news along the pike

Center for Drug Evaluation and Research

January 1998

Volume 4, Issue 1

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Agency Budget Flatlined

CDER Tapped to Support Mandated Programs

By Janet Woodcock, M.D.

The Center has received its final fiscal year 1998 appropriated budget. Our PDUFA budget has not yet been determined. Flatlining of the Agency's budget, except for increases for food safety and tobacco regulation, requires us to absorb, for the fourth year in a row, mandated government salary increases and other cost hikes.

This money had to be taken out of the available operating dollars for the Commissioner's office and all the Centers. This required the Center to shrink its workforce so we can generate money through "underburn"—hiring fewer employees than our ceiling for full-time equivalent (FTE) employees allows. The Center did this last year and generated about $5 million in extra operating money. We are currently under our FTE ceiling because of the recent hiring freeze.

In addition, the Agency was directed by the Appropriations Committee conference report to spend the full amount requested on food safety

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Friedman Cites Resource Constraints

FDA Faces Performance Challenges

Lead Deputy Commissioner **Michael A. Friedman, M.D.,** highlighted the Agency's improved performance under continuing resource restraints in a major speech to the Food and Drug Law Institute at its annual meeting in Washington Dec. 9. "That 1997 has been a perfectly splendid year of unprecedented achievement and that the Agency remains vigorous, healthy and dynamic is a testimony to the excellent FDA staff," Friedman said.

Overall workload at FDA has increased about 12 percent annually for the last several years, he said. In that context, he highlighted the Office of Generic Drug's record 416 generic drugs approved in a 12-month period. The number of new drug and biologic applications has increased 50 percent since 1992, and the review of these products continued at 96 percent on-time performance. At the same time, the median time to approval for drugs and biologics has been dropping steadily and stands at 12 months for the cohort submitted in fiscal year 1996 .

(Continued on page 10)

ORM Announces New Office

Office of Post-marketing Drug Risk Assessment

By Murray Lumpkin, M.D.

Over the next six to eight months, the Office of Review Management will transform the Division of Pharmacovigilance and Epidemiology (DPE) from a division in the Office of Epidemiology and Biostatistics into a new Office of Post-marketing Drug Risk Assessment (OPDRA). The remaining biometric portion of the present OEB will become part of a renamed Office of Biostatistical Sciences and will continue to be headed by Robert O'Neill, Ph.D. The directors of both offices will report to the Deputy Center Director (Review Management), as do all of the present office directors in ORM.

Current plans call for the new office to have at least two divisions of Drug Risk Assessment: DDRA I and DDRA II. These two divisions will perform the same kind of work—one division for half the products in the Center, the other division for the other half.

In contrast to the current branch structure in DPE, which is organized along discipline lines,

(Continued on page 9)

Joe's Notebook

We're All Just a Moment Away . . .

When I worked at NIH, one of my jobs was to explain research programs on stroke and neurological injury to the public. Many callers, survivors themselves, would remind me that I was only temporarily able-bodied. Any moment, they said, might find me joining the ranks of the so-called "disabled." You might recall my tale in the August issue of the *Pike* when for 12 days in the hospital I thought those predictions were coming all too true, too soon. In the what-goes-around-comes-around department, the nurse educator even gave me pamphlets with stroke information that I had written. While I still have my own little pharmacy lined up in a kitchen cabinet at home, I am happy to report that my physicians say that I am now neurologically normal—although my friends and family had doubts about that before my incident.

In the it's-a-small-world department, it's with a great deal of personal pleasure that the *Pike* is able to bring you **Wendy Cheng's** story (page 6) of her confrontation with the sudden onset of deafness. As a footnote to her story, during OTCOM's holiday party, Wendy was able to play violin accompaniment to our seasonal caroling. But there's more to Wendy's and my stories than the simple reminder there are real people who benefit from the work that you do everyday.

One of the groups I worked with at NIH was the Neural Prosthesis Program, responsible for funding the research that led to cochlear implants. Terry Hambrecht, who heads the program, is further evidence that real people, not just abstractions about research, development and approval are the true motivators and innovators. You see, Terry obtained his M.D. and engineering degrees so that he could find a way to help his best friend in high school walk again after a paralyzing accident. Just last year FDA approved another of the projects supported by Terry's program—an implant that will restore hand grip for certain quadriplegic persons.

If you've ever been on a quest for that perfect gift or personal item, you'll certainly appreciate the tale **Russ Rutledge** shares with you about his discovery of treasure in our community backyard. **Chris Nguyen** wants you to know that the Division of Training and Development can't do its job alone. Be sure to extend our personal thanks to all those who volunteered to teach courses last academic year. You'll find them on page 8.

In the all-good-ideas-seem-to-go-unrecognized department, you may recall last month's *Pike* article about First Responder training. Well, it turns out that **Matt Zell,** ODE IV's management officer took the training when it was offered by CDRH. He found it excellent—better than the first aid training he had in the Coast Guard—and started the ball rolling to have it offered to employees at CDER's remote sites. Ultimately, it turned out that ODE IV footed the bill for the training as well.

In the things-never-change-they-just-go-electronic department, I started in this business many years ago delivering the morning paper to my neighbors. Later, when I was in South Korea, my buddies and I would load our outfit's newspaper onto jeeps and drive them to all the far-flung battalions.

