news along the pike

February 1997

Center for Drug Evaluation and Research

Volume 3, Issue 2

Inside . . .

Pike's Corners . . .

Center Sets Records for Drug Reviews

269 NDA Actions, 196 Efficacy Supplement Actions in 1996

By Murray Lumpkin, M.D.

There are many metrics by which our review performance is judged: quality, quantity, timeliness, predictability, value added—and they all point to a year of performance superlatives. All CDER staff are to be highly congratulated on an outstanding performance this year.

One review performance highlight of calendar year 1996 consisted of 269 actions taken on original new drug applications (NDAs) and 196 actions taken on efficacy supplements. This is a 25 percent increase in the number of actions taken on original NDAs over those taken in 1995 and a 6 percent increase in the actions taken on efficacy supplements over those taken in 1995.

Of these 269 NDA actions, 131 were approvals. This represented a 60 percent increase over the 82 NDAs that were approved in 1995. Interestingly, even though the numbers of approvals soared, the "FDA review time" and the "total time to approval" both

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212 New Generics Approved, 33 First Ever

By Ted Sherwood

The Office of Generic Drugs (OGD) had another impressive year of approvals for abbreviated new drug applications (ANDAs) and abbreviated antibiotic applications (AADAs). Last year, OGD approved 212 abbreviated applications, a record high for the 1990s. Plus, the Office issued 25 tentative approvals for drug products that cannot be granted full approval or cannot be marketed until the innovator or brand product's patent or exclusivity terms expire.

Additionally, 33 of the final approvals represent first-ever generic drugs— the first time a generic drug is available for a brand-name product. Examples of first-time approvals include: an anticonvulsive, clonazepam (generic for Klonopin); an antipsychotic, clozapine (generic for Clozaril); a duodenal ulcer therapy agent, sucralfate (generic for Carafate); and a diuretic, triamterene and hydrochlorothiazide (generic for Dyazide). These four drugs alone have an $800 million

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CDER Report to Industry Highlights Progress

In a report to pharmaceutical industry leaders, CDER highlighted its successes for the last year. The report contains extensive data about the Center's drug review performance for 1996.

The electronic version of the report in Acrobat PDF format will be available shortly on the Center's Web site at:

http://www.fda.gov/cder/letter96.pdf

In an introductory letter, Center Director **Janet Woodcock** outlined some of CDER's priorities for the coming year:

- Meeting or exceeding the current performance goals established by the Prescription Drug User Fee Act (PDUFA).
- Clarifying the Center's policies on prescription to over-the-counter switches.
- Implementing further reforms in the Investigational New Drug process.
- Taking steps to decrease total drug development time now that PDUFA has succeeded in bringing drug review times

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Joe's Notebook

What's This "We" Stuff, Anyway?

If you thought this was my wife's smart answer to my query about where "we" placed some vital but now missing component to a household project, you'd be partly right. If you thought February, in which we celebrate Valentine's day and Black History Month led me to make a connection between teamwork and diversity, you'd be partly right. But, if you suspected your editor is stretching to link these to CDER's transformation and improved public health, you'd be on target for this editorial. You may have wondered what possessed me to make all these connections.

Another source that generated the connection was the Wednesday CDER Scientific Seminar that kicked off the month. **Dr. Leigh Thompson,** former chief scientific officer at Eli Lilly & Co., presented a persuasive medical and scientific argument on the benefits of diversity in the drug development process—not just in the clinical phase, mind you, but also in preclinical development. Thompson also suggested that the teams involved in drug development need to do some outside-the-box thinking. For example, is the team goal approval of the NDA or long-term marketability? As I listened to Thompson, I couldn't help but reflect on a project I was involved with last year: helping promote the breakthrough emergency treatment for acute stroke. The use of the therapy, approved by the FDA last summer, still hasn't spread much beyond the university-based medical centers that conducted the clinical trials. The point is, no matter how good one team is in meeting its goal, the larger project, improving public health, depends on that team's goals and products being linked in a chain with those of other teams.

A Great Big Thank You

By Lucy Rose

There are a great many thank-you's to pass around as OTCOM completes its first year (see pages 9 and 10). As is always true when starting anything new, the year was full of challenges, such as hiring new staff, blending existing organizations with new ones and working to earn the respect of our customers.

Through it all, though, the staff of this remarkable organization, OTCOM, has shown total dedication to the Center's mission, an unprecedented flexibility, a willingness to grow and learn and a contagious sense of humor that has supported all of us through our growing pains.

