news along the pike

FEBRUARY 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

VOLUME 6, ISSUE 2

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Center Reports Drug Review Statistics for 1999

83 New Drugs, 35 NMEs, 97 Efficacy Supplements OK'd

BY MURRAY LUMPKIN, M.D.

In calendar year 1999, CDER took 190 actions on original new drug applications and approved 83 of them, 28 of which were priority reviews. Of the approvals, 35 were for new molecular entities, and 19 of these were priority approvals.

The Center approved 97 efficacy supplements, which are new uses for already approved drugs, and 1,419 manufacturing supplements.

There were 16 approvals for "orphan" products to be used in patient populations of 200,000 or fewer.

New Drug Applications: The median total time to approval for NDAs acted on in 1999 was 12.0 months, the same as in 1998. Approval time represents the total review time at the Agency plus industry response time to the Agency's requests for additional information. The median review time—FDA time only—was 11.8 months, 2 percent quicker than the 12.0 months of the year before. Twelve of the 1999 NDAs were for orphan uses.

(Continued on page 8)

186 Generic Drugs, 43 First Time; 56 Tentative Approvals

BY NASSER MAHMUD

In 1999, CDER received 296 applications for generic drugs and approved 186, including 43 that represent the first time a generic drug was available for the brand name product. In 1998, there were 345 applications, 225 approvals and 46 first-time approvals. Examples of first-time approvals for 1999 include nicotine gum, used as a smoking deterrent, and profpofol injectable emulsion, used as a sedative for maintenance of anesthesia during surgery.

The Center also issued 56 tentative approvals in 1999 compared to 40 in 1998. A tentative approval has its final approval delayed due to an existing patent or exclusivity on the innovator's drug product. Examples of tentative approvals include lovastatin tablets, a cholesterol lowering agent, and fluoxetine hydrochloride capsules, used for depression.

The numbers used this year reflect conversion to a new counting system in which certain variations in a drug product are counted as a single application. Thus, the totals should not be compared to those in previous *Pike* reports.

Nasser Mahmud is a regulatory management specialist in the Office of Generic Drugs.

CDER Group Wins FDA Review Science Award

A group of Center scientists were presented the FDA and CDER Excellence in Review Science Award at the 2000 FDA Scientific Achievement Awards ceremony on Feb. 15 as part of the annual FDA Science Forum held in Washington.

FDA Scientific Achievement Awards

Excellence in Review Science—Biopharmaceutics Classification System Working Group: **Ajaz S. Hussain, Ph.D., Lawrence J. Lesko, Ph.D., Ko-yu Lo, Ph.D., Vinod P. Shah, Ph.D., Donna Ann Volpe, Ph.D.,** and **Roger L. Williams, M.D.** For development and implementation of a biopharmaceutics classification system to establish a mechanistic basis for correlating *in vitro* drug product dissolution and *in vivo* bioavailability.

CDER Scientific Achievement Awards

Excellence in Analytical Science—**Hsien-Ming James Hung, Ph.D.** For outstanding achievements in the development of new statistical methodologies for clinical trials that significantly enhance the scientific basis of the FDA's regulatory decisions.

Excellence in Laboratory Science—Cardiopulmonary Pharmacology Research Team: **Douglas P. Chadwick, Eugene H. Herman, Ph.D.,** and **Jun Zhang, M.D.** For establishing animal models of insidious anthracycline induced cardiotoxicity, discovering a cardioprotective approach and linking the cardiotoxicity to a monitorable interspecies biomarker.

JOE'S NOTEBOOK

The Broad Street Pump Handle

Visual representations of evidence should be governed by principles of reasoning about quantitative evidence. For information displays, design reasoning must correspond to scientific reasoning. clear and precise seeing becomes as one with clear and precise thinking.

—Edward R. Tufte
Visual Explanations, 1997

For it's fifth anniversary issue, the *Pike* is running its traditional February Page One articles on drug review performance for the previous year. I'll be the first to admit that numbers in a line of words are rarely as informative as they can be in a graphical presentation. Later, the Center will produce the *Report to the Nation* with the appropriate graphs.

Involved as I am with that project, I was privileged to take a one-day seminar this past fall with Professor Tufte, Yale University's guru of the visual display of information. Tufte's main example of effective presentation of evidence for decision making was a surprise—a classic of epidemiology—Dr. John Snow (1813-1858) and the 1854 cholera epidemic in London.