So if you haven't yet, why not make a New Year's resolution to try out TeamLinks and the Adobe Acrobat Reader. Nothing warms the heart of an editor more than a satisfied reader. **Mary Jane Mathews** from Office of Pharmaceutical Science writes in an E-mail to the Editor:

"Just a note to tell you that the new way you're sending the *Pike* is great. I don't even have to think about when it's coming out—it's just there and all I have to do is click and then print."

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).

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

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Ombudsman's Corner

What You Say: Part III

By Jim Morrison

In the first two columns of this series, I discussed five of my top eight hindrances to communication between CDER and the world outside. They were a lack of accurate and timely information to applicants on the progress of their application; problems with setting up meetings; requests for information that seem unnecessary or personally motivated; rigidity in applying guidelines; and poor-mouthing to explain delays.

Working in the confidential world of trade secrets and proprietary information, we sometimes underestimate how much companies know about their competitors' products and research. We are surprised when an applicant challenges a guideline or a request for a new analysis or data by telling us their competitor's product got approved without such an analysis or data. To some applicants, the regulatory scheme should be simple: develop standards for proving the safety and effectiveness of a drug class, and apply the same standards to all other members of the class forever. The problem with that philosophy, of course, is that science constantly changes as we learn more about new drugs. Requirements that were not contemplated before become essential for a new application, and what seemed essential for the first member of a class may seem unimportant when the fifth one comes up for review.

Recognizing how such changes in the ground rules may be perceived by applicants is the key to communicating new requirements effectively. Care must be taken that new requirements are explained in light of new information, lest applicants come to believe that we are really favoring competitors already in the market by throwing added road blocks in the path of newcomers.

Closely related to the problems stemming from evolving science are those caused by changes resulting from divisional reorganizations or reassignments of reviewers. Needless to say, such an abrupt change may leave an applicant bewildered and angry when the result is conflicting advice or a different review outcome.

We are making strides in developing better consistency across divisions in the application of policies and practices. But continuity is equally important. We must honor advice and commitments made by previous reviewers of an application, unless to do so would lead to an unsafe or ineffective product on the market. Such commitments should not be made lightly, they should be documented, and they should be altered only for significant reasons, with the concurrence of the division director. In fact, the new legislation recognizes that we shouldn't deviate without appropriate justification and supervisory concurrence. It requires that we adhere to our guidances and that we seek public comment as part of the process for general guidance documents.

Finally, I want to make a plea for rationality in regulation. I have heard people say: "I know it doesn't make much sense, but the regulations require that . . ." The law and the regulations were written to make sense. If your interpretation of them does not make sense in dealing with a particular case, you should reassess the interpretation you're using. Discuss it with your colleagues and supervisor and get an opinion from the Chief Counsel's office. Even if you sometimes feel that you are just passing along guidance or recommendations to the regulated firm, please take responsibility for what you tell the firm. If the logic of what you are saying is not clear in your mind, it won't be clear in theirs. That is the essence of communication.

So that completes my list of communication mishaps. If you have some you would like to contribute to my list, please give me a call (4-5443) or e-mail me at MORRISONJ.

Jim Morrison is the Center's Ombudsman.

Draft Guidance Issued on PBM Promotional Practices

On Jan. 5, FDA published a draft guidance concerning those promotional activities by pharmacy benefits management companies (PBMs) or similar enterprises that are performed on behalf of sponsors of medical products. The U.S. health care environment has seen an increase in the number of drug, biologic and device sponsor partnerships with PBMs and other health care organizations. Medical decisions are now often influenced by the promotional activities of health care payers who may have a financial incentive to move market share of particular medical products.

This could have serious health implications for patients if treatment decisions are influenced by false or misleading information. For example, drug "switching"—the substitution of one therapy for another—is one way that managed care organizations control cost and enforce formularies. Switches based on inadequate information could be dangerous, particularly for patients dependent upon chronic therapy.

This draft guidance results from several in-depth analyses of PBM involvement in medical decision making, conducted by FDA, the Health Care Finance Administration and the HHS Office of the Inspector General. FDA began its investigation of this issue in 1994 when the third of three pharmaceutical sponsor/PBM mergers took place. FDA's activities included a major public hearing and solicitation of public comment in 1995.

FDA proposes that medical product sponsors should be responsible for the promotional activities of subsidiary PBMs that violate the Federal Food, Drug and Cosmetic Act. The draft guidance also proposes factors for determining whether a medical product sponsor should be held responsible for violative promotional activities of nonsubsidiary PBMs. Such factors may include the nature and extent of the relationship between the PBM and the medical product sponsor or the assistance a sponsor gives the PBM toward the performance of the violative activity. The draft guidance can be found on CDER's Web site at http://www.fda.gov/cder/guidance/index.htm and then scrolling to Advertising Draft.

New Associate Director for Strategic Planning

Staff to Facilitate Developing Center's Road Maps for Change

By Charlene Cherry

The Special Projects Staff has been established in CDER to facilitate our travels along the expressway to change. Construction of the plan will be coordinated by the Associate Director for Strategic Planning—a new position established by the Center director to help manage the Center's travels through change. Our speed and progress will be closely watched by those who have a stake in what we do.

The FDA Modernization Act of 1997, the Government Performance and Results Act (GPRA), PDUFA 2, the Information Technology Management Reform Act (ITMRA) and the National Performance Review (NPR) provide us with broad direction to our travel destinations. The amount of time and the route we take are critical. "Strategic planning" is the road map we develop to reach the destinations outlined in these laws. How and when we get there depends on how well we plan our route.

