news along the pike

Center for Drug Evaluation and Research

November 1997

Volume 3, Issue 11

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Pike's Corners . . .

Vice Presidential Award

FDA-Industry Partnership Wins Hammer

By Eric Sheinin and Doug Sporn

A partnership between the FDA and the International Society for Pharmaceutical Engineering (ISPE) that will save industry millions of dollars and ultimately benefit consumers has been selected to receive the Hammer Award from Vice President Al Gore. The ceremony honoring the FDA-ISPE team took place Nov. 3, as part of ISPE's annual meeting in Florida.

The award-winning team of ISPE, CDER and FDA's Office of Regulatory Affairs (ORA) Central Region developed a list of similar pharmaceutical manufacturing equipment needed for efficient implementation of the Scale-Up and Post-Approval Changes guidance for immediate release-solid oral dosage form drugs (SUPAC-IR).

The guidance and the "similar equipment list" provide substantive regulatory relief to manufacturers in the filing procedures used for manufacturing equipment changes. By reducing the number of requests that require prior

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Fall Awards Highlight Individuals, Teams

By Jackie Barber

CDER held its first Fall Honor Awards Ceremony Nov. 21—the day President Clinton signed the FDA Modernization Act into law. "This legislation represents an endorsement of what you have been doing," Center Director **Janet Woodcock** told the audience. "I'm struck by the breadth and diversity of the awards. They recognize how important a job everyone in the Center does."

A highlight of the ceremony was the presentation of the first Excellence in Communication and Leadership Excellence awards. To open the ceremony, the Montgomery County Police Color Guard presented the colors, and **Kevin Barber** sang the national anthem. **Ruth Clements** announced each award, and office directors provided an explanation of individual or team contributions. Those honored at the ceremony were:

Vice President Gore National Performance Review Hammer Award

Jane Axelrad, Yuan Yuan Chiu, Charles

(Continued on page 6)

Center's Electronic FOI Reading Room Opens

By Carolann Hooton and Carol Assouad

CDER's new drug reviews and generic drug reviews highlight its Electronic Freedom of Information (FOI) Reading Room that debuted on the Internet Nov. 5. The Center's site is part of the FDA's widely expanded capabilities on its World Wide Web site. The electronic reading room allows users to access and download a wide range of Agency and Center documents and records.

"We have entered a new era of ready access via the Internet to our review work products," commented **Murray Lumpkin, M.D.,** Deputy Center Director (Review Management). "This makes it all the more imperative that our reviews be a true reflection of the thoughtful deliberation and critical analysis that, indeed, do go into our decisions. As many people now will only be able to judge us on what they are able to read, all our reviews must be clear, well-written and fully documented."

In addition, the FDA's homepage has been revamped to make it easier for consumers, health professionals and others to access information suited to their special needs.

(Continued on page 10)

Joe's Notebook

The *Pike* Now a Double Click Away

When you received your e-mail alerting you that this issue of *News Along the Pike* was published, all you had to do was double click your mouse and you could start reading or make a printout—if you were in TeamLinks and had the Adobe Acrobat Reader installed. Those are two big "ifs" for many of you, so I thought I would share with you what the electronic version of the *Pike* offers. But first, thanks to Editorial Board member **Grant Williams** for prompting me to revisit the issue of e-mailing the *Pike.*

You'll notice from Grant's column in this month's Reviewers' Corner that he's become quite familiar with Adobe Acrobat and a flow charting program that most of us don't have. That brings up the main reason for using Adobe: How do we share the output of those programs with others who don't have identical software? A printout is one answer. Many of you, for example, read the *Pike* in hard copy.

There are plenty of good reasons, however, for installing the Acrobat Reader on your computer besides viewing the *Pike* and the Reviewer Diagram Group's examples. Perhaps the best reason is that the Acrobat Reader gives you access to other documents on the X:drive and on our Web site—MAPPs, guidances, organizational charts, reports, Freedom of Information documents—as well as a host of other documents throughout HHS and the Federal Government.

Grant's flow charting exercise also illustrates a second good reason for having an electronic version of the *Pike:* the ability to create links. You can follow a story in the *Pike* across pages by clicking on the "continued on" or "continued from" lines. These are now appearing in blue. You can jump to a story from its index on page 1. You can follow a hyperlink to additional information elsewhere on the World Wide Web. Check out **Carolann Hooton** and **Carol Assouad's** story on the Electronic Freedom of Information Reading Room, and you'll see even more reasons for installing the Acrobat Reader.

I have used all of Adobe's navigation tricks to help make reading the *Pike* on-line more convenient. On the Adobe toolbar, you'll find icons for thumbnails, bookmarks, a hand and printing. The thumbnail icon will display a tiny image of each page. Clicking on the tiny image will display the full page. The bookmark icon will display the headline for each article or column. Clicking on the bookmark will take you directly to the page with the article. Clicking on the hand icon and positioning the mouse pointer over an article will turn the pointer into a small hand with a down arrow. Clicking the mouse will pop the story up to the full width of your browser. Continuing to click will let you follow the story across columns and pages.

Making a printout of the *Pike* can be a bit tricky if you opened the *Pike* from the Internet using one of the latest browsers that integrates the Acrobat Reader. Be sure to click on the printer icon found on the Adobe toolbar, not the one found on the browser's toolbar. The browser icon prints blank pages.

There are a couple of ways to install the Adobe Acrobat Reader on your computer. From CDER's homepage, click on one of the four main buttons. At the bottom of the next page you will find a link to the Adobe Web site where you can download the reader. This is slow but useful if you are not connected to CDER's network.

