roney, Ph.D., Clyde D. Rutledge, John Schmeling, M.D., Robert M. Shore, Harold V. Silver, Milton J. Sloan, Ph.D., Neal J. Sweeney, Ph.D., Rajendra Uppoor, Ph.D., Brenda W. Uratani, Sue-Jane Wang, Ph.D., Mildred A. Wright, Robert J. Yaes, M.D., Josie Yang, Ita S. Yuen, Ph.D.,** and **Joanna N. Zawadzki, M.D.**

Product Quality Research Institute: **American Association of Pharmaceutical Scientists, The Consumer Healthcare Products Association, Generic Pharmaceutical Industry Association, National Association of Pharmaceutical Manufacturers, The National Pharmaceutical Alliance, Parenteral Drug Association, Pharmaceutical Research and Manufacturers of America, Center for Drug Evaluation and Research, Ajaz S. Hussain, Ph.D., Eric B. Sheinin, Ph.D.,** and **Helen N. Winkle.**

Pediatric Oncology Drug Development Working Group: **Patricia C. Delaney, Murray M. Lumpkin, M.D., Richard Pazdur, M.D., Rosemary Roberts, M.D., Karen D. Weiss, M.D.;** PHS Unit Commendation, **CDR Terrie L. Crescenzi** and **CDR Steven I. Hirschfeld.**

CDER Special Recognition Award

Suliman I. Al-Fayoumi, Ph.D.
Janine Davis-D'Ambrogio

(Continued on page 9)

Center's Fall Awards Ceremony Honors 60 Individuals, 40 Teams

(Continued from page 8)

Shirnette D. Ferguson
Valeria Freidlin, Ph.D.
Mamta Gautam-Basak, Ph.D.
Ravi S. Harapanhalli, Ph.D.
Venkateswar R. Jarugula, Ph.D.
Kent R. Johnson, M.D.
Sally J. Lewis
Hong (Laura) Lu, Ph.D.
Shriniwas G. Nerukar, Ph.D.
Christine F. Rogers

ODE III Document Team: **Michael M. Folkendt** and **Florine P. Purdie.**

Castles, Swords and Shields Team: **Tawni M. Brice, Rita R. Hoffman, LCDR Lisa M. Hubbard, Deborah L. Kallgren, Diane V. Moore, LCDR Matthew J. Tarosky** and **Jean A. Yager.**

Project Management and Regulatory Forum Team: **Ignor Cerny, Pharm.D., Christina H. Chi, Susan Cobb, Kim M. Colangelo, Evelyn R. Farinas, Jody L. Ford, Gary M. Gensinger, Mark J. Goldberger, Deborah L. Kallgren, Lorene M. Kimzey, Crystal A. King, Randy Levin, Cecelia M. Parise, CAPT Thomas G. Phillips, Leah W. Ripper, Khyati N. Roberts, Nancy B. Sager, CAPT Margaret A. Simoneau, LCDR Matthew J. Tarosky** and **Jean A. Yager.**

CDER Administrative/Program Management Excellence

Candee D. Chadwick

LuDrean Peterson

Angela F. Poe

CDER Excellence in Communication Award

Crystal L. Rice

AAPS Conference Group: **William M. Adams, Ph.D., Craig M. Bertha, Ph.D., James F. Brower, Monica E. Caphart, Yuan-yuan Chiu, Ph.D., Jon E. Clark, John M. Dietrick, Eric P. Duffy, Ph.D., Bonnie B. Dunn, Ph.D., Florence S. Fang, Ph.D., Patrick J. Faustino, Ph.D., Allan H. Fenselau, Ph.D., Raymond P. Frankewich, Ph.D., Mamta Gautam-Basak, Ph.D., Devinder S. Gill, Ph.D., Ravi S. Harapanhalli, Ph.D., Ajaz S. Hussain, Ph.D., Everett H. Jefferson, Ravindra K. Kasliwal, Ph.D., Donald N. Klein, Ph.D., Sue-Ching Lin, George Lunn, Ph.D., Moheb M. Nasr, Ph.D., Vinayak Pawar, Ph.D., David A. Place, Ph.D., Radhika Rajagopalan, Ph.D., Bryan S. Riley, Ph.D., Nancy B. Sager, Vilayat A. Sayeed, Ph.D., Norman R. Schmuff, Ph.D., Robert H. Seevers, Ph. D., Vinod P. Shah, Ph.D., Eric B. Sheinin, Ph.D., Joseph Sieczkowski, Ph.D., Neeru Takiar, Ph.D., Saleh Turujman, Ph.D., Rajendra Uppoor, Ph. D., Ubrani V. Venkataram, Ph.D.,** and **James D. Vidra, Ph.D.**