Organizationally, the Associate Director for Strategic Planning and the Special Projects Staff are located in the Immediate Office of the Office of Management. Myself, **Susan Carey** and **Cindy Sayer-Marx,** both senior program analysts, currently make up the Special Projects Staff. Another senior program analyst will be added in 1998.

The mission of this group is to nurture the CDER community and stakeholders through the perpetual process of planning for our future. The Special Projects Staff will facilitate and act as consultants throughout the process. Defining the Center's strategic direction will not be the product of a CDER staff function, but the result of the most important thinking done by its customers, managers and employees.

The new staff looks forward to working with everyone involved in CDER's future. Look for future *News Along the Pike* articles for information and updates. Please feel free to contact any of us with your suggestions, ideas or comments (CHERRYC, CAREYS or MARXC).

Charlene Cherry is the Associate Director for Strategic Planning.

Reviewer Affairs Corner

RAC Picks 1998 Officers, Subcommittee Chairpersons

By C. Russ Rutledge

This article will highlight some of the activities of the Reviewer Affairs Committee (RAC) over the past year. The committee is now 4 years old.

For those of you who are unfamiliar with the RAC, it is a communications link between non-supervisory division reviewers and CDER management, including the Center director.

The RAC has a representative and alternate from each review division within CDER. While the RAC is primarily set up to address reviewers' issues, the Office of Compliance divisions are also represented. A current list of RAC representatives may be reviewed on the X:drive in the folder \coorcomm\RAC\roster\roster.98.

Last January, the RAC started contributing articles to *News Along the Pike*. These contained reports of accomplishments and current events of interest to the committee. You can review these articles by calling them up on X:drive in \cdernews\pike97 or on the Internet at http://www.fda.gov/cder/pike.htm.

To recap, January introduced the RAC, its subcommittees and how we operate. February listed the RAC representatives. March was about the Reviewers' Handbook. April solicited suggestions via the RAC's hi-tech suggestion box on the X:drive. Reviewers' Day was previewed in May, while the 1997 survey was reported on in August and September.

If you would like more information, feel free to review the RAC meeting minutes on the X:drive in \coorcomm\rac\minutes.

RAC held its annual election of officers during the Dec. 9 meeting. Outgoing 1997 Chairperson **Janet Higgins** led the meeting and gave each subcommittee a chance to introduce its function. Then nominations were solicited and the vacancies were filled.

The 1998 RAC officers are:

- Chair: **Melissa Maust,** Division of Chemistry I, OGD.
- Vice-chair: **Fred Marsik,** Division of Anti-Infective Drug Products, ORM.
- Project Manager: **Tanya Abbott,** Executive Operations Staff.

Subcommittees do the main work of RAC and are chaired by the following:

- Reviewers' Handbook: **Russ Rutledge,** Division of Manufacturing and Product Quality, OC.
- Comparable Pay: **Harold Geyer,** Division of Anesthetic, Critical Care and Addiction Drug Products, ORM.
- Operational Procedures: **Barbara Elaskoff,** Division of Biometrics II, OEB.
- Networking: **Nakissa Sadrieh,** Division of Medical Imaging and Radiopharmaceutical Drug Products, ORM.
- Bylaws: **Beverly Friedman,** Division of Pharmacovigilance and Epidemiology, OEB.
- CDER Culture: **Lynda Reid,** Division of Dermatologic and and Ophthalmologic Drug Products, ORM.
- Communications and Training: **Melissa Maust.**
- Project Management White Paper: Vacant
- *News Along the Pike* representative (responsible for writing RAC Corner): subcommittee chairs.

C. Russ Rutledge is a compliance officer in the Division of Manufacturing and Product Quality.

PDUFA 2 Targets Improved Drug Development, Review Times

By Murray Lumpkin, M.D.

A phase-in to a 10-month review time by fiscal year 2002 for standard new drug applications and efficacy supplements highlights an expanded list of performance goals agreed to under the 1997 reauthorization of the Prescription Drug User Fee Act (PDUFA). The Center's successes in meeting and exceeding the review performance goals agreed to in 1992 give confidence that it can rise to new challenges. Currently, CDER is reviewing more than 90 percent of priority drug applications in six months or less and standard drug applications in 12 months or less. Review performance goals for priority drugs—those that appear to represent an advance over available therapy—will remain at six months for the five years of the reauthorization.

In addition to performance goals for standard and priority drug reviews, the Center has committed to performance goals for meeting management, clinical holds, resolving major disputes, reaching agreement on certain protocols as well as electronic submission of applications. Performance goals are time frames in which certain actions should occur based on submission cohorts, identified by the fiscal year in which the application is received. A copy of the goals can be found at:

http://www.fda.gov/cder/news/pdfufagoals.htm.

Standard drugs: The performance goal remains at 90 percent reviewed and acted on in 12 months for fiscal years 1998 to 2001. The phase-in to a 10-month review begins in fiscal year 1999 when 30 percent must be reviewed and acted on in 10 months. It climbs to 50 percent in FY 2000, 70 percent in FY 2001 and 90 percent in FY 2002.

Priority drugs: The performance goal remains 90 percent reviewed and acted upon within six months.

New molecular entities: These have the same review performance goals as standard and priority drugs but are reported separately.

