news along the pike

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CENTER FOR DRUG EVALUATION AND RESEARCH

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***PIKE'S CORNERS . . .***



# 2001 Priorities: DFS, Review Standards, External Ties

## *Center Director Reviews Mission, Successes, Challenges*

**BY JANET WOODCOCK, M.D.**

CDER priorities for the year 2001 will be to implement the division files system, standardize our reviews and strengthen our external ties.

DFS electronic document filing and archiving will be a profound change for us. We need to make the transition individually and collectively.

Standardizing our reviews is an essential step in making our information about a drug available to the public and the clinical community. People will support us when we give them something that they can see and value.

Strengthening external ties with our stakeholders—including the clinical community—and building constituencies is going to take resources, but we need to make the investment.

**Mission Review**

During recent years, we have come to a deeper understanding of our mission to assure that safe and effective drugs are available to Americans.

Safe means that the risks of a medicine are managed. It is one thing for us to calculate that benefits outweigh risks for an intended population in a clinical study, but we're only now exploring how big an issue that is when the drug is actually used. We need to make sure that the risk-benefit ratio for a drug is maintained during its life cycle.

Safe also means that the quality of products is assured and that health fraud is pursued. Even though this has been scaled back from lack of resources, we must go after egregious

*(Continued on page 8)*

## *American University Picks Dr. Woodcock for Executive Award*

The American University School of Public Affairs named Center Director **Janet Woodcock, M.D.,** one of two recipients of its Roger W. Jones Award for Executive Leadership at a ceremony Sept. 25. Deputy Under Secretary of the Navy Charles Nemfakos also received the award.

Walter D. Broadnax, Ph.D., dean of the public affairs school, said the award recognizes the ideals of Roger Jones, a career federal executive who believed that government should not be an obstacle to but a catalyst for technological change in society.

Ray Kline, chairman of the selection committee and a former president of the National Academy of Public Administration, presented the awards. Kline said that this year's candidates created "stiff competition, but two real winners emerged."

The awardees were asked to speak on the role of the career executive during transition in the presidency. Both commented on the theme of successfully blending a new administration's political agenda with a federal agency's core programs and functions and the technical ex-

*(Continued on page 3)*

## Compliance Officer Begins Studies for Work in Japan

**BY PATRICK E. CLARKE**

Center employees may occasionally ignore some of the many e-mails that are automatically blipped onto their computer screens. But, for **Monica Caphart,** a compliance officer in the Office of Compliance's Division of Manufacturing and Product Quality, reading e-mail faithfully and having excellent credentials, is leading her on an experience of a lifetime.

Caphart is the third Center employee in a row and one of eight federal government employees chosen this year as a Mike Mansfield Fellow. An intensive two-year program, the fellowships provide for a year in Japan working full-time in professional positions in Japanese government offices, preceded by a first year of full-time study in the United States of the Japanese language and culture.

**Henry Malinoski, Ph.D.,** the Center's first fellow has returned from his one year in Japan; and **Ken Kobayashi, M.D.,** the second fellow, has recently begun his year of work in Japan.

*(Continued on page 7)*

## JOE'S NOTEBOOK

# U.S. Health Trends

Although modern medicines are helping Americans live longer and healthier lives, it isn't easy to make a direct link from what we do at work to better public health statistics. In addition to improved medicines that work better and are easier to take, many other variables come into play, such as lifestyle choices, access to health care, education and genetics.

Nonetheless, you may be interested in some updated statistics from *Health, United States, 2000.* In its 24th year, this annual report—from the Centers for Disease Control and Prevention's National Center for Health Statistics—was released two months ago and contains a wealth of information on Americans' health status and use of health care as of 1998. For instance:

- In 1998, life expectancy at birth reached an all-time high of 76.7 years, and infant mortality remained at a record low 7.2 deaths per 1,000 live births.
- Mortality from heart disease, the leading cause of death, declined 3 percent in 1998, continuing its long-term downward trend. The 1998 age-adjusted death rate for heart disease was about one-half the rate in 1970.
- Mortality from cancer, the second leading cause of death, decreased 1.6 percent in 1998, continuing a decline that began in 1990. Over the preceding 20-year period, 1970-1990, age-adjusted cancer death rates had increased steadily.
- Mortality from stroke, the third leading cause of death, appears to have resumed a downward trend. In 1998, the age-adjusted death rate fell 3.1 percent, declining for a third straight year following a leveling off earlier in the decade. Between 1980 and 1992, stroke mortality had declined at an average rate of 3.6 percent per year.
- Mortality from HIV infection declined 21 percent in 1998, following a 48 percent decline in 1997 and a 29 percent decline in 1996. This three-year decline contrasts sharply with the 1987-1994 period, when HIV mortality increased at an average rate of 16 percent per year.