All of us in OTCOM wish to thank all of the CDER and FDA people who have so generously helped us over the last year—the volunteers who taught CDER courses, those who helped with personnel issues, those who helped with our renovations and moves and the countless other folks who have helped in so many ways. Though our organization is first and foremost a service one, we realize that we are indeed also served by those we serve. We realize we can't do our jobs effectively without you.

People are our most important resource. As we move into our second year, we plan to devote time and energy to both professional development and team building. Our goal is to enhance productivity, efficiency and work satisfaction through the use of teams and work groups.

Our teams have enabled many of us to expand our responsibilities and develop new skills, while continuing to perform our usual work.

We are striving to be totally transparent and accountable. We look forward to your input, both on our past performance, as well as on our future priorities. We always welcome your thoughts, concerns and ideas and know that they will help us improve our services to CDER.

news along the pike

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

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

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Ombudsman's Corner

Shakespeare's Advice on Career Development

By Jim Morrison

About a third of the issues brought to me concern internal CDER matters. Often the immediate cause of the complaint is not the real problem. Unfortunately, as in many scientific organizations, the press of technical work in CDER often becomes overriding, and we don't take enough time to attend to the human side of the enterprise. As a result, talented people sometimes find themselves underutilized or placed in positions for which they are not best suited or for which they have not been adequately prepared.

The problems that result from unwise management of human resources are tremendously destructive to the fabric of any organization. In CDER we are working through the transformation process to improve the way we manage all of our resources. But in the meantime, there are some things you can do to improve your lot in life if you find yourself in one of these career blind alleys.

To quote Shakespeare, "The fault is not in our stars, . . . but in ourselves that we are underlings." In *Julius Caesar*, Shakespeare described a support group run amok. Today, as in ancient Rome, assassination is never a viable remedy for problems with management. But there are other ways by which you can take charge of your own situation.

One method is to participate in a developmental program, such as the CDER Leadership Fellows Program or the FDA Leadership/Executive Development Programs. The CDER Leadership Fellows Program is in the midst of its maiden voyage, with 28 fellows working on projects that will make significant changes in CDER. A date has not been set for opening the next application process.

The FDA Leadership/Executive Development Programs are about ready to announce openings for the next two-year cycle. I have a particular interest in the FDA programs, because I have been for many years the CDER representative to the FDA Management Development Committee, which oversees the programs and makes the selections. These programs are open to GS-13s to 15s and are highly competitive. They have evolved from the old FDA Mid-Level Program, and they offer a rich mix of course work and tailored developmental assignments to different parts of the FDA, including the field.

If you are interested in applying to the FDA Leadership or Executive Development Program, keep an eye out for the official announcement, coming probably in early spring. If you have questions about how to apply, please contact the OTCOM representative who will be identified in the upcoming announcement. For those who may want to talk about how they might fare in the competition or other aspects of the programs, I would be happy to serve as a resource. Please call me (4-5443) or e-mail me (MORRISONJ).

While these two developmental programs apply specifically to people in grades GS13-15, a wealth of other programs target different groups. One in particular is the Center's new Secretary Certification Program sponsored by OTCOM.

Developmental programs are only one aspect of personal and professional development. I always encourage applicants to the programs to develop their own plan and to consider acceptance to one of the programs a nice bonus but not essential to their career progression. In my next column, I will discuss other approaches people have used to get a career unstuck. I invite everyone to share techniques you have used or have seen others use successfully. Give me a call or send an e-mail, and I'll include the best ones in my column.

Jim Morrison is the Center's Ombudsman.

Mentor's Corner

1997 New Reviewers' Mentor Advisory Group Members

By June Cory

This year's New Reviewers' Mentor Advisory Group has members representing a cross-section of the divisions and disciplines within the Center and is ready to help you with mentoring questions. The group meets to discuss issues related to improving the mentoring climate in the Center. For more information on mentoring activities or help obtaining resources, please contact one of the following members:

- **June Cory** (coordinator), Division of Training and Development, 827-3489.
- **Charles Ganley** (chair), Division of Cardio-Renal Drug Products, 594-5300.
- **Tom Abrams,** Division of Drug Marketing, Advertising & Communications, 827-2831.
- **Susan Kummerer,** Division of Medical Imaging & Radiopharmaceutical Drug Products, 443-7515.
- **Joy Mele,** Division of Biometrics II, 443-3520.
- **Vijay Nerurkar,** Office of Generic Drugs, 594-0350.
- **Jack Pevenstein,** Division of Biometrics III, 827-3110.
- **Anthony Proakis,** Division of Cardio-Renal Drug Products, 594-5300.
- **Nancy Smith,** Division of Biometrics III, 827-3111.
- **Jim Timper,** Division of Anti-Infective Drug Products, 827-2193.
- **Dale Wilcox,** Division of Training and Development, 827-3498.