Resubmissions of original NDAs: These are now divided into two "classes." Class 1, involving minor changes, target two-month reviews by FY 2002. For FY 1998, 90 percent need to be reviewed and acted on within six months with 30 percent reviewed and acted on in two months. For FY 1999 and 2000, 90 percent must be reviewed and acted on within four months, with 50 percent reviewed and acted on within two months in FY 1999 and 70 percent in FY 2000. The goal is 90 percent within two months for FYs 2001 and 2002. Class 2 involves items not specifically identified in the PDUFA goals document and 90 percent are to be reviewed and acted on within six months.

Manufacturing supplements: New in PDUFA 2 is that those requiring prior approval from the Center before implementation have a phase-in to a four-month review and action by FY 2002. For FY 1998, the goal is 90 percent within six months. For FY 1999, the goal is 90 percent within six months with 30 percent within four months. For FY 2000, the figures are 90 percent and 50 percent; for FY 2001, 90 percent and 70 percent. For 2002, the goal is 90 percent within four months. The goal for manufacturing supplements that don't require prior approval from the Center before implementation remains at 90 percent reviewed and acted on within six months.

Meeting notification: The Center will respond to an industry request for a meeting within 14 calendar days of receiving the request. CDER will provide the 14-day response for at least 70 percent of the requests in FY 1999, 80 percent in FY 2000 and 90 percent in subsequent fiscal years.

Meeting scheduling: Three types of meetings, based on how critical they are to the drug development process, have time frames within which the Center agrees to schedule the meeting. The times range from 30 days for meetings needed to allow a stalled development program to proceed to 75 days for routine meetings. The Center agrees to meet at least 70 percent of the time frames in FY 1999, 80 percent in FY 2000 and 90 percent in subsequent fiscal years.

Meeting minutes: A phase-in for providing minutes within 30 calendar days is established. The goal is set at 70 percent in FY 1999, 80 percent in FY 2000 and 90 percent thereafter.

Clinical holds: The Center should answer a sponsor's complete response to a clinical hold within 30 calendar days. The phase-in for the goal is 75 percent in FY 1998 and 90 percent in subsequent fiscal years.

Major dispute resolution: When procedural or scientific matters cannot be resolved at the division level and the sponsor files a written appeal, the Center will respond in 30 calendar days. Phase-in for meeting the 30-day goal is 70 percent in FY 1999, 80 percent in FY 2000 and 90 percent in subsequent fiscal years.

Special protocol question assessment and agreement: At the sponsor's request, the Center will evaluate certain protocols and issues, defined in the PDUFA agreement, to assess whether the design, conduct and analysis are adequate to meet scientific and regulatory requirements. Once the Center has agreed to proposed design, execution and analysis, it won't later change its perspective unless public health concerns emerge that were unrecognized at the time of such an agreement. Protocols that qualify for this program include carcinogenicity and stability studies as well as Phase 3 clinical trials that will form the primary basis of an efficacy claim. The Center will assess the protocol and answer specific questions within 45 days. Phase-in for the 45-day goal is 60 percent in FY 1999, 70 percent in FY 2000, 80 percent in FY 2001 and 90 percent in FY 2002.

Information technology: The Center will develop the infrastructure to allow paperless receipt and processing of INDs and NDAs by FY 2002.

Areas without specific implementation time frames include:

Simplification of action letters: The Center will change its regulations and procedures to issue either an "approval" or a "complete response" action letter at the end of the review. The complete response will replace the current "approvable" or "not approvable" letters when the response isn't an approval.

Expedited notification of deficiencies in applications. The Center will send sponsors an "information request" letter identifying deficiencies when each discipline has finished its initial review of its section of a pending application.

Between Silence and Sound

CDER Librarian Reports on First Year with 'Bionic Ear'

By Wendy Cheng

March 21, 1996, seemed to start out like every other day. Little did I know my life would start unraveling that morning. I noticed a slight headache, but it went away shortly. I got dressed and put on my hearing aid. I have a profound hearing loss in my right ear and wear a hearing aid in my left ear to adjust for a severe hearing loss in that ear.

That morning spoken English suddenly sounded slightly distorted, and I made a mental note to get my hearing aid checked.

At work, I found myself straining to lip-read everyone and several times asked my colleagues to repeat words. I had trouble hearing on the phone, which is not normal for me. By Friday morning, I realized my hearing aid was only picking up the lower frequency vowel sounds and not the higher frequency consonant sounds. I could only hear the vowel sounds if the speaker was standing at very close range. Over the weekend, the straining to lip-read my husband, daughter, mother and sisters continued. Worst of all, music sounded distorted, too.

Usually, when voices didn't sound right, it meant there was a problem with the hearing aid. I couldn't wait to find out what was wrong with it.

Monday morning, I was with my audiologist, staring in shock at the audiogram in my hands. Pure tone audiometry tests revealed that in my good left ear, I was now hearing the pure tones at very high intensity levels only. I scored only 20 percent on the speech audiometry test. Normally I score 95 percent to 100 percent. My worst fears were confirmed when my audiologist said my hearing aid was fine.

The otologist next door thought perhaps I had a viral infection in my left ear and checked me into the hospital. I was put on a regimen of steroids and respiratory therapy. Four days later, with no improvement in sight, I was sent home with medication instructions.

Two weeks later, the vowel sounds for speech disappeared into the growing silence.

I had to make adjustments if my life was to be manageable. With a heavy heart, I stopped my violin lessons and canceled my participation in an upcoming string quartet workshop. It was impossible to fathom playing a violin if I couldn't hear it. Instead, I used this time of silence to join Internet mailing lists devoted to hearing loss and taught myself hypertext markup language so I could create a personal Web site.