It's quicker to install from our network's X:drive. For Windows 95, use Explorer to open the folder X:\software\acrobat\acrobat301 and double click on the file you find there. For Mac users, open the folder X:\software\acrobat\mac and do the same.

news along the pike

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

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

Photocopies are available in the Medical Library (Parklawn 11B-40) and its branches (Corporate Boulevard S-121, Woodmont I 200-S, and Woodmont II 3001).

Views and opinions expressed are those of the authors and do not necessarily reflect official FDA or CDER policies. All material in the Pike is in the public domain and may be freely copied or printed.

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

News Along the Pike
CDER Office of Training
and Communications (HFD-200)
Parklawn Building, Room 12B-45
Editor: Norman "Joe" Oliver (OLIVERN)
Associate Editor: Lori Frederick
Phone: (301) 827-1243
Fax: (301) 827-3055

Ombudsman's Corner

What You Say—Part I

By Jim Morrison

How many times have you been certain of what you meant to say, but the party to whom you were speaking didn't take it in the way you expected? It may happen more frequently than you think. I hear about problems of miscommunication all the time, but I get only those cases where someone received a message that provoked them enough to contact me.

In recent sessions of the New Reviewers' Workshop, I have given examples of communications with regulated industry that miss their mark. In this and subsequent columns, I'll share some of these examples and others that pertain to how well we communicate in CDER.

First, there is this one—which I still hear sometimes—that all we can say to an applicant is that the application is "under review." For many years, we were instructed that such information was all we could impart. If there is a single type of communication, or lack thereof, that causes more problems than any other for CDER, it is the failure to keep applicants or other stakeholders apprised of what is happening with the paperwork they have submitted.

I firmly believe that we would receive fewer calls and questions and more good will if we let people know where their application is and when each segment of the review is expected to be completed by the members of the team and their supervisors. So long as you give reasonable estimates and really make a good faith effort to meet them, you will gain credibility and significantly improve CDER's reputation for fairness and efficiency.

Second, the meetings MAPP (4512.1) has helped, but it has not eliminated the problems with scheduling meetings. It seems that it still takes too long to get meetings scheduled in the views of those we regulate who have a lot riding on our decisions. Some of the scheduling problems lie with the overcrowded calendars we all have and the demands created by PDUFA due dates and other pressing work. However, we can get out of this box if we simply stop assuming that all problems are solved by meetings. From my experience, very few are.

Perhaps the issue that is presented by the applicant or by the internal indecision can be resolved by telephone or e-mail. Some issues can be settled by the skillful use of a short consensus paper that is used as the basis for reaching mutual agreement. Many alternatives to meetings are more efficient and effective. Try them, you'll like the way they can free up time on your calendar.

"Many alternatives to meetings are more efficient and effective. Try them, you'll like them and the way they can free up time on your calendar"

In communicating with one another, it is always important to keep in mind that the relative positions of the people communicating greatly affect how the communication is received.

Just as a supervisor talking with a subordinate should be careful in choosing words that will be listened to for any nuance of threat, disapproval or praise, those of us who work in a regulatory agency must be cognizant of the effect our words have on those we regulate.

Dr. Woodcock likes to use the example of how you would react to an IRS auditor and perceive his or her words. The analogy is a good one to keep in mind. I'll continue this discussion of communications in the next issue of the *Pike.*

Jim Morrison is the Center's Ombudsman.

EEO Corner:

Native American/Alaskan Natives Heritage Month Observed

By Noreen Gomez

November has been designated as Native American/Alaskan Natives Heritage Month. It is the time set aside for us to give thanks to the original inhabitants for their contributions to civilization as we know it today.

There are almost 2 million Native Americans living in the United States. The term "Native American" is used to describe the 504 tribes including the 197 Alaskan Native groups, such as the Eskimos and the Aleuts. About 100 tribes have become extinct since the arrival of Europeans on American soil. There are roughly 300 Indian reservations in the United States, the largest of which is the Navajo reservations extending throughout 16 million acres in Arizona, New Mexico and Utah.

Once again CDER salutes its own growing family of Native American/Alaskan Natives for a job well done. Our family includes: **Tawni M. Brice** (Alaskan), consumer safety technician, Office of the Director, Regulatory Policy Staff; **Sharon L. Brownewell** (Cherokee), technical information specialist, Office of Management, Division of Drug Information Resources; **Hartsell L. Whitacre, Jr.** (Cherokee), management analyst, Office of Management, Division of Management and Budget; **Angela M. Youngblood** (Cherokee), telecommunications specialist, Office of Training and Communications, Division of Communications Management; and **Helen N. Winkle** (Cherokee), program manager, Office of Testing and Research, Immediate Office.

An exhibit featuring our Native American/Alaskan Natives, and their tribal affiliations was displayed during November in the Parklawn's 5th floor lobby and WOC II lobby.

Noreen Gomez is an EEO specialist on the Center's EEO Staff.

History Corner

1911: Popular Drug Division Had Extensive Collaborations

By John Swann, Ph.D.

Fourth of four parts.

In 1911 the Federal Government employed fewer than 300 chemists, 70 percent of whom worked in the Department of Agriculture. Moreover, Harvey Wiley strongly believed in the importance of collaborative work with other Federal agencies and with outside institutions and organizations. Thus it is not surprising that other agencies turned to this department—and to the Bureau of Chemistry in particular—for assistance with chemical analyses and therapeutic appraisals. In turn, the Drug Division applied most of these opportunities to enforce the 1906 Food and Drugs Act.