Despite these overall declines in mortality, there are substantial and disturbing disparities among racial and ethnic groups for many causes of death. In 1998, overall mortality for black Americans was 53 percent higher than for white Americans. The 1998 age-adjusted death rates for black Americans exceeded those for white Americans by 78 percent for stroke, 50 percent for heart disease, 33 percent for cancer and almost 700 percent for HIV infection.

Surgeon General and Assistant Secretary of Health **David Satcher, M.D.,** speaking at the U.S. Conference on AIDS in Atlanta in early October, warned that the HIV and AIDS epidemic "has evolved to become increasingly an epidemic of people of color, of women and of the young.''

Citing updated statistics covering the period July 1999 to last June, Dr. Satcher noted that black and Latino women are hard hit, making up 78 percent of the newly reported HIV cases among women. Black Americans, who make up 12 percent of the population, account for more than 50 percent of the estimated 40,000 new HIV infections and almost half of the total cases reported. Latinos make up 11 percent of the population and account for an estimated 19 percent of new HIV infections and 19 percent of total AIDS cases reported.

You can be download a copy of *Health, United States, 2000* from CDC's Web site at http://www.cdc.gov/nchs. This year's report features a special chart book on adolescent health.

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**New Associate Editor.** It's been a full two years since the *Pike* has had an associate editor. Please welcome **Patrick Clarke,** who comes to us from California where he worked in public affairs for the Air Force Reserve.


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

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## *OMBUDSMAN'S CORNER*

# Ignorance Is Not Bliss

**BY JIM MORRISON**

The composer Gian Carlo Menotti once wrote: "A man only becomes wise when he begins to calculate the approximate depth of his ignorance." One benefit from working in CDER is a never-ending depth gauge for ignorance. It isn't that we are dumb, it is just that the science, policies and issues are so extensive and change so frequently that it is not possible for us to ever feel that we have mastered them. Whenever we think we are on top of them, it's time to wake up.

There are both internal and external opportunities for displaying our ignorance. But knowing that we don't know everything is a safety net most of us acquire sometime after adolescence. It is always possible to learn by asking someone or to defer to someone who does know. When we don't know what we don't know, as Yogi Berra might say, we get into trouble.

Each of us has areas of expertise, and collectively CDER has a wealth of knowledge about drug development and regulation. But there are blind spots. For example, too many of us tend to make assumptions about marketing and economic factors that motivate drug companies. And, yes, it does work the other way. Sometimes companies make assumptions about what motivates the FDA rather than asking the Agency.

Just recently I saw such a case of mutual ignorance. Reviewing staff were encouraging a company to pursue studies that might have led to an expansion of the labeling and use of a drug. The company viewed the encouragement as an unwanted requirement. The reviewers could not understand why the company was resisting such sound scientific advice. The situation developed into something of an impasse.

Had the reviewers asked the company about its plans for the drug, they would have learned that the firm viewed the product as very marginal and were unwilling to spend additional resources to develop it further.

Had the company asked the reviewers about their proposals, it would have learned that the reviewers thought they were being helpful and that the suggestions were not intended as requirements. Five minutes of discussion would have prevented weeks of perplexed correspondence.

Even CDER staff who have worked in the pharmaceutical industry are unlikely to know the particular reasons behind the actions or inaction of applicants. Motivations may not be knowable by even the most astute observers. Confidential business deals or commercial strategies may be involved that even the company's regulatory affairs contacts are not aware of. Just know that we can't know enough to predict regularly what people or companies will do, so don't try.

Too often regulated companies assume that FDA is making a request or acting out of bureaucratic ignorance. From my observations, most often FDA staff have legitimate motives and intelligent reasoning behind their requests and actions.