I reached inside myself to think of solutions to everyday communication problems. A late-deafened friend has commented that electronic mail is the greatest invention ever made for persons with hearing loss, and I found this to be very true. While in the hospital, I typed out an e-mail to my colleagues at work, telling them how they could best help me in this new situation. I was thankful that electronic mail is very much a part of the office culture at CDER, otherwise communication would have been much harder. I was to rely heavily on e-mail in the following months and still do today.

The CDER EEO staff kindly loaned me a TTD (telecommunication device for the deaf). Because I could no longer hear the voice phone, I realized I needed to learn to use the relay system for the deaf, specifically a technique called voice-carryover (VCO). I had vaguely heard of this technique in which my voice could be piped over to the other party and I would not have to type my responses on the TTD. I realized very quickly that being able to voice for myself really speeds phone calls, compared with having the relay operator type my responses to the other caller. Unfortunately, no one in FDA seemed to know exactly how VCO worked. In April 1996, the national office for Self Help for Hard of Hearing people sponsored a communications forum at a local community library so I attended the forum and got several copies of the Maryland Relay Service's brochures on voice carryover.

"The last straw came when Abby was diagnosed as having a slight delay in speech development . . . As a mother, I wanted to be involved in all aspects of her development, speech included."

It was difficult for me to tell other FDA staff outside my colleagues that I could no longer hear on the voice phone. Upon learning what happened, one enterprising FDA employee in a district office took it upon herself to learn about the relay service and to initiate a call to me via the relay. That was an encouraging moment during those uncomfortable months.

I decided that attempting to lip-read everyone, especially in staff meetings, was too stressful. So, with the exception of the one person I could lip-read fairly well, I told my colleagues to write down what they had to say. Within a week, I had arranged to get sign interpreting services for staff meetings and two to four hours of one-to-one communication each day. It was hard to have to read signs—the last time I used a sign interpreter was about nine years ago during graduate school. During those early months after becoming deaf, I felt then that I was lucky that I already knew some sign language and was grateful that FDA already had an excellent sign interpreter on the staff. However, reading signs and mentally translating back into English for one or two hours straight at staff meetings was tiring.

By mid-April 1996, I was living an uncomfortable existence as a deafened individual. At the best moments, when my sign interpreters were present or when I was on a functioning TTD troubleshooting computer problems via relay, I almost felt that being deaf was a minor annoyance. At the worst moments, when I couldn't hear my 2-year old daughter Abby talk, follow conversations at home and at work, or hear a string quartet play on television, I was acutely aware of how much I was missing. The last straw came when Abby was diagnosed as having a

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Backyard Treasure

Quest for Sartorial Splendor in Washington State Ends in D.C.

C. Russ Rutledge

I enjoy wearing unusual ties since its one of the few fashion items a man can wear in the work environment without drawing undue attention. Think about it—if a man wears something other than a pair of nice slacks, dress shirt, good shoes, blazer or suit jacket and a tie, it either looks unprofessional or as if he's trying to make a statement. Unfortunately a common reaction to the effort is rolling eyes. The tie is the key to individualism while still staying within the "acceptable" professional appearance envelope. While stripe and paisley ties were the standard neckwear for years, now cartoon character ties are replacing these venerable accessories, and other brightly colored ties are becoming more common.

Finding aesthetically pleasing ties is somewhat more difficult. I love art and search for ties which subtly reflect my tastes. One favorite is based on Edvard Munch's famous painting, "The Scream." In addition to art, wherever I travel, I try to find a tie that is somewhat unique and reflective of the locale. For instance, I have a tie from a trip to Switzerland that depicts the aerial tram climbing the steep mountain slopes to the revolving restaurant perched on top of the Schilthorn.

For several years, I have made visits to relatives and friends in the Pacific Northwest. This is the land of the totem poles. For a keepsake, I have looked for a tie with a totem on it for the past three years. I've searched at Indian reservations, tourist havens and airport gift shops, all to no avail. Most recently I took a trip up to British Columbia and had no luck finding a totem tie there either. After this last trip, I had decided this was turning into a Holy Grail type of hunt, so resigned myself to commissioning an artist to paint a totem tie if I was ever going to have one. I asked my sister to check with her arts and crafts friends in Bellingham and see if one would be willing to take on this project.

Having just got back from this latest Seattle trip, I took a Friday afternoon to see the Blue Guitars exhibit on the second floor of the American History Museum. We in Washington have such a magnificent diversity of museums and art galleries, yet like most other people I know, about the only time I go to see these is when hosting out-of-town visitors. I thought this was silly, so I have recently begun taking "aesthetic Fridays." After marveling over the sensational craftsmanship displayed at the Blue Guitars exhibit, there was still a lot of afternoon left, so I went over to the Natural History museum to reassert my humbleness in front of the Hope Diamond and the other spectacular gem exhibits. With a few minutes left before closing, I decided to pick up a couple of last minute stocking stuffers from the gift shop. And there, in the basement of the Natural History Museum, after all that looking in the Pacific Northwest, I finally found my totem tie. Its funny how we go to so many places and search for treasures, yet often find them in our own backyard.

Russ Rutledge is a compliance officer in the Division of Manufacturing and Product Quality.