In its first decade, the division worked extensively with many other Federal government entities. The division analyzed the composition and the claimed therapeutic effects of alleged cures for tuberculosis, cancer, drug addiction, epilepsy, syphilis and other nostrums for the Post Office Department, toward enforcement of the postal fraud laws.

The division investigated cod liver oils for the Bureau of Fisheries, part of the Department of Commerce and Labor. From time to time division staff also handled requests for analyses from the Congress, the Interior Department and the Bureau of Printing and Engraving.

Drug Division head Lyman Kebler described the occasion when Wiley assigned him the task of analyzing different samples of glue for Printing and Engraving: "I told 'the Big Chief' that I had never tested glue and did not know anything about the subject. In reply the Boss said, 'You know as much about testing glue as anyone in the Bureau.' I further protested that glue was not a drug. He retorted, 'Glue is certainly a drug around here and it is your job.' He had shopped, without success, around the Bureau for someone to do the work, and the Drug Chief was a newcomer and the logical victim. Some of my fellow chemists considered it a good joke."

The Drug Division cooperated with several components of the Department of Agriculture. For example, at the request of the Bureau of Plant Industry, they analyzed samples of hops for arsenic contamination, and they determined the levels of barium in animal feed that could account for a cattle disease known as "loco." They worked with the Bureau of Entomology on beeswax, investigating physicochemical properties of this substance as a function of the type of bees involved and the location of the production. In the process, the division improved upon pharmacopoeial tests for beeswax.

Among collaborations outside the Federal Government, the division examined so-called medicated beverages for the food commissioner of the State of Texas. Many of the brands of soft drinks tested were entirely free of cocaine, yet this alkaloid was present in several other samples, ranging from a trace to about twice the USP dose per 8 ounces of beverage. The division consequently recommended 13 samples for prosecution under the 1906 Act.

Both Wiley and Kebler were charter members of the Council on Pharmacy and Chemistry of the American Medical Association. The AMA established this council in 1905 to provide physicians with a list of approved products not in the U.S. Pharmacopeia or National Formulary. The council evaluated drugs from the standpoint of composition, therapeutic claims and advertising. Council approval or disapproval of a product determined whether or not manufacturers could advertise it in much of the professional medical literature.

Kebler's group investigated dozens of drugs for the council, especially with respect to false, misleading and exaggerated therapeutic claims. The American Pharmaceutical Association was involved with the Drug Division since Wiley's announcement at the 1902 APhA meeting. Kebler and his colleagues assisted APhA in the evaluation of essential oils, crude drugs and the general nature of drug adulteration in America.

The Drug Division of the Bureau of Chemistry was responsible for controlling the vast majority of the nation's supply of drugs for self-medication and prescription use. The division failed to keep pace with problems in the drug supply, for many reasons, including: shortcomings in the 1906 Act, which became only more pronounced with the Sherley Amendment of 1912; Wiley's preferential attention to food problems; insufficient staff; and the need to revise pharmaceutical analyses for many of the products before they could be regulated. But during this first decade of its existence, Kebler and his colleagues organized the Drug Laboratory as effectively as possible given the scientific, legal, economic and human constraints of the day.

John Swann is a historian in the FDA's History Office.

FDA Modernization Act Passed

By Jane Axelrad

The FDA Modernization Act of 1997 was passed by Congress earlier this month and signed by the President. The law contains a full reauthorization of the prescription drug user fee program, including additional fees and goals under an expanded program known as PDUFA 2. Many provisions will affect our work in CDER including, to name just a few:

- Exclusivity for pediatric drugs.
- Expediting the study and approval of fast track drugs.
- Reports of postmarketing approval studies.
- Dissemination of information on off-label uses.
- Manufacturing changes for drugs and biologics.
- Repeal of sections 506 and 507 regarding insulin and antibiotics.
- Pharmacy compounding.

Some of the provisions merely codify what we are already doing. Others will require changes in our policies and procedures. The next *Pike* will have more information.

Jane Axelrad is the Center's Associate Director for Policy.

Reviewers' Corner

The Reviewer Diagram Project—Visualizing Your Process

By Grant Williams

Eager Beaver, a dedicated new CDER reviewer has spent the past weeks pouring over examples of medical officer reviews done by his colleagues and by Long Term, his team leader. He is now feeling quite confident about the prospect of receiving his first new drug application (NDA).

He looks up, startled to see that his door is obstructed by a moving dolly carrying boxes of blue NDA volumes. "Here are the first 30 volumes, where do you want me to stack them? Or do you just want the electronic versions and the data?" asks a friendly voice from behind the stack.

Eager's autonomic nervous system begins to consider how to respond. In the old days he might have responded by giving into that surge of epinephrinoid panic exclaiming: "Long, where are you? Your review document doesn't tell me what to do!"

But not this time. Eager recalls that Team Leader Long read an article in the *Pike* on Reviewer Diagrams and prepared his own diagram to document his personal process of review. Quickly, Eager reaches for the PDF-viewer icon and, with an adept double click, his pulse slows as he moves from one box to the next in the diagram. "Just give me volume 1.1 and the overview of the pivotal studies for now."

With the emergency over, Eager begins to study the diagram with a passion.

While this story is fictitious, it reminds us that there is a very real need for reviewers and mentors to describe and visualize their review processes. The Reviewer Diagram Group, supported by Good Review Practices (GRP) Track II, has been meeting since July 1996 to evaluate how to meet this need. The goals of the project are to:

- Dissect individual review processes and create diagrams.
- Allow reviewers and supervisors to record and visualize the steps in their own review process.
- Communicate an understanding of the framework, content, process and issues involved in review activity.
- Create a final, customizable plan and diagram for each therapeutic area.