During the 1830s and 1840s, when severe cholera epidemics threatened London, Snow had become interested in the cause and transmission of the disease. He published a brief pamphlet in 1849 suggesting that cholera is a contagious disease caused by a poison that reproduces in the human body and is found in the vomit and stools of cholera patients. He believed that the main, although not only, means of transmission was contaminated water. However, Snow's argument was only one of many theories proposed at the time.

Snow was able to prove his theory in 1854, when another severe epidemic of cholera occurred in London. Through painstaking documentation of cholera cases and correlation of the comparative incidence of cholera among subscribers to the city's two water companies, he showed that cholera occurred much more frequently in customers of one water company. This company drew its water from the lower Thames, after it had become contaminated with London sewage. The other company obtained water from the upper Thames. The rate of cholera in customers of the first company was 315 deaths per 10,000 households compared to 37 deaths per 10,000 households served by the water company drawing from the cleaner upper Thames.

A striking incident during this epidemic has become legendary. In the neighborhood surrounding the intersection of Cambridge and Broad Streets, the concentration of cholera cases was so great that more than 500 people died in 10 days. Snow investigated and concluded that the cause was centered around the Broad Street pump. He described his findings to an incredulous but panicked assembly of local officials. They had the pump handle removed, and the epidemic was contained. Removing the pump handle and cleaning the water supply were successful disease control measures carried out some 40 years before the true bacterial cause of cholera was discovered. The pump handle has become a symbol for effective epidemiology.

The Centers for Disease Control and Prevention appropriately enough have a succinct tribute to Snow on their Website at http://www.cdc.gov/ncidod/dbmd/snowinfo.htm

To learn a great deal about Snow's times and science, read his original treatise on cholera, examine his data tables and view his famous map of the Broad Street outbreak, be sure to visit the UCLA School of Public Health's Website devoted to Snow at http://www.ph.ucla.edu/epi/snow.html.

To borrow my copy of Tufte's book, send me an e-mail. You can read how the workers in a brewery a block from the Broad Street Pump were saved from the epidemic by the owner's policy of free beer for employees!

news along the pike

The Pike is published electronically on the X:drive in Cdernews and on the World Wide Web at:
http://www.fda.gov/cder/pike.htm
Photocopies are available in the Medical Library (Parklawn Room 11B-40) and its branches (Corporate Boulevard Room S-121 and Woodmont II Room 3001).
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Please contact a member of the Editorial Board or:

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

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

OMBUDSMAN'S CORNER

Happy Anniversary to the *Pike*

BY JIM MORRISON

At times, it seems my memory of FDA predates recorded history. My tenure here really began with the Bureau of Drugs in the early 1970s. From that perspective, the changes have been spectacular. But since this is the fifth anniversary of the *Pike*, in this column my reflections go back only as far as 1995, which is also the year the CDER Ombudsman position was created. The major focus of activity in CDER then was the 1992 Prescription Drug User Fee Act. The Center was getting into the tough part of the goal dates for NDAs.

Judging by complaints from the industry, it was still too early to tell if PDUFA was going to be a success or if it would be another failed attempt to revolutionize new drug reviews. There was a dwindling backlog of pre-PDUFA applications, but some review divisions were struggling to get their work done on time. Inside CDER, however, there was a clear mandate to make PDUFA work, and there was a sense of urgency that meant reviewers were working harder, smarter and longer hours. However, just doing more of the same was not the long-term solution.

In February of 1996, Center Director **Janet Woodcock, M.D.,** led about 30 senior managers in a go-away. CDER had management go-aways before, and some in attendance were skeptical that anything more would come from this one. But instead of focusing on planning or budgets, this one focused on taking a step back, on breaking down the barriers to communication among CDER's diverse offices and on figuring out what CDER was about and what it needed to do to adapt to a changing world. The participants in that go-away became the CDER Change Team.

The result was a palpable change in the climate in CDER. There was a growing cohesiveness, collegiality and a renewed sense of direction. To illustrate the extent of the change in CDER, I'll cite one example. In the fall of 1996, during one of many sessions to acquaint first- and second-line supervisors with the change process and to get their input, we had an exercise to write a headline for the Washington *Post* for a date in the year 2000. Several of the working groups produced a headline that read something like: "CDER Wins Prestigious Award for Outstanding Achievement." Although that mock headline was viewed as an improbable stretch at the time, just two years later, CDER and the Agency won the Ford Foundation's prestigious Innovations in Government award.