Cochlear Implant Bridges Gap Between Silence and Sound

(Continued from page 6)

slight delay in speech development and was referred to an early infant-toddler intervention program. As a mother, I wanted to be involved in all aspects of her development, speech included. To make a long story short, I underwent cochlear implant surgery a year ago December and was hooked up to my new speech processor a month later.

This month I will be celebrating my first anniversary of life with a bionic ear. What a year it has been! After several adjustments to the speech processor, I can now hear all the vowel sounds of speech. It feels good to be able to hear voices again and converse more easily with colleagues and family. And five months after hookup, I gingerly picked up my violin again. I'm just happy I can make music for my enjoyment, although perfect intonation remains an elusive goal.

About the only everyday annoyance I have to deal with is that the speech processor is encased in metal and sets off metal detectors at security checkpoints all over CDER buildings. Still, this is a minor inconvenience compared with the benefits that the implant gives me.

However, using the phone continues to be a challenge, so I use it for short conversations now and only with voices in certain registers. Part of the problem seems to be related to the fact that the implant works best when combined with lip-reading. The speech encoding strategy in the speech processor doesn't seem to translate all the consonant sounds for speech accurately. In addition, staff meetings involving more than five people or in large conference rooms are still problematic since the microphone on the implant doesn't pick up voices located more than a foot away. I'm still investigating possible solutions to this problem.

I now have a greater awareness of how many more listening situations need to be made accessible to people with hearing loss. I dream of the day when CDER all-hands staff meetings can be captioned live or when the new FDA campus will have assistive listening devices for the hearing impaired wired in the sound system of all conference rooms.

My kudos go to our colleagues in the Ear, Nose and Throat Devices Branch at the Center for Devices and Radiological Health, who review and approve quality hearing aids and cochlear implants.

In my opinion, these devices truly help those with hearing losses enjoy the sounds of life.

Wendy Cheng is a librarian in the Medical Library.

DTD Honors Instructors for '96-'97 Academic Year

By Chris Nguyen

The Division of Training and Development, Office of Training and Communications, held an Instructors' Awards Ceremony Dec. 5. The ceremony honored those in CDER who volunteered their time and expertise to teach courses during the 1996-1997 academic year: The courses and instructors were:

- *Basic and Clinical Immunology:* **Shukal Bala, Marc Cavaille-Coll, Walla Dempsey, Ken Hastings,** and **David Schwartz.**
- *Basic Statistical Methods:* **Ruthanna C. Davi, Barbara A. Elashoff, Nancy L.P. Silliman** and **Nancy D. Smith.**
- *Basic Topics in Statistics: ANOVA and Regression:* **Michael Elashoff.**
- *Basic Topics in Statistics: Survival Data Analysis:* **Katherine B. Meaker.**
- *Clinical Pathology:* **Gary K. Chikami, Jim Farrelly, Lois Freed, Ken Hastings, Roswitha Kelly, Mercedes Serabian, Satish Tripathi** and **Andrea Weir.**
- *Clinical Pharmacokinetics:* **Raymond Miller.**
- *Clinical Trials in Drug Development: an Introduction to the Design Conduct and Review of Clinical Trials:* **Aloka Chakravarty, Victor Raczkowski, Kathy Robie-Suh, Grant Williams** and **Steve Wilson.**
- *Introduction to Drug Regulatory Procedures:* **Edwin Dutra, Bette Barton, Bronwyn Collier, Evelyn Farinas Kenneth Feather, Donald Hare, Brenda Holmes, Melvin Lessing** and **Denise Zavagno.**
- *Neonatal Pharmacology:* **Marietta Anthony, Paula Botstein, Jean Fourcroy, Sid Stolzenberg** and **Gloria Troendle.**
- *New Reviewer's Workshop:* **Carol Assouad, Rose Cunningham, Heidi Jolson, Karen Kapust, Jim Morrison, Lana Pauls, Lisa Rarick, Nancy Smith** and **Steve Wilson.**
- *Overview of FDA Legal Activities:* **David M. Fox.**
- *Physiology and Toxicology of Reproduction:* **Joy Cavagnaro, Thomas F.X. Collins, Robert Osterberg, Sidney Stolzenberg** and **Robert Sprando.**
- *Presentation, Power and More:* **Carol Assouad, Jack Pevenstein.**
- *Regulatory Science:* **Wallace Adams, Dennis Bashaw , Nilambar Biswal, Albinus D'Sa, Zan Fleming, Paul Goebel, Tony El Hage, Ralph Harkins, Chuck Hoiberg, Thomas Laughren, Robert Osterberg, Nancy Ostrove, Toni Piazza-Hepp, Eric Sheinin, Kasturi Srinivasachar, C.T. Vishwanathan** and **Grant Williams.**
- *Special Topics in Reproductive Toxicology and the New ICH Guidelines:* **Sid Stolzenberg, Thomas F.X. Collins, Robert Sprando, Sheila Weiss** and **Ed Fisher.**
- *Successful Meetings and Minutes:* **Chin C. Koerner.**
- *Topics in Clinical Trials:* **Susan Ellenberg, Martin Himmel, Thomas Laughren, Robert O'Neill** and **Robert Temple.**
- *Topics in Applied Statistics: Multiple Endpoints and Multiple Comparisons in Clinical Trials:* **Abdul Sankoh** and **Mohammad F. Huque.**

Awards were also presented to the Committee for Advanced Scientific Education chairperson, **Zan Fleming,** and subcommittee chairpersons, **John Senior** and **Frank Sistare.**

Chris Nguyen is an employee development specialist in the Division of Training and Development.