Over the past year, the group has evaluated various flow charting software and methods for sharing diagrams. In recent efforts, reviewer outlines of process have been converted to diagram form using Micrografx ABC Flowcharter, and then have been published and re-linked in Acrobat Exchange. The widely available Acrobat Reader allows users to view the diagram and to follow the links to different levels of the diagram. The Acrobat file can be shared with colleagues as an attachment to e-mail.

Four draft examples of review process diagrams are available for viewing:

- David Lepay's diagram comes from his experience as a medical officer in the Division of Antiviral Drug Products. This diagram outlines activities for a 6-month review, including activities before and after NDA submission.
- Brad Leissa's diagram reflects his experience as a medical officer in the Division of Anti-Infective Drug Products, and includes a section on conceptual approach, a section on sequential process steps and a link to a review document outline for the division.
- Joy Mele's diagram comes from her experience as a statistical reviewer at CDER.
- Grant Williams' diagram reflects his experience as a medical officer in the Division of Oncology Drug Products, and is an example of documentation of a microprocess, determining time to progression from the primary electronic data in patients with cancer.

When you view the diagrams, open the file in Acrobat Reader, then click on the shadowed boxes to follow the diagram to a different level. The examples can be found on the X:drive where you find this issue of the *Pike*, in the cdernews folder, as lepay.pdf, leissa.pdf, mele.pdf and williams.pdf. If you're reading this on-line and are connected to CDER's network, just click on a bulleted example above and you'll be linked right to it.

The next step for this project is to collect a library of representative diagrams from experienced reviewers in each review division and to make them available on a common drive or CDER's intranet. If you are an experienced NDA reviewer and would like to participate in this process, send me an e-mail (WILLIAMSG).

Members of the Reviewer Diagram Group are **Julie Carlston, Brad Leissa, David Lepay, Joy Mele, Nancy Smith, Madeline Vanhoose, Grant Williams** and **Janet Woodcock.**

Grant Williams is a medical officer in the Division of Oncology Drug Products.

Communications Corner: November's Tip—How to Deal with Conflict

To handle conflict among your team members:

- Ask those who disagree to paraphrase one another's comments. This may help them learn if they really understand one another.
- Work out a compromise. Agree on the underlying source of conflict, then engage in give-and-take and finally agree on a solution.
- Ask each member to list what the other side should do. Exchange lists, select a compromise all are willing to accept.
- Convince team members they sometimes may have to admit they're wrong. Help them save face by convincing them that changing positions may well show strength.
- Respect the experts on the team. Give their opinions more weight when the conflict involves their expertise, but don't rule out conflicting opinions.

Source: Making Teams Succeed at Work, Alexander Hamilton Institute, 70 Hilltop Road, Ramsey, NJ 07446 in *communications briefings,* 16(4).

CDER's Fall Awards Ceremony Honors Individuals, Teams

(Continued from page 1)

Hoiberg, Frank Holcombe, Shirkant Pagay, Rashimakant Patel,Eric Sheinin, John L. Smith, Doug Sporn, and **Roger Williams.**

CDER Administrative/Program Management Excellence Award

Julie L. Basore.

Frances V. LeSane.

Gloria Marquez Sundaresan.

Tammy L. Mueller

Carol T. Norwood.

CDER Excellence in Communication Award

Rachel E. Behrman, M.D., M.P.H.

Roger C. Gregorio.

Paul J. Motise.

Norman J. Oliver.

ODEIV/FDA Team: **Funmilayo O. Ajayi, Ph.D., Renata Albrecht, M.D., Sue Bell, Ph.D., CDR James D. Bona, M.P.H., Susan A. Cobb, Philip M. Colangelo, Ph.D., LT CDR Carmen L. DeBellas, Walla L. Dempsey, Maureen P. Dillon Parker, CAPT Anthony W. DeCicco, James G. Farrelly, Ph.D., Pauline Fogarty, Gino Girardi, M.D., Mark J. Goldberger, M.D., Holli A. Hamilton, M.D., Kenneth L. Hastings, Pharm.D., Robert J. Hopkins, M.D., LT Lisa M. Hubbard, CDR Lauren C. Iacono-Connors, Ph.D., David B. Katague, Ph.D., Joyce A. Korvick, M.D., John A. Lazor, Ph.D., Brad G. Leissa, M.D., Paul S. Liu, Ph.D., John D. Mahoney, Nasim R. Moledina, M.D., Kjeld Molvig, Toni-Marie Nearing, Leah M. Palmer, Pharm.D., Toni D. Piazza-Hepp, Pharm.D., Alexander T. Rakowsky, M.D., David B. Ross, M.D., Ph.D., Kellie Schoolar Reynolds, Pharm.D., Chandrahas G. Sahajwalla, Ph.D., Janice M. Soreth, M.D., LT Kimberly A. Struble,** and **Linda J. Utrup, Ph.D.**

CDER Leadership Excellence Award

Mohammad F. Huque, Ph.D.

Lana G. Kostecka.

Vinod P. Shah, Ph.D.

Frank D. Sistare, Ph.D.

Kimberly L. Topper.

Liang Zhou, Ph.D.