June Cory is a member of the Division of Training and Development.

Administrative Management Corner

New Time Reporting Initiative in CDER

By Charlene Cherry and the Time Reporting Team

How are CDER's resources used? Center Director **Janet Woodcock** would like to have the answer to that question at her fingertips. Who's asking her the question and why? Anyone who has an interest in drug development—Agency and Center managers, members of Congress, leaders in the pharmaceutical industry and the American public. Why? Because people want to know what we're doing, how we're doing it and how much it is costing. It all fits in with the big picture of reinvention, reengineering, downsizing, transforming and the economy.

Should we be able to answer these questions? Yes. Can we now? No, not completely.

To many of us, time reporting is not a popular concept. It gets in the way of doing our real work. Some of us are time reporting already, but most of us are not. For those of us who are not time reporting, get ready; we will be by Oct. 1. That's the date Dr. Woodcock has mandated for implementation of a time reporting system that captures all CDER work activities and includes input from all CDER employees.

The Center already has an on-line time reporting system that is used to track activities taking place under the Prescription Drug User Fee Act. This system allows Center management to answer some questions about how we use our resources, but not all. The system also provides information used to obtain CDER's share of user fee funds from FDA. The scope of this existing system will be refined and enhanced to include all major categories of CDER activities.

The Management Analysis Branch (MAB) of the Division of Planning, Evaluation and Resource Management (DPERM) in the Office of Management is developing the new system. We have developed draft activity lists and identified points of contact from each division. We will soon begin the process of fine-tuning these activity lists with the division contacts. We anticipate that the Senior Management Team will finalize the activity lists by mid-March, and then systems development will go into full swing.

The Time Reporting Team consists of **Richard Allen, Charlene Cherry** (project manager), **Kristin Crown, Anne Henig, Don Kim** and **Dan Luckabaugh**—all from DPERM—and **Vikki Levi** from the Division of Information Systems Design.

If you have questions on the new time reporting system contact: Charlene Cherry, 827-0517 (e-mail: CHERRYC) or Richard Allen, 827-0524 (e-mail: ALLENR).

Charlene Cherry is the MAB branch chief in DPERM.

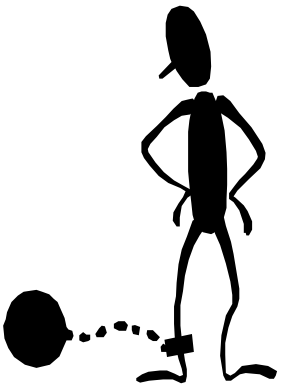
Project Management Corner

Phone Logs . . . Need I Say More?

By Susan Cusack

Here's a bit of trivia for you: The old punishment of attaching a ball and chain to a prisoner's leg was called "The Log." I will refrain from further comparisons.

Most CSO/Project Managers keep some form of record of informal telephone communications with industry, fondly referred to as a phone log. In response to my article about Meeting Minute templates, **Art Shaw** sent me an e-mail describing a Word Perfect macro that he developed for this purpose.



The phone log system he created consists of a macro, a table form and a button he created for his button bar. "When I receive a phone call," Art said, "I simply press the button on my button bar and a series of query screens appears to fill in information about the caller and notes on the call. When I am done the file is kept open to allow some editing or amplification of the notes. I periodically print the file to keep a permanent record."

Art also pointed out that the file created is searchable. "If John Jones of Mega Chemical Co. is on the phone, I can open the phone log file and do a quick word search to find out what I told John Jones the last time he called."

Art demonstrated his system for me, and I have been trying it for a couple of weeks. It is simple to use. Although it took a little discipline initially to open the macro when I was talking, it has ultimately saved me a lot of time. The search capabilities sure beat thumbing through a book, trying to remember when you talked to someone and then trying to find a record of the conversation. Which brings me to another feature that I like. The macro automatically inserts the time and date. I love that! I have confessed before that at any given time, I am not likely to know what day it is. Anything that keeps me oriented is appreciated. That feature alone encouraged me to activate the macro while I was talking.