Awards are fine, but are there more lasting indicators that CDER has changed in five years? From my perspective, while the number of complaints has stayed fairly constant, the attitude of complainants has changed. Five years ago, complainants from the industry and members of the public were angrier and were very willing to buy into the image of CDER as a group of hide-bound bureaucrats who delighted in putting roadblocks in the path of progress.

While there is still a small minority of people out there who cling to that image, those who contact me and who know CDER have a greater respect for us and an expectation that whatever problem they have encountered is an aberration that can be fixed. The edge in people's voices is generally gone, as is most of the anti-FDA sentiment. No award or public relations campaign can bring about that change in attitude. People believe their own experiences over PR. The surest way to win people over is one person at a time, and CDER has been doing just that.

No five-year retrospective would be complete without some mention of where we are headed in the next five years. The Internet is changing the way people think about information. It is also raising expectations about how much information should be instantly at everyone's fingertips. One of CDER's most important challenges over the next five years will be to fill the demand for better information about health care and medicines.

This demand is coming, not only from the public, but also from health care professionals and other stakeholders. With the number of Internet sites numbering in the tens of millions and increasing daily, there will be more misinformation about drugs and dietary supplements out there spreading confusion. As people realize the need to get information from reliable sources, they will grow to depend on sites such as FDA's.

CDER needs to be there with accurate information, displayed in an easy to use format that is updated constantly. To do that, we will need to completely rethink the way we handle information within CDER.

CDER has come a long way in the past five years in transparency and openness. The *Pike* has been part of that progress. It has become a popular and trusted source of information about CDER, not only for staff here but perhaps more so for people outside the organization. That underscores the need for even more openness and transparency by CDER. The challenges in the next five years will be tough, but if the past five years are any indication, CDER will successfully meet those challenges.

Jim Morrison is the Center's ombudsman.

Employees Give Back During CFC Campaign

BY DAVE MOSS

FDA in the Metro area exceeded its goal of $775,000 in the Combined Federal Campaign by more than $40,000 and exceeded last year's contributions by more than $100,000. Well over half of all FDA employees contributed and the average contribution was up nearly 20 percent over last year. CDER employees led the way with their most generous campaign ever, exceeding last year's contributions by more than $50,000. Clearly the generous folks in CDER and the rest of the Agency are giving back to their communities and helping those less fortunate than themselves.

Center Director **Janet Woodcock, M.D.,** chaired this year's FDA Campaign. **Dave Moss** served as the Agency campaign manager. **Tim McGovern** led the CDER campaign with assistance from **Tim Mahoney**, OCD coordinator; **Tom Cunningham,** ORM coordinator; and **Candee Chadwick,** OPS coordinator. Of course, numerous team captains, keyworkers and volunteers were key to the success of this year's campaign.

(Continued on page 4)

INFORMATION TECHNOLOGY CORNER

OIT Creates New Desktop Management Team

Does the rate of computer-related change ever concern you? New operating systems, work applications, growing security risks, all seem to be coming at us with lightning speed. To cope with these changes OIT's Division of Infrastructure Management and Services has created a new group called the Desktop Management Team.

The team's focus is to manage change and prevent potential hardware and software conflicts that could impact CDER's productivity. They also assist the Help Desk and the desktop support technicians when PC configuration issues arise.

The team's current endeavors include:

- Hardware and software testing, evaluation and configuration.
- Level II request evaluation.
- Standard desktop and laptop system load creation and testing.
- McAfee virus file updates.
- Service level agreements.

Two projects that will be implemented soon are the McAfee 4.0.3 version upgrade and the EASE NT migration for timekeepers and supervisors. The division's goal is to manage the complex, fast-changing IT environment while at the same time providing the best service possible to the CDER community. Look for future articles in the *Pike* describing our upcoming projects.