CDER Team Excellence Award

Antineoplastons Review Team: **Robert J. DeLap, M.D., Ph.D., CDR Steven I. Hirschfeld, M.D., Ph.D., John R. Johnson, M.D., Grant A. Williams, M.D., CDR Paul F. Zimmerman, Library Renovation Team, David E. Graham,** and **Carol L. Knoth.**

Maxipime® Review Team: **Aloka G. Chakravarty, Ph.D., LT CDR Carmen L. DeBellas, Elizabeth A. Duvall-Miller, David W. Feigal, Jr., M.D., Daphne Lin, Ph.D., David B. Ross, M.D., Ph.D.,** and **Janice M. Soreth, M.D.**

New Drug Policy Development and Case Review Team: **Kathleen R. Anderson, Rita R. Hoffman, Fred Richman,** and **CAPT Robert J. Tonelli.**

SUPAC-SS Task Force/Working Group: **Wilson H. DeCamp II, Ph.D., Francis R. Pelsor, Pharm.D., Donald J. Schuirmann, Paul Schwartz, Ph.D., Vinod P. Shah, Ph.D.,** and **Surendra P. Shrivastava, Ph.D.**

Virtual Journal Team: **Renata Albrecht, M.D., Carol S. Assouad, Steven A. Aurecchia, M.D., Belle Burkhart, Julie S. Carlston, Yuan-yuan Chiu, Ph.D., Gail Y. Chotoff, Diana L. Clark, Ph.D., Joseph J. DeGeorge, Ph.D., G. Alexander Fleming, M.D., Lori A. Frederick, Charles J. Ganley, M.D., William R. Gillespie. Ph.D., Ralph D. Harkins, Ph.D., Deborah J. Henderson, Deborah L. Kallgren, Lydia C. Kaus, Ph.D., Brad G. Leissa, M.D., David A. Lepay, M.D., David M. Moss, Robert E. Osterberg, Ph.D., Jack B. Pevenstein, Janet L. Rose, John R. Senior, M.D., Eric B. Sheinin, Ph.D., Nancy D. Smith, Ph.D., Paul K. Stauffer, Lisa L. Stockbridge, Ph.D., Jonathan K. Wilkin, M.D., CAPT Stephen E. Wilson, Dr.P.H., Pamela G. Winbourne, Janet Woodcock, M.D.,** and **Xavier J. Ysern, Ph.D.**

Medical Library Renovations Team: **David Graham,** and **Carol Knoth.**

ONDC Leadership Team: **Stanley W. Blum, Ph.D., Chi-wan Chen, Ph.D., Peter H. Cooney, Ph.D., Wilson H. DeCamp II, Ph.D., Eric P. Duffy, Ph.D., Albinus M. D Sa, Ph.D., Bonnie B. Dunn, Ph.D., John J. Gibbs, Ph.D., Charles P. Hoiberg, Ph.D., David B. Katague, Ph.D., Steven R. Koepke, Ph.D., Eldon E. Leutzinger, Ph.D., Stephen P. Miller, Ph.D., Stephen K. Moore, Ph.D., Hasmukh B. Patel, Ph.D., Guiragos K. Poochikian, Ph.D., Moo Jhong Rhee, Ph.D., John E. Simmons, Ph.D., Eva Tolgyesi, Ph.D., Robert J. Wolters, Ph.D., Rebecca H. Wood, Ph.D.,** and **Duu Gong Wu, Ph.D.**

CDER Support Staff Excellence Award

Margo L. Bennett.

John L. Cesaletti.

Jamie M. Metz.

William L. Myers.

Mary C. Norris.

Rose M. Smith.

Nadine Warren.

Division of Reproductive and Urologic Drug Product Support Staff: **Stephanie M. Cafarelli, Dannette M. Locklear, Jennifer L. Mercier.**

CDER Special Recognition Award

Suresh Doddapaneni, Ph.D.

Howard S. Spungen.

1997 Diversity Day Planning Committee: **Cynthia P. Adams, Noreen A. Gomez, Lanh Green, M.P.H., Patrick F. Guinn, Marta L. Locklear, Ting Eng Ong, Guyann V. Toliver,** and **Zulema A. Miguele.**

(Continued on page 7)

Information Technology Corner

Let Help OIT Help You Obtain Optimum Performance

By Heather A. Chafin

Getting a new desktop computer? Where is your new one coming from? Where is your old one going? Processing your computer through the Office of Information Technology (OIT) for cleaning ensures that the computer you are receiving or giving away runs at its optimum performance level.

But what are optimum performance levels and how do they affect you? Having optimum performance levels means that the computer you are receiving or giving away will be checked for viruses, cleaned of all unnecessary and sensitive files, and upgraded with the latest and greatest versions of all Centerwide core software, like SmarTerm, TeamLinks and, if the budget allows, MS Office.

Also, each computer has its own network "ID," which allows it to function within the CDER network. Computers that aren't processed through OIT could have duplicate or missing network IDs, and this will prevent them from working within the network and accessing the Internet. Also, computers have to be reconfigured for home use to ensure e-mail or network access and to remove any software not purchased for use outside the Center.

How can you make sure you and your computer are primed for optimum performance? Anytime a computer is being moved from one physical location to another, whether it is going to another workspace within your division or home for work-related computing, please contact your division's property control officer (PCO), who will place a sticker on the PC with the proper information. Once this sticker is affixed, your PCO will make sure the PC is sent to OIT for cleaning. This process ensures that you and others in your division will receive the best computer equipment possible.

A list of PCOs can be found on the OIT intranet site. Simply type oitweb/oit in your browser's address block. Click on the Support Assist button and then the bullet for PCO Information. *Heather A. Chafin is a computer specialist in OIT's Technology Support Services Staff.*

CDER Fall Honor Awards Ceremony Marks Individual, Team Achievements

(Continued from page 6)

FDA/ISPE Team for Development of a Similar Pharmaceutical Manufacturing Equipment List: **Joseph X. Phillips, Robert P. Best, Larry W. Kranking, and Russ Somma, Ph.D.**

FDA EEO Achievement

Mercedes S. Albuerne, M.D.