CDER Stability Technical Committee: **Richard C. Adams, Ali H. Al-Hakim, Ph.D., Chi-wan Chen, Ph.D., Kenneth J. Furnkranz, Dale L. Koble, Ph.D., David B. Lewis, Ph.D., CAPT Yana R. Mille, Suresh Pagay, Ph.D., Barry Rothman, Robert H. Seevers, Ph.D., Eric B. Sheinin, Ph.D., Jeb S. Taylor** and **Kimberly A. Topper.**

ORA Training Group: **Eric P. Duffy, Ph. D., Bonnie B. Dunn, Ph.D., Eric B. Sheinin, Ph.D.,** and **Paul S. Stinavage, Ph.D.**

Postapproval Changes Implementation Group: **Peter H. Cooney, Ph.D., Bonnie B. Dunn, Ph.D., Steven R. Koepke, Ph. D., Melissa J. Maust, Bryan S. Riley, Ph.D., Nancy B. Sager, Vilayat A. Sayeed, Ph.D.,** and **Eric B. Sheinin, Ph.D.**

DIA/FDA Joint Project Management Workshop Team: **Matthew A. Bacho, Doris J. Bates, Ph.D., Kim M. Colangelo, Bronwyn E. Collier, Jody L. Ford, Tia M. Harper-Velazquez, Pharm.D., Deborah L. Kallgren, Natalia A. Morgenstern, Lana L. Pauls, Jack S. Purvis, Mary Jane Walling, Jena M. Weber** and **Jean A. Yager;** PHS Unit Commendation: **CAPT Joseph M. Buccine** and **LCDR Kassandra C. Sherrod.**

CDER Information Technology Excellence Award

Division Files System Project Team: **Gary M. Anderson, Christine A. Aragon, Gregory V. Brolund, Charles C. Burdette, Melissa R. Chapman, Janet L. Gentry, Chris Luce, Sabina Mesalic, Warren Miller, Scott M. Shippey, Glen M. Tiffany** and **Carolyn A. Yancey.**

OPS IT Initiatives Team: **Troy Livingstone, Richard G. Sponaugle, Jr.,** and **Obinna Ugwu-oju;** PHS Unit Commendation: **LTJG Jeen S. Min.**

Division of Pharmaceutical Analysis Information Technology Migration Team: **James S. Black, John M. Brinsko, Don C. Cox, Corinne E. Gomez, Mark A. Gray, Gurminders J. Khalsa, Rudolph F. Kulousek, Wendy A. Lee, Sandra J. Logan** and **Jan D. Meisler.**

CDER Leadership Excellence Award

Aloka G. Chakravarty, Ph.D.

Joseph C. Famulare

Edwin Rivera Martinez

Agnes A. Nguyenpho

Toni D. Piazza-Hepp, Pharm.D.

William P. Rickman

Albert T. Sheldon, Ph.D.

Robert L. West

Charlotte A. Yaciw

OPS Office Directors: **Gary J. Buehler, Yuan-yuan Chiu, Ph.D., Lawrence J. Lesko, Ph.D.,** and **James T. MacGregor, Ph.D.**

CDER Excellence in Mentoring Award

Roswitha E. Kelly

Lori Marie Gorski

Bioequivalence Population Pharmacodynamic Modeling Team: **Andre J. Jackson, Ph.D.,** and **Gur Jai Pal Singh, Ph.D.**

Chemistry I Mentoring Group: **Devinder S. Gill, Ph.D., Albert J. Mueller, Ph.D., Paul Schwartz, Ph.D.,** and **Michael J. Smela, Jr.**