March IT Training

Monday	Tuesday	Wednesday	Thursday	Friday
		1 **Excel 97 Intro** 9:00-12:00 **Word 97 Intro** 1:00-4:00	2 **Word 97 Formatting** 9:00-12:00 **Word 97 Tables** 1:00-4:00	3 **PowerPoint 97 Intro** 9:00-12:00 **PowerPoint 97 Charts** 1:00-4:00
6	7 **CDER Standard Letters 5.0** 9:00-11:00	8	9	10
13 **DFS** 9:00-12:00 **NEST** 1:00-4:00	14 **NEDAT** 9:00-12:00 **JMP Intro (Session 1)** 1:00-4:00	15 **Creating PDF Review Documents** 9:00-12:00 **MS Project for Project Managers** 1:00-4:00	16 **Access 97 Intro & Tables** 9:00-12:00 **Access 97 Queries & Reports** 1:00-4:00	17 **Access 97 Form Design** 9:00-12:00 **Access 97 Report Design** 1:00-4:00
20	21 **JMP Intro (Session 2)** 1:00-4:00	22 **CDER Standard Letters 5.0** 9:00-11:00	23	24
27	28 **DFS** 9:00-12:00 **JMP Intro (Session 3)** 1:00-4:00	29	30	31

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

Help Desk FAQ

How do I map a network drive?

To map a network drive:

- Right click My Computer or Network Neighborhood, and then click Map Network Drive.
- Click the Path box, and then type the path to the resource you want. For example, many in the Center map the drive letter X to \\CDFDA\COMMON.
- To reconnect every time you log into the network, check the Reconnect at logon box
- Click OK

Remember when calling the Help Desk that the drive letter is arbitrary. Please provide the technician with the full path. Contact the Help Desk (HELP, 7-0911) for more details.

Inventory of Pre-Y2K Systems

If an item was received or created as part of your official duties, it is a record and should be managed accordingly. Electronic files, computer systems and databases can be records, too. The information that records contain must be accounted for, maintained and disposed of when no longer needed.

This process is mandated by the Federal Records Disposition Act (44 U.S.C. Chapter 33). Disposition instructions can be found in a records control schedule, a document reviewed and approved by the National Archives and Records Administration.

Last summer, the FDA was tasked by HHS and NARA to account for a list of information systems that were slated for retirement or disposal because of Y2K concerns. Many of the systems were not readily identifiable, having been discontinued or migrated to other systems.

OIT's Division of Data Management and Services and Division of Applications Development Services compared the list to CDER's current systems inventories and assembled the necessary disposal proposals. The FDA Records Office has now reviewed and approved those recommendations, and the disposal instructions will be implemented.

This was a collaborative effort by all involved and may lead to similar reviews of CDER's information systems and databases.

Contact **Scott Zeiss** (ZEISSS) for more information.

QA Development Project

A peer review of the revised guidance document on project planning was held Feb. 23. The guidance document includes a project plan template. All five guidance documents on Configuration Management are now approved and are posted on the project Web page on the CDER intranet http://oitweb/oitActivities/qa_development/.

The OIT point of contact is Vali Tschirgi (TSCHIRGIV).

Successful CFC Campaign

CDER Leads Way at FDA

(Continued from page 3)

The financial support of Federal workers emerges as crucial to the well being of communities in the National Capital Area. Thanks to everyone who participated and contributed to this year's campaign!

Dave Moss was FDA's CFC campaign manager.

TRAINING AND DEVELOPMENT CORNER

CDER's Accreditation for Continuing Medical Education Renewed

BY NANETTE MCATEE

The Accreditation Council for Continuing Medical Education recently renewed for two years CDER's accreditation status as a provider of continuing medical education. The Division of Training and Development's CME program underwent a rigorous onsite inspection in June.

Accreditation assures both physicians and the public that continuing medical education activities sponsored by CDER meet the ACCME's high standards. The ACCME evaluates the overall continuing medical education programs of institutions according to standards adopted by all seven of its sponsoring organizations:

- American Board of Medical Specialties.
- American Hospital Association.
- American Medical Association.
- Association for Hospital Medical Education.
- Association of Medical Colleges.
- Council of Medical Specialty Societies.
- Federation of State Medical Boards.

With ACCME accreditation renewed, CDER can continue to award continuing medical education credit to training and education programs that:

- Target physicians.
- Are consistent with CDER's mission.
- Meet the requirements outlined by the ACCME.

If you are involved in developing an educational activity for physicians and are interested in pursuing CME credit, contact **Dale Wilcox** (WILCOX, 7-4580) during the initial planning of the event. DTD will:

- Guide you through the accreditation process.
- Maintain an activity file on the event.
- Issue credit to participants of the event.