New Drug Approved to Prevent Osteoporosis in Women

The Center has approved raloxifene (Evista), one of a new class of drugs for the prevention of osteoporosis in postmenopausal women. Clinical data on raloxifene indicate that it acts like estrogen, though to a lesser degree than estrogen, in increasing bone density.

In respect to lipid metabolism, there were no statistically significant differences between estrogen and raloxifene groups in lowering total cholesterol levels; however, raloxifene did not increase levels of HDL as estrogen did. Also, raloxifene did not adversely affect breast and uterine tissue in clinical trials.

The approval of raloxifene on Dec. 10 gives an estimated 19 million Americans at risk for osteoporosis—80 percent of them women—another possible avenue for preventing osteoporosis, a progressive thinning of bone mass and reduced bone strength. Under FDA guidelines, drugs to treat or prevent osteoporosis must be shown to preserve or increase bone density and maintain bone quality. The effect of raloxifene on actual bone fracture risk is not yet known but is being evaluated in ongoing trials.

The effects of raloxifene on bone mineral density were studied in three large trials of approximately 1,800 postmenopausal women for 24 months. Women taking 400 mg to 600 mg of calcium and 60 mg of raloxifene daily had a greater increase in bone density compared with women taking only calcium supplementation. There was no evidence of an increased risk of breast or endometrial cancer in women who received raloxifene up to two and one-half years in the clinical trials.

The most serious side effect associated with raloxifene was increased risk of venous thromboembolic events (VTEs)—blood clots that form in the veins and may break off and travel to the lungs. The 2.5 fold increase in the risk for VTE in women treated with raloxifene was similar to that reported for women on hormone replacement therapy.

Other commonly reported side effects were hot flashes and leg cramps. Women with a history of blood clots in their veins should not use raloxifene, nor should women who are pregnant or may become pregnant, because of potential danger to the fetus. Abnormalities were observed in fetuses of rats given the drug.

Post-marketing Drug Risk Assessment to be New Office

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the new office will have a structure in which epidemiologists and risk assessors will be combined into drug risk assessment teams within the new divisions. This is a structure similar to that in the ODE review divisions in ORM. As with the review teams in the ODEs, members of these risk assessment teams in the new divisions will bring their individual discipline expertise to the overall process of assessing the new risk data.

These divisions will not handle review activities related to post-marketing risk assessment, they will also be actively involved with their biometric colleagues in exploring and defining new methodologies and quantitative approaches to investigating post-marketing safety concerns.

In addition, the new office and divisions will be responsible for maintaining and utilizing the Center's cooperative agreements with various epidemiologic databases and in maintaining its partnerships with post-marketing risk assessment colleagues in other drug regulatory agencies.

As more drug products are being developed well and expeditiously—and thus approved more expeditiously—the imperative to have an outstanding system of post-marketing drug risk surveillance, assessment and management is all the greater. This is especially true during the early post-marketing life of a drug and whenever information is obtained that could potentially alter a product's risk-benefit profile. Risk management might include new labeling, "Dear Health Care Practitioner" letters, restricted distribution programs or marketing termination.

For the past two years, CDER has been working on developing the Adverse Event Reporting System (AERS), a state-of-the-art information technology system for receiving, storing and analyzing the more than 250,000 individual reports of suspected drug-related adverse events the Center receives each year. AERS will be the first system in the world that actually implements the various information technology and safety reporting agreements reached as part of the International Conference on Harmonization. This trailblazing effort will be a major step forward and light years ahead of our present system for handling these reports.

Murray Lumpkin is Deputy Center Director (Review Management)

Acting Division Director Named for DPE Transition Period

Ralph Lillie will be the acting director of the Division of Pharmacovigilance and Epidemiology (DPE) during its transition to the new Office of Post-marketing Drug Risk Assessment. Lillie has been working with the division recently to complete the acceptance testing of the AERS system. With a bachelor's degree in pharmacy from Rutgers and an M.P.H. in epidemiology from Uniformed Services University of Health Sciences, Lillie is a 23-year veteran of the Public Health Service. In addition, he served in the Navy for five years, including medical support service in Vietnam. After stints as a consumer safety officer in the divisions of Metabolic and Endocrine Drug Products and Oncologic Drug Products, Lillie served as a consumer safety officer for the newly formed Division of Anti-Viral Drug Products in 1988, eventually serving as supervisory consumer safety officer and assistant division director in subsequent years.

Most recently he has led the Center's effort to complete the new information technology system that the Compliance and Pharmaceutical Science offices are now using to communicate with the field offices.

During his service to the Center, Lillie has continued to practice pharmacy at the NIH Clinical Center and at the Whitman Walker Clinic in Washington. He has received several outstanding and commendable service PHS awards.

Jolson Named to Head Anti-Viral Drug Products Division

Starting Jan. 18, **Heidi M. Jolson, M.D.,** will be the new director of the Division of Anti-Viral Drug Products in ODE IV. Originally from Washington, Dr. Jolson attended Georgetown University where she received her B.S. (*magna cum laude*) and M.D.(*cum laude*). Dr. Jolson also holds an M.P.H. from the Johns Hopkins School of Hygiene and Public Health.

After completing an internal medicine residency at University Hospital in Boston, she became a clinical instructor in medicine at Boston University School of Medicine and an instructor in medicine at Harvard Medical School. Dr. Jolson has completed an infectious diseases fellowship that consisted of training in the Public Health Service's epidemiology training program and service as a fellow in infectious diseases at the Veterans Administration Medical Center in Washington. She is board certified in both internal medicine and infectious diseases.