CDER Project Management Excellence

Michelle Dillahunt

Elizabeth A. Duvall-Miller

Katrina S. Garry

Susan C. Lange

CDER Support Staff Excellence Award

Sandra J. Benton

Kristin D. Cook

Shanell L. Owens

Margaret A. Stephens

Chemistry I Support Staff: **Brooksie M. Cooper** and **Eugenie S. Patrick.**

(Continued on page 10)

OCPB SCIENCE DAY

Utility of Genomics to Individualized Drug Therapy Discussed

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

At the ninth science day held Oct. 24 by the Office of Clinical Pharmacology and Biopharmaceutics, William Evans, Pharm.D., presented the keynote address on how genetic makeup might predispose a person to respond to a given drug and how such information might be used to individualize drug therapy for patients. Dr. Evans is executive vice president and deputy director of St. Jude Children's Research Hospital in Tennessee and a professor of clinical pharmacy and pediatrics at the University of Tennessee.

His research focuses on the pharmacokinetics and pharmacodynamics of anticancer drugs in children, exploring the mechanisms for interindividual differences in drug disposition and the biological and pharmacological basis for heterogeneity in response to antileukemia therapy.

Dr. Evans' presentation was titled "Pharmacogenomics: Translating Functional Genomics into Rational Therapeutics, Childhood Acute Lymphoblastic Leukemia as a Model." His talk focused on pharmacogenomics as the hereditary basis for interindividual differences in drug response. Pharmacogenomics is generally defined as the genetic basis that differentiates responders from non-responders to a given drug.

Human genetic polymorphism contributes to the variability in drug metabolism, he said. Dr. Evans used drug therapy in childhood ALL as an example of how pharmacogenomics can be used to provide rational therapeutics. Polymorphism in the enzymes that metabolize mercaptopurine can lead to toxicity or therapeutic efficacy in ALL patients. He concluded that pharmacogenomics can be used to optimize the selection of cancer therapy for individual patients based on the genetics of the host and the tumor.

Our second guest speaker, **Richard Pazdur, M.D.,** Director, Division of Oncology Drug Products, provided a medical regulator's perspective on the use of genomics in cancer therapy. He agreed that genomics has a role to play in finding useful therapeutics for some cancers that

(Continued on page 11)

Center's Fall Awards Ceremony Honors 60 Individuals, 40 Teams

(Continued from page 9)

CDER Team Excellence Award

Conjugated Estrogens Team of the Complex Drug Substances Coordinating Committee: **Wallace P. Adams, Ph.D., Mei-Ling Chen, Ph.D., Yuan-yuan Chiu, Ph.D., Carol E. Drew, Henry D. Drew, Ph.D., Thomas Layloff, Ph.D., David T. Lin, Ph.D., Diane V. Moore, Moheb M. Nasr, Ph.D., Larry A. Ouderkirk, Rashmikant M. Patel, Ph.D., Moo Jhong Rhee, Ph.D., Robert H. Seevers, Ph.D., Michael J. Smela, Jr.,** and **Roger L. Williams, M.D.;** PHS Unit Commendation: **CAPT Yana R. Mille.**

OCPB Metabolic and Endocrine Review Team: **Hae-Young Ahn, Ph.D., Steven B. Johnson, Pharm.D., Robert M. Shore, Pharm.D.,** and **Xiao-Xiong Wei, M.D., Ph.D.**

OGD WWW Team: **CAPT Timothy W. Ames, LT Gregory S. Davis, Richard G. Sponaugle, Jr., Paul K. Stauffer, LTJG Emily S. Thomas** and **Sally Winthrop.**

Chemistry Manufacturing and Controls MYLOTARG Review Team: **Xiao Hong Chen, Ph.D., Eric P. Duffy, Ph.D., CAPT David Hussong, Cheng Yi Liang, Ph.D.,** and **Marjorie A. Shapiro, Ph.D.**

Beltsville Research Facility/MOD I Consolidation Team: **Arthur R. Byrant, Valerie A. Flournoy, Richard M. Hogart, Almetia L. Hoskins, James R. Marsh, Tammy L. Mueller** and **Sylvester West.**

Laboratory Consolidation Team, Division of Product Quality Research: **Charles R. Brownell, Charlotte A. Brunner, Anthony B. Civarella, Patrick J. Faustino, Ph.D., Everett H. Jefferson** and **Jeb S. Taylor.**