In addition to the ACCME accreditation, CDER is also approved by the American Council on Pharmaceutical Education to provide continuing pharmacy education.

Programs that have an audience consisting of pharmacists may pursue CPE credit with assistance from DTD.

Obtaining Your CE Credit

If you wish to request a CDER continuing education number—or have forgotten your number—please contact **Karen Zawalick** (ZAWALICKK, 7-1449). Make a note of your CE number and use it when you complete the evaluation forms for programs offering CE credit. This CE number identifies you with the CDER continuing education activities in which you participated. This information is maintained in a database in the Division of Training and Development and is for CDER employees only.

To request a report on your CDER CE activities, please contact Karen two weeks in advance of your need for the information. Karen will provide you with a hard copy for your records.

Nanette McAtee is a regulatory health education specialist in DTD.

EQUAL OPPORTUNITY CORNER

Soul Food Sharing Event at WOC II Marks Black History Month

BY GLORIA MARQUEZ SUNDARESAN

Once upon a time, two women had routinely lunched together, sharing homemade food that each had prepared and exchanging menus and food preparation tips. They raved about each dish and complimented each other on how tasty the food was—and they were happy.

The women continued their ritual until they finally decided that their love for cooking and eating had to spread. So, one day they brought in extra food for others to taste at lunch time. Sure enough it, was an instant hit. After that, there was no turning back.

By popular request that small event turned into a large one at Woodmont II. It became known as the Soul Food Sampling, and the two women decided to hold it during February to celebrate Black History Month appropriately.

The lucky residents of WOC II have been enjoying this special treat since 1998—one big festive lunch in the month of February. This year's event coincided with Valentine's Day, making two parts of the body happy at once—the tummy and the heart.

The array of tasty, ethnic food at this year's event was phenomenal. There were several kinds of fried chicken, BBQ ribs, pig's feet and liver smothered with onions; salads; an array of vegetables including greens, cabbage, string beans, potatoes and broccoli; and desserts galore.

Those who missed this year's Soul Food Sharing will have to wait until next year's Black History Month. Those of us who participated have 12 months to shed the calories we counted and enjoyed.

The two women who co-chaired this event for the last three years are **Carol Hall,** OPS, and **Jody Moore,** Executive Operations Staff. Other members of the organizing committee are **Joy Bennett,** ODE I; **Vikki Kinsey,** Executive Operations Staff; **Diane Smith,** EEO Staff; **Lisa Springs,** HFD-120; and VIP honorary member, **Bill Myers,** OPS.

In addition to the Soul Food Sampling, CDER set up the display "Black American Women of Hope" in the Parklawn Building's main entrance. Also, the EEO Staff has sent e-mail biographies about notable African American men and women. So far, we have featured:

- Patricia Roberts Harris, who died in 1985, a former Secretary of the Department of Health Education and Welfare, predecessor to the Department of Health and Human Services.
- Benjamin Carson, M.D., one of the world's most gifted neurosurgeons and a member of the faculty at the Johns Hopkins University
- Marian Wright Edelman, founder of the Children's Defense Fund.

Contributing to these e-mail biographies were **Estela Barry,** a retired CDER pharmacologist, and **Robert White Jr., M.D., FACP,** a medical officer in the Division of Oncology Drug Products.

Gloria Sundaresan is a member of the EEO Staff.

PROJECT MANAGEMENT CORNER

Task Force for Team Best Practices Issues Progress Report

Members of the Reviewer Affairs Committee and the Project Management Staff collaborated to form a Task Force for Team Best Practices. The task force orchestrated a pilot workshop to identify team best practices on Dec. 9. Workshop participants consisted of a random selection of reviewers and project managers from across the Center.

The workshop was designed to create a comfortable atmosphere in which a free exchange of ideas and opinions would develop. The object of the workshop was to solicit perspectives, insights and recommendations on best practices for multidisciplinary reviews. A dynamic and vibrant exchange of information was achieved. Participants appeared to be energized by the opportunity to express their views regarding the team review process.