FDA Commendable Service Award

Clare A. Gnecco, Ph.D.

Josephine M. Jee.

Robert R. Linkous.

Warren F. Rumble.

Paul Schwartz, Ph.D.

Mahboob Sobhan, Ph.D.

Joseph K. Winfield, M.D.

OGD Microbiologists: **Andrea S. High, Ph.D., James L. McVey,** and **Kenneth H. Muhvich, Ph.D.**

Postmarketing Safety Evaluation Team: **Min Chu Chen, M.S., Robert A. Eaton** and **Susan Lu**

PHS Unit Commendation

CDR David Banks.

CDR Nancy Chamberlin, Pharm.D.

CDR Beverly J. Friedman, M.B.A.

CAPT Roger A. Goetsch, Pharm.D.

PHS Outstanding Unit Citation

Protease Inhibitor Review Team: **CDR Lauren C. Iacono-Connors, LT Kimberly A. Struble.**

PHS Outstanding Service Medal

CDR Robert K. Leedham, Jr., M.S.Pharm.

CAPT Ralph B. Lillie, M.P.H.

PHS Unit Commendation

Master Queue Task Group: **CAPT David Holovac, CDR James W. Wilson III.**

PHS Commendation Medal

CDR Harold Davis, M.D.

CDR John J. Feeney III, M.D.

CAPT Thomas H. Hassall, M.S.

CDR Mary I. Lambert, M.N., R.N.

FDA Group Recognition Award

Carcinogenicity Assessment Committee: **Paul A. Andrews, Ph.D., Conrad H. Chen, Ph.D, Jasti B. Choudary, Ph.D., Joseph F. Contrera, Ph.D., Albert F. DeFelice, Ph.D, Joseph J. DeGeorge, Ph.D., William R. Fairweather, Ph.D., James G. Farrelly, Ph.D., Glenna G. Fitzgerald, Ph.D., Kenneth L. Hastings, Ph.D., Abigail C. Jacobs, Ph.D., Dou H. Jean, Ph.D., Alexander W. Jordan, Ph.D., Laraine L. Meyers, Ph.D., Sharon Olmstead, Robert E. Osterberg, Ph.D., Lillian Patrician, Charles A. Resnick, Ph.D., Hilary V. Sheevers, Ph.D.,** and **Ronald W. Steigerwalt, Ph.D.**

PHS Unit Commendation

CAPT Ching-Long J. Sun, Ph.D.

FDA Outstanding Achievement Award

K. Gary Barnette, Ph.D.

Marion V. Brooks.

Christa Childs.

Dale P. Conner, Pharm.D.

Angelica Dorantes, Ph.D.

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

Devinder S. Gill, Ph.D.

Samuel D. Maldonado, M.D.

Melissa J. Maust.

Mehul U. Mehta, Ph.D.

Janie P. Saunders.

Jackie Barber is CDER's awards officer.

Pediatrics Corner

Public Gives Input on Proposal for Pediatric Use Information

By Khyati Roberts

On Aug. 15, the FDA published a proposed rule in the *Federal Register* for new regulations requiring pediatric studies of certain new drug and biological products (see August *Pike*). As a part of this rulemaking, FDA, in cooperation with the American Academy of Pediatrics (AAP), held a public meeting on Oct. 27 to discuss this proposed regulation.

The meeting included several panels in the morning that discussed specific questions and subject areas relating to the regulations followed by an afternoon session that was opened up to interested parties who wished to present comments. A total of eight participants presented their comments in the afternoon. The panel discussions in the morning consisted of recognized experts in the field, including members of the pharmaceutical industry and representatives from patient/consumer groups. Following is a list of the discussions and panelists:

Panel 1: When Are Studies Needed?

- Definition of "widespread use."
- Severity of illness.
- Study requirements for new molecular entities vs. drugs already on the market.

Panelists were Sanford N. Cohen, Wayne State University School of Medicine, Children's Hospital of Michigan; Susan DeLaurentis, Pediatric AIDS Foundation; Thomas A. Hazinski, Vanderbilt University Medical Center; and Anthony R. Temple, McNeil Consumer Products Company.

Panel 2: Comments on Testing.

- Extrapolating from adult, pharmacokinetic, and safety data.
- Defining dose ranging.
- What age ranges should be tested?
- Should neonates be included or excluded?
- How patients need to be enrolled?

Panelists were Arthur J. Ammann, American Foundations for AIDS Research (AmFAR); Wendy Goldberg, Patient/Family Representative; D. Gail McCarver, Children's Hospital of Michigan Alan Sinaiko, University of Minnesota; and Stephen P. Spielberg, Merck Research Laboratories.

Panel 3: Special Challenges to Testing Children.

- What conditions warrant waivers and deferrals?
- Should formulation constitute waiver?
- Discussion of cost issue and industry burden.
- Ethical issues surrounding the testing of children (i.e., informed consent).

Panelists were Emmett Clemente, Ascent Pediatrics; Charles R. McCarthy, Kennedy Center for Bioethics, Georgetown University; Hugh Tilson, Glaxo Wellcome; and Philip D. Walson, Children's Hospital, Columbus, Ohio.

Panelists and presenters spoke to a committee of three AAP and five FDA members. Serving on the Committee for FDA were **William B. Schultz,** Deputy Commissioner for Policy; **Randolph F. Wykoff,** Associate Commissioner for Policy; **Ann Witt,** Special Counsel to the Deputy Commissioner for Policy; **Paula Botstein,** Acting Director, Office of Drug Evaluation III, CDER; and, **Elaine C. Esber,** Associate Director for Medical and International Affairs, CBER. AAP representatives on the Committee were **Robert M. Ward,** Chairman, Committee on Drugs; **Catherine Wilfert,** Chairman, Committee on Pediatric AIDS; and, **Ralph Kauffman,** Former Chairman, Committee on Drugs.