Physical Pharmacy Team, Division of Product Quality Research: **Charles R. Brownell, Everett H. Jefferson, Robbe C. Lyon, Hullahalli R. Prasanna** and **Jeb S. Taylor.**

USP Reference Standards Team: **Joy C. Bayliss, Sylvia H. Colson, Charles T. Dieter, Valerie A. Flournoy, Richard M. Hogart, Almetia L. Hoskins, Susan Jenney, Richard E. Kolinski, Terra G. Lipe, Anjanette P. Smith** and **Anna M. Wokovich.**

Oncology Active Controls Trials Research Team: **Gang Chen, Ph.D., Ning Li, Ph.D.,** and **Mark D. Rothmann, Ph.D.**

Influenza Postmarketing Safety Team: **Debra B. Birnkrant, M.D., Debra Boxwell, Heidi M. Jolson, M.D., Stanka Kukich, M.D., Robert J. Meyer, M.D., Barbara A. Styrt, M.D.,** and **Virginia L. Yoerg;** PHS Unit Commendation: **CAPT Teresa C. Wu.**

New Data Initiative Working Group: **Allen D. Brinker, David J. Graham, Cynthia J. Kornegay, Parivash Nourjah, Ph.D.,** and **Judy A. Staffa.**

OPDRA Active Surveillance Team for Potential Medication Errors Due to Name Confusion: **Mary J. Dempsey, Parivash Nourjah, Ph.D., Peter P.S. Tam** and **Yi Tsong: P**HS Unit Commendation: **LCDR Sammie G. Beam, CAPT Thomas G. Phillips, CAPT Evelyn M. Rodriquez, CDR Anne E. Trontell** and **CDR Kathleen Uhl**

OPDRA Antipsychotics QT Prolongation Safety Assessment Team: **Syed R. Ahmad, M.D., Julie G. Beitz, M.D., Allen D. Brinker, M.D., Min Chu Chen, R.Ph., Cindy M. Kortepeter** and **Kathleen M. Phelen, R.Ph.;** PHS Unit Commendation: **CAPT Joslyn R. Swann** and **CDR Anne E. Trontell.**

OPDRA Short Form Development Team: **Mary J. Dempsey** and **Patrick F. Guinn;** PHS Unit Commendation: **CAPT Michael F. Johnston** and **CDR Denise P. Toye.**

Jackie Barber is CDER's Incentive Awards Officer.

Regulatory Decision-Making Issues Highlighted at OCPB Science Day

(Continued from page 10)

have had a low response or survival rate to drug therapy. He noted that these low rates may be due to our inability to identify certain subpopulations with a particular cancer that may respond to a particular therapy. Some trials enroll large patient numbers of a particular cancer type and find that a drug may have a low response or survival rate. A subpopulation of responders may have been diluted out because of large enrollment. He noted that identifying subpopulations or responders in cancer patients might benefit drug therapy and survival outcome.

Intramural Presentations

A talk from **Abimbola O. Adebowale, Ph.D.,** titled "The Relationship Between *In Vitro* Dissolution and *In Vivo* Absorption of Propanolol Hydrochloride from an Aqueous Polymeric Dispersion Extended Release Delivery System: Level A Correlation," began the day's intramural presentations. Dr. Adebowale discussed the development and demonstration of Level A *in vitro/in vivo* correlation for three formulations propranolol. She concluded that this relationship could be utilized to predict *in vivo* behavior using dissolution data as a surrogate.

Sang M. Chung, Ph.D., discussed his and his co-workers research on "Profound Effect of Plasma Protein Binding on the Polarized Transport of Furosemide and Verapamil in the Caco-2 Model." The research evaluated the effect of using human plasma as a medium compared to aqueous buffer. Dr. Chung's results showed that more physiologically relevant media such as human plasma might have a pronounced effect on the polarized permeability or transport clearance of highly protein bound drugs.

Xiaoxiong Wei, M.D., Ph.D., provided an overview of "Roles of Pharmacogenetics and Pharmacogenomics in Drug Therapy and Drug Development." Pharmacogenetics determines the variability in drug response, which may be related to variability in pharmacokinetics such as absorption, distribution, metabolism and excretion profiles of a drug in individuals and pharmacodynamic variability such as receptor polymorphism.