All comments and recommendations on the qualities of successful and unsuccessful teams were captured and compiled in a report sent to the participants. Here are some recommendations from the pilot workshop on methods that could enhance team interactions:

- Delineation of roles and expectations for all disciplines to assure efficient use of all the expertise among the team members in the review process.
- Use of team member expertise without disciplinary borders.
- Development of mutual respect and trust among team members.
- Consistent participation by team members, intra-discipline group discussions of science issues and communication to other disciplines such as microbiology, chemistry, statistics, medical, toxicology, pharmacology, project management, post marketing and scientific investigation.
- Effective team communications.
- Good listening skills among team members to encourage innovation and problem solving.
- Team empowerment by management and trust in the team's ability to review.
- Proactive vs. reactive communication with sponsors.
- Informing sponsors of FDA questions and new issues prior to meeting to allow them to come prepared.
- Use of teleconferencing vs. face-to-face meetings.
- Informing sponsors of new issues and possible decisions to avoid surprises during face-to-face meetings.
- Team members should be fully prepared and ready to participate to assure efficient use of meeting time.
- A pre-established agenda should be developed to enhance meeting productivity. Questions and answers should be identified prior to sponsor-applicant meetings. Based on these prior agreements on answers, the team should develop a unified position.
- Debriefings directly following a sponsor-applicant meeting are helpful to assist in the development of minutes and to assure accuracy.
- Rewarding a job well done by management in the form of an e-mail, a certificate or a get together over lunch.

Additional workshops are tentatively planned for March and April. Ultimately, all the information gathered through these workshops will be made available throughout CDER.

Task force members and authors: Sousan Altaie, Debbie Kallgren, Robert Leedham, Fred Marsik, Lana Pauls, Luqi Pei, Jean Yager, Maryjane Walling and Millie Wright.

REVIEWER AFFAIRS CORNER

Subcommittees Perform Majority of Work; Survey Still in Development

C. RUSS RUTLEDGE

The Reviewer Affairs Committee accomplishes most of its work through its subcommittees. For example, the Team Model Subcommittee has worked with Jean Yager and the Project Management Staff in developing the team best practices concept and helped conduct the December workshop described in the Project Management Corner above.

You can visit the RAC intranet homepage at http://cdernet/rac/index.htm to learn more about our subcommittees. Membership on the various RAC subcommittees is open to any CDER employee or team leader. Being a RAC representative is not a prerequisite.

If you are interested in contributing to a subcommittee project, please contact the subcommittee chair or your division RAC representative. You can find their names on the RAC intranet site.

You may also submit comments on any of the subcommittee projects through your RAC representative or directly to the subcommittee chair.

For instance, OIT and others submitted comments to improve the Reviewer's Handbook. These were presented during one of the committee's monthly meetings. The next edition of the handbook is being drafted, so now is a good time to submit your comments to your division RAC representative or the subcommittee chair, Russ Rutledge (RUTLEDGEC).

With the union now representing the Center's nonsupervisory employees, the question of whether it is appropriate for the RAC to continue to represent the concerns of primary reviewers to senior management has occupied the committee.

To determine the opinion of CDER's reviewers on these fundamental questions, RAC designed a survey modeled after last November's RAC Corner.

Several scenarios were discussed including disbanding the RAC, reestablishing it as a union subcommittee, or collaborating with the union in a "sister" relationship. The survey questions were forwarded to the CDER Senior Management Team, labor management for wording and the NTEU for review.

The wording of the survey still has details to be worked out so that it is acceptable to all parties. The committee is confident these issues will be resolved shortly and that the opinion of CDER reviewers on the issue can be determined and reported.

C. Russ Rutledge is a compliance officer in the CDER Office of Compliance's Division of Manufacturing and Product Quality.

OTR Advances Regulatory Applications of Computational Toxicology

By Joseph F. Contrera, Ph.D., Edwin J. Matthews, Ph.D and R. Daniel Benz, Ph.D.

The accomplishments of the Office of Testing and Research in the area of computational toxicology were highlighted at the 2000 FDA Science Forum held Feb. 14-15. The Regulatory Research and Analysis Staff in OTR has been engaged in toxicology database and computational toxicology research since the early 1990s.

Computational toxicology is the application of computer technology and information processing to analyze, model and predict toxicological activity based on chemical structure activity relationships. See the April 1998 issue of the *Pike* or our intranet site for more information.

Last year, OTR initiated a CDER Computational Toxicology Consulting Service that is accessible to FDA staff on our CDERnet site at http://cdernet/pharmtox/comptox/comptox.html. This is a review and scientific support service where Regulatory Research and Analysis Staff performs computational toxicology evaluations of compounds submitted by FDA reviewers and other FDA scientists.