It is never inappropriate for companies to discuss with the Agency the reasons behind their actions. Likewise, it is appropriate for CDER staff to engage applicants in a discussion of their aims and plans for a proposed product. Of course, it is not legitimate for CDER staff to press companies for financial information.

Not only is it difficult for companies to discern what motivates the Agency, but CDER staff should not assume they always know what other parts of the Center or the Agency are doing. In our ignorance we sometimes unknowingly create a Catch 22. But believe me, regulated companies are very good at knowing when they are presented with a Catch 22.

I don't know how the notion that "ignorance is bliss" ever got started (perhaps a misquote from a poem), but from where I sit, ignorance is anything but blissful.

*Jim Morrison is the Center's ombudsman.*

# American University Selects Dr. Woodcock for Top Executive Award

*(Continued from page 1)*

pertise of its career employees. Nemfakos said that managing a transition from one administration to the next is a subset of the broader challenge of managing the transformation of government and governance from doers to managers and entrepreneurs. Dr. Woodcock noted that a change in administrations reflects the will of the people and is an important component of ensuring accountability for government agencies.

The award recognizes:

- Superior leadership resulting in outstanding organizational achievements.
- Commitment to the continuity of government by developing managers and executives.

Through a major restructuring of the Center, implementation of project management, strategic planning, process improvements, training, identifying and publishing key policies and a strong commitment to information technology, Dr. Woodcock led the Center during the reform of the drug review process. The successful retooling of the drug review process has given Americans access to beneficial new drugs more quickly, and drugs approved in the United States remain the world's standard against which success in the industry in measured.

Dr. Woodcock led changes to the Center's organization, quality of science and management that moved decision making downward and enhanced the roles of medical scientific and management disciplines. Her strong commitment to the continuity of government involved all levels of the Center in the development of clear, shared mission, vision and operating principles.

Recognizing the need to develop future leaders systematically, she instituted the Leadership Fellows Program, which has graduated 80 fellows. She has enhanced the science base of the Center through extensive in-house training.

She began an internal grants program for CDER scientists to fund research projects that establish and validate regulatory science and review.

*PROJECT MANAGEMENT CORNER*

# Site Tours, Shadowing Program Undergo Successful Pilot Runs

**BY JEAN YAGER, DEBORAH KALLGREN, JULIEANN DUBEAU AND MAUREEN PELOSI**

The four of us, members of the Center's Project Management Training and Certification Subcommittee, conducted a successful trial run in July of two training initiatives for project managers: the Site Tours and the Shadowing Program (January *Pike*).

We traveled to Glaxo Wellcome in Research Triangle Park, North Carolina, to evaluate a sample program agenda and format for its usefulness to project managers and to determine its potential value as a training venue for reviewers. We agreed that the program increased everyone's understanding of the drug development process.

This initiative, first announced in the *Federal Register* in November, encourages voluntary participation from interested pharmaceutical companies. The training follows a detailed agenda created by the host firm with guidance from the Project Management Program Staff.

CDER pays travel costs for its employees. To guarantee a neutral training experience, Center participants cannot be actively involved in the review of any pending new drug application or efficacy supplement from the host firm or engage in specific discussions of any applications during either the tour or shadow visit. This ensures that the visit is not used to debate or create regulatory policy.

The facilities tour requires one day, and the shadowing experience takes place over two days. The tour of the manufacturing facility may be separate from the shadowing experience or, as in this case, when the manufacturing site is near the research and development facility, both experiences may be combined into a three-day comprehensive visit. We originally envisioned that the two programs would be targeted separately to junior and senior project managers. We discovered, however, that combining the programs is the best approach.

### Site Tour

The first day of the program included an orientation to the firm's drug development facilities. Although the content was oriented to junior project managers, the four of us found it informative.

The morning was spent touring the pilot plant, the pharmaceutical development analytical laboratories and the pathology and toxicology laboratories. In the pilot plant, small batches of test drugs are made in a vat the size of a toaster. It was particularly fascinating to compare the miniature version to the room-sized vats used to make batches of marketed drugs.

After lunch, we took a short ride to the factory for a tour of the firm's manufacturing facilities. There were many interesting activities to observe and learn more about, such as product dissolution and paddle speeds, manufacturing and packaging processes for metered-dose inhalers, pathology and histology laboratories and the numerous control steps taken to ensure product sterility and quality.