Pharmacogenomics differentiates responders and non-responders for a given drug based on the patient's genetic makeup. Dr. Wei briefly updated the current development of DNA chip technology and single nucleotide polymorphism information. He concluded that pharmacogenetics and pharmacogenomics provide us the basis for individualized drug therapy.

He Sun, Ph.D., presented a paper on "Using Concordance Correlation Measures in Longitudinal Pharmacokinetic and Pharmacodynamic Data Modeling for Informative Regulatory Decision Making." The purpose was to encourage the use of concordance correlation measures instead of using statistical significance assessments in PK and PD modeling. A statistically significant predictor or covariate should not be included in a PK and PD model (and thus should not lead to alteration of regulatory action) if its addition leads to little or no changes in both global and cross-sectional prediction performance.

Two proposed measures, the concordance correlation coefficient and the proportional reduction in penalized quasi-likelihood function, were discussed. They were compared to the commonly used statistical measures for sensitivity, stability, interpretation and practical applicability with simulated and real data sets. Dr. Sun said that the two measures satisfy the basic requirement for measures of association and provide a practical tool for PK/PD model selection. He concluded that these proposed measures would significantly contribute to making regulatory decisions based on steady global and local prediction performance.

Joga Gobburu, Ph.D., gave the final presentation, titled "Role of Exposure-Response in Regulatory Decision Making: an Example." He illustrated the use of clinical pharmacology knowledge in characterizing the *in vivo* behavior of a pain relief drug. Effectiveness and safety data from a submission were employed to construct an exposure-response surface using nonlinear mixed effects modeling.

Dr. Gobburu said that the models relating exposure (dose, concentration) to effectiveness and safety endpoints were helpful in appreciating the pharmacodynamics of the drug.

He also said the models helped in assessing the clinical significance of typical pharmacokinetic studies conducted to explore potential prognostic factors, such as drug interactions and disease status. Dr. Gobburu illustrated an efficient and simple method to evaluate clinical significance of potential prognostic factors.

Posters

There were five poster presentations including two from OCPB upper management:

- Pharmacokinetics of intravesical mitomycin C in a Phase III trial: Population-based analysis vs. conventional analysis, **Jenny H. Zheng, Ph.D.,** and others.
- Pediatric dosing recommendation of Drug X, **Veneeta Tandon, Ph.D., Dan Wang, Ph.D,** and **Dennis Bashaw, Pharm.D.**
- Modeling and simulation in drug development: Application to a drug for an unmet need, **Vanitha J. Sekar, Ph.D.,** and **Joga Gobburu, Ph.D.**
- Deriving concentration-response relationship from dose-response studies without pharmacokinetic samples, **Peter Lee, Ph.D.**
- Regulatory research comparing dosing of commonly approved drugs in the United States and Japan, **Henry Malinowski, Ph.D.**

Prizes

The top three prizes for presentations went to Drs. Gobburu, Wei and Chung in order. The top three poster prizes went to Drs. Sekar, Tandon and Zheng, respectively. Upper management did not compete for awards.

A committee representing the three divisions and immediate office in OCPB organizes science day. The members are: **Susan Banks,** Dr. Fadiran, Dr. Gobburu, Dr. Velazquez Kieffer (chair), Dr. Kumi, **Wes Metz** (Deputy Director, OCPB), **Lillian Riley, Sandip Roy, Ph.D.,** Dr. Sekar, **Monique Walkelamp-Barnes, Ph.D.,** Dr. Wang and **Hellen White.**

More detailed abstracts are available on CDERnet at http://cdernet/ocpb/index.html.

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

Kelsey's Connection to Drug Safety Dates to Elixir of Sulfanilamide

(Continued from page 1)

Medal for Distinguished Service, the highest award the government gives to civilians. She was the second woman to receive this award.

While best known for her work on thalidomide, Dr. Kelsey notes that her connection to drug safety goes back to the elixir of sulfanilamide scandal of 1937 in which a poisonous solvent in a patent medicine killed 107 persons, mostly children.