OTR toxicology databases were used to support the development of numerous safety guidances for the International Conference on Harmonization. Computational toxicology is currently being used to support regulatory decisions regarding the necessity, nature and extent of testing for excipients, contaminants or degredants that are identified late in the NDA process. In collaboration with the Center for Food Safety and Applied Nutrition and support from the Office of the Commissioner, computational toxicology modules were developed to meet new review requirements for food contact substances in the 1997 FDA Modernization Act. The regulatory application of this and other computational toxicology software to meet these requirements is underway at CFSAN.

A large-scale predictive performance study of OTR developed software modules demonstrated improved capability to predict the carcinogenic potential of pharmaceuticals in rodents with increased specificity, sensitivity and predictivity compared to previous versions or other software. The intranet site contains a link to the study (Reg. Tox. Pharm. (1998) 28, 242-264).

Other modules are under development including reproductive toxicity, teratology and genotoxicity. In collaboration with the Offices of Post-Marketing Risk Assessment and Biostatistics, an effort is underway to assess the feasibility of modules that incorporate the results of the clinical Adverse Event Reporting System to predict clinical adverse events.

CDER possesses a unique resource of scientific information from both clinical and animal studies for pharmaceuticals that has applicability beyond the area of pharmaceuticals. Toxicology and clinical adverse event databases have been created at CDER, and the challenge now is developing effective ways to convert this information into useful knowledge to advance the science of risk and hazard assessment.

Computational toxicology offers a means of rapidly analyzing large databases to identify relationships and patterns that can be used to support regulatory and product discovery decisions. The power of computational toxicology software increases with the size and diversity of the program's data set. Technology now makes it possible to analyze information from the combined toxicology databases of CDER and other centers. Such a knowledge base would improve the scientific basis of regulatory decisions, increase consistency, facilitate the regulatory review process and stimulate new product development.

Joseph Contrera is director, Edwin Matthews an expert computational toxicologist and Daniel Benz a toxicology database specialist in OTR's Regulatory Research and Analysis Staff.

Office of Compliance Mourns Passing of Management Officer Anita Harrell

By Edward Miracco

It is with great sorrow that we report the death of **Anita Harrell,** a member of the CDER family since 1978 and administrative and management officer for the Office of Compliance for almost two decades. She passed away on Feb. 12 after an extended illness.

Anita began her FDA career as a technical information clerk for the Drug Listing Branch. She was promoted in quick succession to drug listing clerk, administrative clerk, administrative assistant and to administrative officer in 1981. In 1995 she received her promotion to the position of Management Officer. During her tenure she received numerous FDA performance awards including an Outstanding Achievement Award in 1990 and the Administrative-Program Management Excellence Award in 1998.

Anita was a devoted Baltimore Orioles fan and an avid admirer of Cal Ripkin, Jr., whom she fondly referred to as "Cal, Jr." Her season tickets to the ball games were one of her greatest joys, joys that she often shared with her friends at work. She also loved her two cats, Tipper and Tiger. Her office friends are quick to recount the feline antic stories that brought smiles to all.

Anita's co-workers are also quick to point out that she always had time to help them with work issues. She was known as a person who would drop everything to assist, often correcting what appeared to be the uncorrectable and solving seemingly unresolvable administrative issues. I can personally attest to this, having been guided by Anita through the insanity of a relocation from New York to the D.C. area about 11 years ago.

In spite of her serious illness, Anita came to work until two weeks before her death. She never complained. She just did her job with competence, an almost indescribable gentleness, and always with dignity.

Stephanie Gray, CDER Office of Compliance Office Director and Anita's supervisor for the past six years, said it best during a recent dedication when she stated that Anita was a model of courage and kindness and an inspiration to the many whose lives she touched. She will indeed be missed and knowing her will be forever cherished by her extended family at CDER.

Edward Miracco is a consumer safety officer in the Office of Compliance.

Center Approves 83 New Drugs, 35 NMEs, 97 Efficacy Supplements

(Continued from page 1)

Priority approvals: Last year's approvals included 28 priority drugs. Priority drugs are considered to be of potentially exceptional public health value. They receive a faster review because they represent a major advance in medical treatment. The median total approval time for these priority applications was 6.1 months, 5 percent faster than the median of 6.4 months in 1998. The median FDA review time was 6.1 months. Nine of the orphan drugs approved in 1999 received priority approvals.