In 1991, Dr. Jolson joined FDA as a medical reviewer in the Division of Anti-Viral Drug Products and became a medical group leader in that division. In 1996, Dr. Jolson became deputy division director in the Division of Reproductive and Urologic Drug Products. In addition to her review and management responsibilities, Dr. Jolson has served the Agency in several notable capacities, including the DHHS Chronic Fatigue Interagency Coordinating Committee, the CDC-sponsored Hantavirus Task Force and numerous pandemic influenza meetings sponsored by the National Institute of Allergy and Infectious Diseases. She is chair of the CDER new reviewers' orientation working group, chair of the pregnancy registry working group and a member of the women's health subcommittee. She has received both the FDA Commendable Service Award and the FDA Award of Merit.

CDER Budget Tapped, Center's Travel Takes Heavy Hit

(Continued from page 1)

and tobacco initiatives, even though the whole amount was not added to our appropriation compared with last year's budget. Therefore, another $16 million had to be generated. This was accomplished by taking a "tap" or contribution, out of each Agency component's budget, resulting in another drop in available operating funding.

The Senior Management Team went over proposed expenditures this year in excruciating detail. I had to make very hard decisions about funding cuts, because the money was just not there. Budgets have been distributed to each Center component. A number of very good programs—including some of our laboratory research, support for some library functions and funding of regulatory research—had to be decreased. There is currently no Center funding for coordinating committee work. Central funding of a number of activities was also eliminated.

A decrease to take particular note of is in the per capita allocation. This is the money each unit receives to do its day-to-day work, including travel. This year's budget dictated a 40 percent reduction in appropriated per capita allocations to all positions. Because of this reduction, less money will be available for meeting or speaker travel. We need to plan to budget the available funds throughout the year.

I ask everyone in the Center to make a concerted effort to control travel costs this year. Although our participation in meetings is important for outreach, we don't have to be constantly visible. We should speak at meetings only if the message is one we need to convey and there are not other ways to deliver it. I have reduced the travel allocation in the office of the Center Director by more than 80 percent. I personally will make very few trips this year. With the demands of the new legislation and PDUFA 2 implementation on top of our usual work, this is truly a year to stay home and get the job done.

At some point during the year we should receive additional PDUFA funds. This money will be directed at very specific activities, however, and will probably not be available as additional operating dollars.

I thank everyone for your energy and commitment during these difficult times. Although the budget is hard to deal with, I am confident that we will manage and move on to better years.

Growth in Science, Resource Constraints Create Challenges

(Continued from page 1)

"Please remember that this is not an academic exercise in speeding up the review process," Friedman said. "There are real patients waiting for these medications. We estimate that more than 11 million Americans received a newly marketed drug this year that would not have been available until 1998 without PDUFA. For many, these drugs provide significant—sometimes life-saving—benefits." According to Friedman, the financial cost for the accelerated review times has worked out to $8 for each of the 11 million persons receiving a new drug.

Friedman said the FDA faces the challenge of sustaining this performance with constrained resources. "How can the Agency continue to manage a 12 percent annual average increase in the total number of all types of applications it receives and continue to produce performance gains of 17 percent a year, if FDA's budget grows at an annual rate of 1.3 percent in constant dollars?" Friedman asked.

Pressures for speed, accuracy and safety of products are not likely to be eased anytime soon, he said, because the steady rise in the number of new medical therapies is a direct consequence of a robust science environment. As industry and Federal investments in research have grown, the payoff has been a drug development pipeline full of promising therapies.

"No single agency will ever have all the technical expertise required to evaluate every novel product pouring out of the nation's laboratories," Friedman said. The FDA is seeking new ways to leverage the expertise of its sister agencies, such as the National Institutes of Health and the Centers for Disease Control and Prevention.

FDA's success in its mission depends on high-grade information and sharing its information. "Although we currently provide large amounts of useful data to the public," Friedman said, "we will have to find more and better ways to get facts to the physicians, patients and consumers making complex choices about the therapies they need and the products they buy."

The Agency is rapidly advancing into the world of electronic information management. This transition places a great burden on the review centers but it also offers tremendous efficiencies.

"Whether it is total electronic filing, FOI, adverse events reporting or clinical trial databases, new approaches to managing information will change how we do business in ways we cannot yet fully imagine." Friedman said.

"We all believe that our performance will be better, probably faster, but certainly the startup will stretch our resources to the limits."

12 Receive Kudos at FDA Ceremony

A dozen CDER scientists were honored at the 1997 FDA Scientific Achievement Awards ceremony on Dec. 9, held at the Natcher Conference Center, on the National Institutes of Health's Bethesda campus, in conjunction with the FDA Forum on Regulatory Sciences.

Hao Zhang, M.D., received an Excellence in Laboratory Science Award. An Excellence in Review Science Award was presented to the microbiologists in the Office of Pharmaceutical Sciences : **Peter H. Cooney, Ph.D., Vivian Greenman, Andrea S. High, Ph.D., Patricia F. Hughes, Ph.D., David Hussong, Ph.D., James L. McVey, M.S., Kenneth H. Muhvich, Ph.D., Paul S. Stinavage, Ph.D., Neal J. Sweeney, Ph.D., Carol Keller Vincent, M.S.,** and **Brenda Uratani, Ph.D.**