"My mentor in pharmacology had close connections with FDA and thought it would be a great learning experience for young graduate students to be involved in toxicology testing of the elixir of sulfanilamide," Dr. Kelsey said.

"The urgency of the situation, the intensive round-the-clock toxicology studies and the subsequent changes in the law relative to the control of drugs made a deep and lasting impression on me as a graduate student," she added.

Dr. Kelsey helped open the door to women in medical and scientific research. She received her doctorate in pharmacology in 1938 from the University of Chicago and became an instructor and assistant professor there. In 1950, after many years of course work, she earned her medical. degree, also from Chicago.

"I feel very honored," Dr. Kelsey said of her induction into the hall. "I am pleased to be honored along with women that I admire, especially those that I personally have worked with in science and medicine."

Dr. Kelsey joins a group of 19 American women inducted into the hall of fame this year, bringing the total number of hall inductees to 176. For more information, see the Web site for the National Women's Hall of Fame at http://www.greatwomen.org.

ICH Eyes July for Accepting Common Technical Document Submissions

By Justina Molzon, M.S. Pharm., J.D.

SAN DIEGO—The 5th International Conference on Harmonization took place here Nov. 9 to 11, marking the tenth anniversary of this important harmonization activity for Japan, the European Union and the United States. The conference followed meetings of the ICH Steering Committee and its expert working groups during which they reached consensus on a final harmonized Common Technical Document.

Changes to the names and structure of some sections were made from the version released for comment this summer (August *Pike).* The aim is for FDA and the regulatory agencies in the other regions to be able to accept voluntary submissions that comply with the CTD by July.

Meanwhile, in Rockville, CDER's and CBER's technical and regulatory experts had begun their review of existing regulations and guidances with the aim of eliminating those superceded by the CTD and bringing others into compliance with the CTD. There appear to be no major conflicts with existing regulations, according to technical experts in both centers. Other steps toward implementation will include internal training and public meetings for transparency.

Center Director **Janet Woodcock, M.D.,** discussed these Agency concerns in her speech at ICH 5 on "FDA Perspectives on Implementation of the CTD."

The San Diego conference drew more than 1,400 participants, including about 200 from regulatory agencies and other governmental and intergovernmental agencies. They heard detailed presentations about the CTD.

In the keynote presentation, FDA Commissioner **Jane Henney, M.D.,** referred to the CTD and its expected electronic counterpart as a "natural extension of the information age" and described the opening of a door to greater communication between regulatory authorities.

Use of ICH guidances has had a positive contribution on the international drug regulatory approval process and speeded the availability of new medicines to the public, according to results of a survey presented at the conference.

The ICH partners announced "Principles of ICH Global Cooperation" that target improved global cooperation with non-ICH partners. The conference also provided an opportunity to reflect on some case studies on the experience of developing and implementing ICH guidelines.

Progress on the electronic version of the CTD, which is currently expected to reach draft consensus in May and final consensus by the end of 2001, was also presented.

During the closing plenary session, the "Way Forward" for ICH was presented. A position paper on the "Future of ICH" endorsed by the steering committee was also provided to the conference participants. The paper emphasizes that ICH intends to focus its activities on:

- Implementing and maintaining existing guidances.
- Preventing disharmony.
- Encouraging scientific dialogue and harmonization in additional areas such as new technologies or therapies and postmarketing activities.
- Undertaking efforts towards global cooperation with non-ICH regions and countries.

In addition, the paper reaffirmed public health protection as a foundation of the ICH harmonization activities. It was also announced that the 6th International Conference on Harmonization would take place in Japan in fall 2003.

A number of harmonized documents, in addition to the CTD, were completed prior to the conference. The following guidances reached Step 2 of the ICH process and will be released for consultation in the three ICH regions:

- Good Manufacturing Practices for Active Pharmaceutical Ingredients (Q-7A).
- Safety Pharmacology (S-7).
- Revision of the Stability Guidance (Q-1A).
- Revision of Toxicokinetics/Pharmacokinetics Guidance (S-5/M-3).
- Stability Guidance on Matrixing and Bracketing (Q-1D).

More information is on the ICH Web site at http://www.ifpma.org/ich1.html.

Justina Molzon is the Center's Associate Director for International Affairs.