> "We came away with a much greater understanding of the complexities of worldwide drug development."

We concluded that the facilities tour had been a tremendous success and that this overview information would be extremely valuable to project managers in the first one to two years of their careers. The experience also gave us a greater appreciation for the complexities of drug development and the business aspects such as marketing, finance, international marketing and pricing, which must be factored into the decision-making process. We concluded the tour by playing a board game on drug development to reinforce the knowledge acquired during the day.

### Shadowing Program

The second and third days provided us with the opportunity to experience regulatory affairs and project management contributions in an industry setting. The firm's shadowing program, targeted at more experienced project managers, was creative, using an informal lecture and dialog format.

We reviewed project management activities at key stages of drug development, from early discovery and proof-of-concept through the marketed product's lifecycle. In addition, we discussed regulatory affairs contributions to various aspects of drug development, including global dossier preparation, report review, labeling and advertising review. We provided our hosts with an overview presentation on the role of the project manager in the review team and discussed various review management issues.

### Lessons Learned

There is no substitute for learning about drug manufacturing by touring an actual plant, observing the process and learning from our regulatory, project manager and scientist counterparts on their home turf. We also concluded that it would be a better learning experience to combine the Site Tour and the Shadowing Program when possible. We realized that both programs would be as valuable for reviewers as they are for project managers. While project managers are able to address issues from the process management point of view, reviewers could speak to them from their scientific perspectives.

We came away with a much greater understanding of the complexities of worldwide drug development. Our discussions with the host firm were frank, open and focused on identifying ideas for improving project management in an evolving worldwide regulatory environment.

We currently have a number of agendas from other interested pharmaceutical companies of all sizes and ranges in our queue. We plan to continue the program, preferably using the combined format.

By the close of this year and contingent upon funding, we hope to have a group of CDER reviewers representing the multidisciplinary review team participate in a site tour and shadowing experience. We are confident that they will come away as impressed and excited by this learning opportunity as we are.

*Jean Yager is the head of and Deborah Kallgren is a project manager on the Project Management Program Staff in OTCOM. Julieann DuBeau, Division of Gastro-Intestinal and Coagulation Drug Products, and Maureen Pelosi, Division of Oncology Drug Products, are project managers in ORM.*

# New Technologies Are Coming. What Can You Do To Prepare?

Recent e-mails, articles and demonstrations have introduced several new hardware and software technologies that are coming soon to CDER. Each of these systems will greatly affect the way we perform our work.

**Infrastructure Improvement**

Fiber optic cable and equipment have been run to several CDER buildings to provide increased network speed and performance. Once the new connections are activated, changes will have to be made to network addresses on PCs, printers and local servers for buildings at Metro Park North 1 and 2, Nicholson Lane Research Center, Wilkins Avenue and Twinbrook Parkway. We will notify you before, and our staff will be available to handle any concerns that may arise during the scheduled configuration.

When the network upgrade is complete, the new equipment will support only PC communications among Center buildings. All Macs should have already been removed from the network; but, if any are still connected, please disconnect them and transfer their functionality to PCs as soon as possible.

PC standardization and fiber optic equipment will provide a faster, more stable network environment. Please contact the Help Desk (HELP, 7-0911) for any computing questions.

**Microsoft Outlook**

E-mail has become an integral part of everyday life in the Center. Some of us use ALL-IN-1, some use TeamLinks and some work back and forth between the two. Since the FDA has mandated that Microsoft Outlook will be the standard e-mail system for the Agency, everyone in the Center must migrate from these two e-mail systems to Outlook.

This migration brings about many issues related to storage capacity, training and maintenance. In order to anticipate issues that may arise when the entire Center migrates to Outlook, users within OIT are starting to pilot the new e-mail system. From this pilot, we can confirm the steps needed to successfully transition the Center to MS Outlook.

Policy and procedure on e-mail migration and storage will be released closer to the Centerwide release of Outlook.

We will continue to update you on the pilot process and the eventual rollout. Contact the Help Desk (HELP, 7-0911) for all of your e-mail related questions.

**Don Duggan** (DUGGAND) is the Outlook rollout project manager.

**Division Files System**

Demonstrations on the new features of DFS (Division Files System) 2.0 have been ongoing throughout the Center. OIT Training and Document Room staff, as well as Document Room Subcommittee members, have been on hand to answer and document questions that arise during the demonstrations.