All of the comments presented will be included in the record and considered during FDA's rulemaking process. The proposed rule can be found in the *Federal Register*, Vol. 62, No. 158, Friday, Aug. 15, 1997, page 43900. Transcripts of the meeting are available on the World Wide Web at http://www.fda.gov/cder/meeting/transcript/1027pedi.htm.

Hard copies of the transcripts may be obtained from Dockets Management Branch (12420 Parklawn Drive, Rockville, MD 20857; docket number 97N-0165).

Khyati Roberts is project manager for the Pediatric Subcommittee.

FDA Warns Against Drug Promotion of "Herbal Fen-Phen"

The FDA has become aware of the increasing promotion of various dietary supplement-type products as "natural" herbal alternatives to the prescription drug combination commonly known as "fen-phen."

So-called "herbal fen-phen" products are being marketed over the Internet and through weight loss clinics, print ads and retail outlets as natural alternatives to the prescription drugs fenfluramine and phentermine (commonly referred to as "fen-phen"). FDA considers these products to be unapproved drugs because their names reflect that they are intended for the same use as the anti-obesity drugs, fenfluramine and phentermine. The agency is warning consumers that these unapproved drugs have not been shown to be safe or effective and may contain ingredients that have been associated with injuries.

Two anti-obesity drugs, fenfluramine and dexfenfluramine, have been voluntarily withdrawn from the marketplace because of safety concerns. FDA believes the use of unapproved alternative products may increase as a result of the withdrawal. Herbal fen-phen products contain none of these prescription drugs.

The main ingredient of most herbal fen-phen products is ephedra, commonly known as Ma Huang. Ephedra is an amphetamine-like compound with potentially powerful stimulant effects on the nervous system and heart.

FDA has received and investigated more than 800 reports of adverse events associated with the use of ephedrine alkaloid-containing products since 1994. These events ranged from

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Interim Recommendations Issued for Diet Drug Exposure

The Department of Health and Human Services issued preliminary recommendations for the medical management of people who took the diet drugs fenfluramine or dexfenfluramine. The recommendations, published in the Nov. 14 issue of *Morbidity and Mortality Weekly Report,* were developed jointly by the Food and Drug Administration, the Centers for Disease Control and Prevention and the National Institutes of Health.

"Since these drugs were withdrawn from the U.S. market last September, many people who took them have been asking what they should do," said FDA's Lead Deputy Commissioner **Michael Friedman, M.D.** "We in the government, together with the medical community, have developed these recommendations to provide guidance based on the best information we have at this time."

The recommendations are based on current knowledge about the association of these drugs with the development of heart valvular disease. The valvular damage can cause regurgitation—a backflow of blood into a heart chamber—that may in some cases lead to heart and lung disease.

Of immediate concern for patients with valvular disease is the possible increased risk of bacterial endocarditis—an often serious and potentially fatal infection of the heart's lining—following certain invasive medical and dental procedures.

Until more complete information is available, the Department recommends the following measures for people who have taken fenfluramine or dexfenfluramine:

- Anyone who has taken fenfluramine or dexfenfluramine for any period of time, either alone or with another drug or drugs, should see their doctor for a medical history and physical examination to determine whether there are signs or symptoms of heart or lung disease.
- Anyone who has taken these drugs for any period of time, either alone or with another drug or drugs, who has signs or symptoms of heart or lung disease, such as a new heart murmur or shortness of breath, should have an echocardiogram performed.
- An echocardiogram should be strongly considered for any patient who has taken these drugs, either alone or with another drug or drugs—regardless of whether they have signs and symptoms of the heart or lung diseases—BEFORE having any invasive procedure for which the American Heart Association recommends antibiotic prophylactic treatment to prevent the development of bacterial endocarditis. This will provide an accurate determination of whether or not the person needs the antibiotic treatment.

These interim recommendations may be updated as new information becomes available.

On Sept. 15, at the request of the Food and Drug Administration, Wyeth-Ayerst Laboratories and Interneuron Pharmaceuticals, which manufactured and marketed fenfluramine under the brand name Pondimin and dexfenfluramine under the brand name Redux, voluntarily withdrew these products from the market (see September's *Pike*). The withdrawal was based on initial echocardiographic findings in five surveys indicating that approximately 30 percent of patients in these surveys who took these drugs had valvular abnormalities, even though most had no symptoms. This is apparently much higher than would be expected in the general population, where additional preliminary reports suggest that significant valvular regurgitation occurs in less than five percent of the general population of young and middle-aged adults in the United States.

Studies are underway and others are planned to learn more about the clinical significance of these findings; the natural course of the valvular lesions (that is, whether they generally disappear, become worse or stay the same once the drugs are stopped); and what factors, if any, may increase an individual's susceptibility to their development.

More information, including a set of questions and answers, is available on CDER's Web site at: http://www.fda.gov/cder/news/feninfo.htm. and on CDC's site at http://www.cdc.gov.

Comment Period Extended to January

The comment period for the Pregnancy Labeling Part 15 Hearing is being extended to Jan. 12 from the original November 12 deadline.

See the August *Pike* for details.

"Herbal Fen-Phen" Name Makes Product Unapproved Drug

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episodes of high blood pressure, heart rate irregularities, insomnia, nervousness, tremors and headaches to seizures, heart attacks, strokes and death.