New Molecular Entities: Thirty-five of the new original drugs were new molecular entities, and 19 received priority reviews. NMEs contain an active substance that has never before been approved for marketing in any form in the United States. The median total approval time for these products was 11.6 months, 3 percent faster than the 12.0 months in 1998. The median FDA review time was 10.0 months. Sixteen of the 30 NMEs approved in 1998 received priority reviews. Eight of the 1999 NMEs received approval for orphan uses.

Efficacy Supplement Approvals: In calendar year 1999, the Center took action on 184 efficacy supplements and approved 97, including nine that were given priority reviews. The median total approval time was 10.4 months, and median FDA review time was 10.2 months. Efficacy supplements are new uses for already approved drugs and often represent important new treatment options for patients. In 1998, CDER took action on 173 and approved 124, including 13 that received priority reviews. In that year, median total approval time was 11.8 months, and median FDA review time was 11.7 months. Four of the 1999 efficacy supplements were for orphan uses.

Manufacturing Supplement Approvals: In calendar year 1999, the Center took action on 1,747 manufacturing supplements, of which 1,419 were approvals. CDER approved 1,375 manufacturing supplements in 1998. The chemists, project managers, the Division of Scientific Investigations and the field inspectors all deserve congratulations for their performance with manufacturing supplements.

Murray Lumpkin is Deputy Center Director (Review Management).

'CDER Live!' Videoconference on DTC Advertising Scheduled for March 16

By Elaine Frost

CDER and the Drug Information Association are co-sponsoring their fifth satellite videoconference on March 16 from 1 p.m. to 3:30 p.m. Eastern time. Called "Perspectives on Direct to Consumer Advertising," this edition of "CDER Live!" will focus on DTC promotion of prescription drugs.

The program will provide comprehensive coverage of the history, law and regulations governing this area, as well as a lively discussion of the different perspectives on DTC promotion. Also discussed will be results from FDA's consumer survey that examined patients' attitudes, reported behaviors and experiences in physicians' offices, both in general and as a function of their awareness of DTC promotion.

The first part of the program will present DTC promotion in the broad context, addressing its history, relevant law and regulations and different perspectives on its benefits and risks.

The second part of the program will consist of an in-depth discussion of recent guidance and enforcement actions, recommendations for how to work with the Division of Drug Marketing, Advertising and Communications.

DDMAC has the lead for developing this edition of "CDER Live!" Several of its staff will form the panel. They will discuss the advisory process and results of their recent research.

FDA employees are welcome to view the program at the following sites:

- Parklawn Room 13B-39.
- Corporate Room S-100.
- Woodmont II Conference Room G.

There is no prior registration.

The program is intended for the pharmaceutical industry and its advertising companies. They should contact Michael Hunter at DIA (215) 591-3316 for costs of subscribing to the satellite broadcast or Webcast and for registration information.

Elaine Frost is a public affairs specialist in OTCOM.

CDER Lab Forms Partnership with Germans

Graduate Students Work at Nicholson Lane Research Center

The Division on of Product Quality Research in the Office of Testing and Research has formed a partnership with the laboratory of a small, non-profit agency in Germany. The agency, known as the Zentrallaboratorium Deutscher Apotheker or ZL, is located in Eschborn and has sponsored two graduate students to work in DPQR's cell culture laboratory.

The German agency will pay the students' expenses, and CDER will supply lab space and supplies.

"We have similar research interests and it makes a nice fit," said research chemist **Donna Volpe, Ph.D.** Volpe will supervise the students and helped them make a smooth transition to the Nicholson Lane Research Center.

"The students will gain experience in using our techniques, the ZL and CDER will gain data for common projects, and we get extra help. It's a win-win situation for all concerned," Volpe said.

Stefanie Schulte-Loebbert, from the J.W. Goethe University in Frankfurt, will study the *in vitro* permeability and dissolution of St. John's Wort components.

Britta Klaembt, from the University of Heidelberg, will characterize and evaluate an epithelial cell model of *in vitro* drug permeability according to CDER's biopharmaceutical classification system guidance.

"We hope this collaboration can serve as a model to other FDA research laboratories as a way to optimize their resources," said **Celeste Bové,** a health science administrator with the Office of Testing and Research.