Many of the questions are answered at the demonstrations and many will be answered in updated user and policy guides to be available closer to the release date of the software. Also, the OIT training classes will be updated to reflect the changes in DFS 2.0.

DFS classes are scheduled throughout the fall. Refer to the OIT Web for training registration and updated user documentation. Please contact the Help Desk (HELP, 7-0911) for all DFS related issues.

**New IT Procurement Process**

On Oct. 10, we introduced a new, streamlined process for ordering information technology products and services that changes the way requests are handled—from filling out the HHS-393 form to placing the requisition with a purchasing agent.

To help guide you, we redesigned the IT procurement intranet site to provide specific information on what to buy and how to buy it. On the site, you will find simple, easy to follow procedures to take you through each step. Information on the hardware and software supported by OIT is current and will be regularly updated. A frequently-asked-questions page provides answers to common queries about IT procurement. The redesigned IT Procurement Web site is located at http://oitweb/procurements/default.htm.

**Mark Magee** (MAGEEM, 7-3531) is the IT procurement point of contact for advice and guidance about IT purchases.

The new procurement process is Phase 1 of a project to reengineer the entire IT procurement process. Phase 2 of will focus on the receipt and distribution of IT products and services, and Phase 3 will address long-term acquisitions planning. These last two phases will be implemented in January.

## November IT Training

| Monday | Tuesday | Wednesday | Thursday | Friday |
|---|---|---|---|---|
| | | 1<br>**E-Doc Query** (RetrievalWare) 9:00-12:00<br>**E-Doc Query** (RetrievalWare) 1:00-4:00 | 2<br>**E-Doc Query** (RetrievalWare) 9:00-12:00<br>**E-Doc Query** (RetrievalWare) 1:00-4:00 | 3<br>**E-Doc Query** (RetrievalWare) 9:00-12:00<br>**E-Doc Query** (RetrievalWare) 1:00-4:00 |
| 6<br>**E-Doc Query** (RetrievalWare) 9:00-12:00<br>**E-Doc Query** (RetrievalWare) 1:00-4:00 | 7<br>**E-Doc Query** (RetrievalWare) 9:00-12:00 | 8<br>**Intro. Word** 9:00-12:00<br>**Word Formatting** 1:00-4:00 | 9<br>**Word Tables** 9:00-12:00<br>**DFS 2.0** 1:00-4:00 | 10 |
| 13 | 14<br>**JMP Session 1** 1:00-4:00 | 15<br>**CDER Standard Letters System** 9:00-12:00<br>**DFS 2.0** 1:00-4:00 | 16 | 17<br>**PEDS Tracking System** 9:00-12:00 |
| 20 | 21<br>**JMP Session 2** 1:00-4:00 | 22 | 23 | 24 |
| 27 | 28<br>**JMP Session 3** 1:00-4:00 | 29 | 30<br>**NEDAT** 9:00-12:00<br>**DFS 2.0** 1:00-4:00 | |

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

*DRUGS IN THE NEWS*

# FDA Approves Two New Uses, Three New Drugs

Based on the Heart Outcomes Prevention Evaluation study, known as HOPE, FDA on Oct. 6 approved a new use for the antihypertensive drug ramipril (Altace)—reducing the risk of heart attacks, strokes and death in patients who are at increased risk for these problems.

The HOPE Study was a large multicenter randomized placebo-controlled study of more than 9,000 patients in Canada, the United States and South America, of whom 4,600 received Altace.

Ramipril-treated patients in the HOPE study experienced a 22 percent reduction, compared with placebo, in the risk of myocardial infarction, stroke or death from cardiovascular causes over five years of follow-up. This resulted in a significant reduction in the risk of death from any cause.

Benefits of treatment were similar in subgroups distinguished on the basis of age, gender, underlying heart disease, diabetes and the use of concomitant medicines.

FDA on Sept. 28 approved mifepristone (Mifeprex) for the termination of early pregnancy, defined as 49 days or less, counting from the beginning of the last menstrual period.