Many ephedra-containing herbal fen-phen products also contain *Hypericum perforatum,* an herb commonly known as St. John's Wort and sometimes referred to as "herbal Prozac." The actions and possible side effects of St. John's Wort have not been studied under carefully controlled trials either alone or in combination with ephedra.

Other herbal fen-phen products contain 5-hydroxy-tryptophan, a compound closely related to L-tryptophan, a dietary supplement widely used in this country until 1990. Used primarily as a sleep aid, L-tryptophan was pulled from the market after it was found to be linked to more than 1,500 cases, including about 38 deaths, of a rare blood disorder known as eosinophilia myalgia syndrome.

FDA regards any over-the-counter product commercially promoted as an alternative to prescription anti-obesity drugs (such as phentermine and fenfluramine) to be a drug.

The Agency is taking appropriate regulatory action to remove such products from the market.

FDA, Engineer Society Win Vice President's Hammer Award

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approval from the FDA before implementation, the list saves manufacturers time and money.

In June 1996, ORA and the Center asked the leadership of the ISPE for technical assistance in developing the similar equipment list. The ISPE agreed and quickly developed a plan with CDER and ORA. In just four months, the partnership was able to present a first draft of the list during an open industry forum. This draft was subsequently made available for comment under Good Guidance Practices on Aug. 14 this year. The "final" document was made available to the industry on Oct. 23.

"This project demonstrates the benefits of cooperation between government and industry," said **Doug Farbrother** from the Vice President's National Performance Review Office, who presented the award. "It reduces red tape, saves FDA's and manufacturers' resources and helps hold down the cost of health care, without lowering the product standards."

The award was accepted by **Joseph X. Phillips,** Deputy Director Central Region, ORA, **Roger Williams, M.D.,** Deputy Center Director (Pharmaceutical Science) and **Larry Kranking, Ph.D.,** ISPE president, on behalf of their organizations' staffs who worked together on the project.

"We turned to ISPE because they have a worldwide network of over 10,000 engineers with broad-based experience with manufacturing equipment," Phillips said. "We have had an excellent relationship with ISPE over the years and have proven we could accomplish important tasks together. The similar equipment list is another tangible example of how the consumer can benefit when industry and government collaborate."

FDA is continuing to work with ISPE on similar equipment lists for modified release and nonsteril, semisolid drug products.

The Hammer Award is given to Federal employees and their private sector partners who have advanced the Vice President's National Performance Review by cutting red tape, improving service to customers and helping build a better and more cost-effective government.

CDER members of the partnership include: **Jane Axelrad,** Associate Director for Policy; **Yuan-Yuan Chiu, Ph.D.,** Deputy Director, Office of New Drug Chemistry (ONDC); **Charles Hoiberg, Ph.D.,** Director, Division of New Drug Chemistry I, ONDC; **Frank Holcombe, Ph.D.,** Director, Division of Chemistry II, Office of Generic Drugs (OGD); **Shrikant Pagay, Ph.D.,** chemist, Division of New Drug Chemistry III, ONDC; **Eric Sheinin, Ph.D.,** Director, ONDC; **John Smith, Ph.D.,** chemist, Division of Chemistry II, OGD; **Douglas Sporn,** Director, OGD, **Roger Williams, M.D.,** and **Janet Woodcock, M.D.**

The similar equipment list, which has been published in the Federal Register, is now available on the Center's Web site. (From CDER's home page choose the Regulatory Guidance button and then select Guidance Documents at http://www.fda.gov/cder/guidance/index.htm. In the Chemistry section, pick *SUPAC-IR: Immediate Release Solid Oral Dosage Forms Manufacturing Equipment Addendum.*)

CDER Opens Electronic Freedom of Information Reading Room

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Internet users can now directly access such documents as warning letters, inspection operation manuals, monthly import detention lists, medical device reports and other often-requested material without having to go through the time and paperwork of filing a traditional FOI request. The CDER electronic reading room index is found at http://www.fda.gov/cder/foi/index.htm. The FDA's electronic reading room can be reached at http://www.fda.gov/foi/foia2.htm.

The Electronic Reading Room is one of the latest features to be added to the FDA Web site to enhance its value to Internet users and comply with the Electronic Freedom of Information Act Amendments of 1996. Under that law, CDER is required to post to the Internet in redacted form any material dating from Oct. 1, 1996, that is requested through FOI three or more times. As of Nov. 1 of this year, the information must be posted within 20 days of the request.

To further enhance its Web site, FDA has also revised the homepage to offer users more ways to find the particular types of information they are looking for. The new options provide specialized menus of selections for consumers, industry, health care professionals and other user groups. These menus will help users to access information on a given subject from throughout the Agency, regardless of the FDA center or office where it originated.

The Electronic Reading Room is a joint effort of the Freedom of Information Staff and Medical Library, both part of the Office of Training and Communications. Those who helped make CDER's electronic reading room a reality include: **Carolann Hooton, Roy Castle, Paul Stauffer, Karen Kapust** and many other FDA and CDER staff.

Carolann Hooton is director of the FOI Staff, and Carol Assouad is director of the Medical Library.

New Review Division Director Named

Lilia Talarico, M.D., has been named director of the Division of Gastrointestinal and Coagulation Drug Products. Originally from Naples, Italy, Dr. Talarico graduated from the University of Naples Medical School. Following postgraduate training in pediatrics at the University of Naples, she completed a U.S. medical internship at Monmouth Medical Center in New Jersey. She has also completed research fellowships in pathology at Harvard University School of Medicine and in hematology at Tufts University. She is board certified in internal medicine and in hematology and oncology. Prior to joining CDER in 1989, Dr. Talarico served as associate professor of medicine at Boston University Medical Center.