"The approval of mifepristone is the result of the FDA's careful evaluation of the scientific evidence related to the safe and effective use of this drug," said FDA Commissioner **Jane E. Henney, M.D.,** "The FDA's review and approval of this drug has adhered strictly to our legal mandate and mission as a science-based public health regulatory agency."

Under the terms of the approval, mifepristone will be distributed to physicians who can accurately determine the duration of a patient's pregnancy and detect an ectopic pregnancy.

Physicians who prescribe mifepristone must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding—or they must have made plans in advance to provide such care through others.

More detailed information about this product is available on FDA's website at http://www.fda.gov/cder/drug/infopage/mifepristone/.

FDA announced on Sept. 26 the approval of arsenic trioxide (Trisenox) for the treatment of patients with acute promyelocytic leukemia (APL) who have not responded to or have relapsed following the use of all trans-retinoic acid and anthracycline-based chemotherapy, which is considered first-line therapy.

Development of arsenic trioxide, an orphan drug, was rapid. It was approved only three years after the study of the drug was first started in the United States.

APL is a cancer of the white blood cells, characterized by a rapid accumulation of abnormal white blood cells in the bone marrow and blood resulting in anemia, susceptibility to infections, bleeding, and hemorrhage.

An estimated 1,500 new cases of APL are diagnosed each year, of which an estimated 400 patients will not respond to or will relapse from first-line therapy.

On Sept. 15, FDA issued an accelerated approval for the combination of lopinavir, a new protease inhibitor, and ritonavir, a previously approved protease inhibitor, to treat HIV infection in adults and children older than 6 months. The low dose of ritonavir in the combination product inhibits lopinavir's metabolism and results in blood levels of lopinavir that enhance its effectiveness against HIV.

The new drug is used in combination with other anti-HIV drugs and was studied in six controlled and one expanded access clinical trials. More information in available on CDER's Web site at http://www.fda.gov/cder/drug/infopage/kaletra/default.htm.

FDA announced on Aug. 31 the approval of the antimicrobial ciprofloxacin (Cipro) for use in individuals who have been exposed to inhaled anthrax. Ciprofloxacin is approved to reduce the incidence or progression of inhalational anthrax following exposure to aerosolized *Bacillus anthracis*, the bacterium that causes anthrax.

Inhalational anthrax is an extremely rare disease, resulting from exposure to contaminated animal hides and hairs, usually in an industrial setting. The causative organism, *B. anthracis*, is a spore-forming gram positive rod that can be used as a biological weapon.

Inhalational anthrax is thought to be the most likely form of this infection to result from the intentional use of an aerosolized preparation of spores of *B. anthracis*.

*PIKE'S PUZZLER*

# Test Your Anatomy Knowledge

BY TONY CHITE

**1. Which of the following bones is not found in the human wrist:**

a. capitate b. trapezium c. navicular d. trapezoid

**2. The human talus:**

a. is the ankle bone.
b. is the second largest of the tarsal bones.
c. articulates with the tibia, fibula, calcaneus and navicular bones.
d. none of these
e. all of these

**3. One of the tendons that binds the popliteal fossa laterally and medially is the:**

a. Achilles b. hamstring c. patellar d. trefoil

**4. A ligament is a band of fibrous tissue that connects:**

a. bones b. muscles c. cartilages d. nerves e. both a and c

**5. A bilaterally symmetric lymphoid gland consisting of two pyramidal lobes situated in the anterior superior mediastinum is the:**

a. thymus b. thyroid c. adrenal d. parathyroid

Answer Key: 1c, 2e, 3b, 4e, 5a.

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

# User Fee Growth Limits FDA Flexibility, Top Agency Officials Say

*(Continued from page 8)*

review.

Other FDA components have become squeezed for funds as the requirement to match user fees with appropriated funds has adsorbed an ever-increasing portion of FDA resources. These include postmarket functions such as adverse event reporting, advertising review and inspections of manufacturing plants as well as other premarket programs such as reviews of over-the-counter drugs, generic drugs, medical devices and blood products.

"There's a perception by some that having the regulated industry provide funding for review may compromise the Agency's independence and objectivity," Henney said. "We have no evidence for this but even the perception of a conflict of interest is a worrisome issue that must be addressed, for it threatens the confidence of consumers in the integrity of FDA's reviews."

Center Director **Janet Woodcock, M.D.,** and Center for Biologics Evaluation and Research Director **Kathryn Zoon, Ph.D.,** said the user fee program demonstrated that FDA could meet stringent goals when adequately funded. Dr. Woodcock said that the public has benefited from faster access to new therapies. She pointed out that industry has been encouraged to develop therapies for formerly intractable conditions. She and Dr. Zoon commented that the PDUFA II proliferation of timelines that need to be tracked has become burdensome.

Consumer and patient groups stated their philosophical opposition to user fees. Both types of groups would prefer that FDA programs be fully funded with taxpayers' dollars to buttress the Agency's reputation for impartiality. Consumer groups said that FDA's acceptance of user fees and recent drug withdrawals have created a perception that consumer safety is compromised. Patient groups, while skeptical of user fees, generally applauded the faster access to approved drugs. Some supported expansion of user fees to cover other FDA activities.

Representatives of research-based drug firms and biotechnology companies supported user fees linked to performance goals. They applauded the predictability that user fees had provided for the Agency, the industry and patients. They opposed expanding user fees without linking them to specific performance goals. Representatives from the generic trade groups split over user fees to support generic drug review. One group opposed them, noting that the relationship between review time and time to market is not as clear cut and predictable for generics as it is for new drugs. Generics often face patent and other legal challenges to their entry onto the market.

A physicians' group representative noted that his organization was initially critical of user fees but now supported the program with performance goal links. He expressed his group's concern that other FDA programs were being squeezed. A pharmacists' group representative supported expanding user fees to other FDA programs related to drugs.

Two academic researchers presented data showing that user fees have been so successful in speeding the U.S. drug review process that they created conditions that make the United States the country of first choice for launching new drugs.

More background material, Dr. Henney's remarks, a recent *FDA Consumer* article on user fees and an on-line comment form can be found at http://www.fda.gov/oc/pdufa2/meeting2000.html. FDA is accepting comments to help it prepare for negotiations until Oct. 31.

# Compliance Officer to Examine Japanese Manufacturing Issues

*(Continued from page 1)*

"I'm on the foreign inspection cadre and did a foreign inspection last year in Japan," explained Caphart. "When I saw the announcement, I thought it would be a great opportunity."

Another FDA employee chosen for the opportunity this year is **Capt. Ronda Balham** of the Office of Orphan Products Development. Balham is not only interested in how Japan evaluates the medical products for patients with rare diseases but also in exploring ways in which both countries might cooperate on standards for reviewing devices and for conformity in labeling and postmarket surveillance.

Caphart noted that her office was a key player in the European Mutual Recognition Agreement and that Japanese officials have expressed interest in a similar agreement. "Getting to know more about our Japanese counterparts would assist in furthering that process if and when it occurs," she said.

Caphart has asked for four placements, one of which would be to work in an office that is the exact equivalent of her office. She also wants to work at their pharmacopoeia, which unlike the private U.S. Pharmacopoeia, is part of the Japanese government.

"I've also asked for some time with their industry," she said. "Because we interface with our industry here, I'd like to see how Japan does it." Finally, she is going to try to get a one- to two-week internship in the Diet, the Japanese legislature. "Because our good manufacturing practice laws are passed by Congress, I want to see how the Japanese government handles similar issues."

She began 10 months of full-time language and culture training in September in Virginia., to be followed by two months of in-country language training.

"Learning more about the culture is what I'm most looking forward to. I've always been interested in other cultures," said Caphart. "I was born in Indiana but was raised in Liberia, as my parents are Liberians."

Caphart is hoping the trip won't be all work. "I have a slight artistic streak and dabbled in drawing while in high school and college. I've always been interested in arts and crafts," said Caphart who is interested in learning origami, the Japanese art of folding paper into different shapes. "Currently I do cake-decorating, and I'd like to see if Japan has some unique forms of cake decorating."

The other member of the Caphart household, Caphart's 11-year-old daughter, Feeta, is just starting sixth grade. "She's so excited to be going, Caphart said. "She's wants to start learning Japanese right away."

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# Internal, External Challenges Point to New Wave of Change

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fraudulent treatments that pose a health risk.

Appropriate advertising and making information about a drug available for physicians, nurses and patients play critical roles in the safe use of drugs.

Effectiveness means that drugs are adequately studied with proper endpoints and standards. Patients need the drugs of today, not drugs of a century ago. It is still a challenge for us to pursue old, ineffective drugs and get them off the market. Product quality is also a part of effectiveness.

We have a role to play in improving the armamentarium to fight disease and can encourage development of drugs that will have a clinical advantage. We know that drug therapy can be better individualized. Safety and effectiveness will increasingly mean "safe and effective for me." Women's groups and pediatric advocates want the information to know that drugs work in their populations.

Availability includes having generic drugs that provide economic access to treatments and over-the-counter drugs that provide ready access. The review process should not be seen as a barrier. People with no treatment options should have investigational drugs available. Again, information is a key part of assuring availability.

Congratulations are due to CDER for achieving an incredible piece of our mission. The Center is a successful, high performance organization, and many of its achievements were only a vision a few years ago. We are leading the international effort on standard setting and are well respected by consumers as a source of authoritative information on drugs. We also enjoy the respect of the industries we regulate and the scientific organizations involved in the pharmaceutical sciences.

**Challenges**

Unfortunately, the clinical community doesn't understand our role and doesn't regard themselves as our customers. Many clinicians believe we are obstacles to the drugs they want for their patients.

A similar lack of understanding and a failure to view themselves as our customers underlie our relations with consumer and patient advocacy groups. Consequently, we are a regulatory agency without a strong public constituency, and our appropriated resources are shrinking (see story below).

Media and activist charges that FDA standards are compromised by the user fee program may have an effect on consumer confidence in the Agency. We need to address concerns related to conflict of interest, human subject protection in clinical trials and growing public worries about the influence of money in a "biomedical-industrial complex."

We need to adequately support our people and make sure everyone is heard in decision making.

**Responding**

The good news is that we are poised on the threshold of a new wave of change and some of our long-term investments are coming to fruition. We will never get all the resources we want or need, so we must wisely use those we have.

We need to achieve a balanced program serving our internal needs and external customers. Internally we need to support our people, improve our processes and invest in the future. Components include scientific seminars and rounds, the master reviewer program, matrix management, computerization, standardized re view templates and matching our scarce research resources against urgent needs.

We will serve the public's need better with the new OTC label and prescription drug package insert. They will provide a uniform look and feel with all the important information up front. Our Web site is an important resource for our customers. More meetings with patient and consumer groups will pay dividends. An example was the incredible turnout we had for the OTC public hearing (July *Pike*). Our international cooperation will also pay important dividends.

For the short term, we need to finish projects and initiatives such as the prescription drug package insert and review standardization.

For the longer term, we need to apply the concepts of risk management, find innovative ways to enhance our enforcement activities, employ knowledge and decision management tools on the electronic data we will accumulate and enhance the Center's scientific base to deal with the next generation of drugs.

We are a successful organization that still has challenges ahead. Investment in our people, technology and in building constituencies will provide the critical edge we need to face these challenges.

*Editor's note: Dr. Woodcock's article is based on her "State of the Center" address at the Sept. 6 Scientific Seminar. Slides from the presentation are available on the CDERnet by selecting the Seminars button at http://cdernet.cder.fda.gov/dtd/index.htm.*

## FDA Hears Pros, Cons of User Fees at Public Meeting

**BY NORMAN J. OLIVER**

At a public meeting Sept. 15 to evaluate the Prescription Drug User Fee Act program, top FDA officials outlined its successes and detailed how the need to match user fees with appropriated funds has constrained other programs. They listened to testimony for and against user fee renewal from 17 groups representing patients, consumers, industry, health professionals and academia. The law sunsets in 2002, and the fees and resources it provides will also expire without further legislation.

"While the results of PDUFA have generally been positive in our premarket review function for drugs and biologics, there's been a significant impact on the Agency's other functions," said FDA Commissioner **Jane Henney, M.D.** Among the benefits, Henney noted that overall approval times for drugs and biologics have dropped from 23 months to 12, approvals for priority products fell from 12 months to 6. About 18 months have been shaved from development times representing cost savings of $2 billion a year to industry.

The proportion of FDA resources devoted to human drug review has increased from 17 percent in 1992 to 28 percent in 1999. User fees, which accounted for 7 percent of drug review costs in 1993 at the beginning of the program, now nearly equal 50 percent of funds spent on drug

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