If this sounds like a tool that you would like to try, notify me by e-mail (CUSACKS) or just keep your eyes open. A demonstration of this system will be scheduled in the near future and announced via e-mail. If you can help convert this macro for Microsoft Word users, have other hints, tools, tidbits or templates to share, please let me know.

Susan Cusack is a consumer safety officer in the Division of Medical Imaging & Radiopharmaceutical Drug Products.

May Help 1 Million with Adult-Onset Diabetes

Endocrine Drugs Approves First Insulin Resistance Reducer

The Division of Metabolic and Endocrine Drug Products approved the first antidiabetes drug designed to target insulin resistance. Troglitazone (Rezulin) is for patients with adult-onset diabetes who have to take insulin and still have inadequately controlled blood sugar levels. The drug offers these people the possibility of reducing or eliminating their dependence on insulin, while improving control of blood sugar levels.

The division's approval, the first for the drug worldwide, came within six months of submission of the new drug application. The review team for troglitazone included **Hae Young Ahn, Alexander Fleming, Mike Fossler, Mike Johnston, Dan Marticello, Robert Misbin, Stephen Moore, Herman Rhee, Solomon Sobel** (Division Director**), Ron Steigerwalt, Baldeo Taneja** and **Xavier Ysern.**

Diabetes affects about 16 million Americans and can cause damage to the eyes, kidneys, heart and peripheral circulation. Type II, often called non-insulin dependent diabetes mellitus, usually starts in adulthood and is commonly associated with being overweight and affects nearly 90 percent of all people with diabetes in the United States. Approximately 3 million people with type II diabetes require insulin injections. Troglitazone is expected to help about 1 million of them.

The drug, the first in its chemical class, improves what seems to be an important underlying cause of adult onset diabetes—resistance of the body to insulin. In two clinical trials, involving more than 500 patients, troglitazone was shown to significantly improve patients' ability to use insulin (produced in the body or through injection) in managing their diabetes.

A Radio Classic

Office of Compliance's Bill Russell On Air

By Edward Miracco

Bill Russell recently joined the Nontraditional Drug Compliance Team in CDER's Office of Compliance. No, Bill is not the legendary Boston Celtic who battled Wilt "The Stilt" Chamberlain in the '50s and '60s while racking up a fistful of National Basketball Association championships. Our Bill came from the Office of Generic Drugs where he was a project manager in Chemistry Branch IV. Additionally, he is currently a lieutenant in the Public Health Service.

Although some may not think that Bill has a past as storied as the famous NBA star, there's no denying he has had some interesting experiences. For example, how many of you know someone who has served in two branches of the U. S. armed forces? Bill served in the Air Force from 1973 to 1978 as a pilot flying F-4C Phantom jet fighters and as a navigator/bombardier in B-52D bombers. After graduating from the University of Houston School of Pharmacy in 1986, he served as a pharmacist in the Navy, assigned to the Naval Hospital in Portsmouth, Va., where he was stationed from 1988 to 1991.

Although he has loads of stories to tell about his days in the armed services, he most enjoys talking about his music activities. Bill has been a music radio commentator at various times since 1976. He started in Grand Forks, N.D. While stationed there, he offered some "helpful" comments to a local FM station manager about a particular announcer's pronunciation difficulties with opera. The next thing he knew he was challenged to "do it better" and made his microphone debut. He continued his operatic announcing in Houston in 1978 on two stations, but abruptly quit in 1981 when it "stopped being fun."

Bill has recently resumed his avocation and can be heard every Tuesday at 7 p.m. on his show, "The Operaphile," broadcast on the Chesapeake, Va., FM station, WFOS. On the show Bill profiles a different opera star, company or topic each week. He also broadcasts on the first Sunday of each month at 7 p.m. when he selects and plays a complete opera. Additionally, on Saturdays at 6 p.m. he shares duties with two other announcers for a program, "Discurio," devoted to historic instrumental or orchestral selections. Bill, however, admits to sneaking in an opera selection from time to time.

Bill also writes about opera and classical music. He has a monthly column devoted to opera, music in general, a particular performer, or as Bill puts it, "anything else that strikes my musical fancy" in the journal of the Houston chapter of Mensa. Bill has been a member of Mensa since 1979 and has been writing this column for 17 years. He also recently began contributing opera reviews to the British magazine, "The Record Collector."

Bill said his taste for opera started at the age of 16 when he went to the library and borrowed the 1907 Enrico Caruso rendition of "Vesti La Giubba" from "Pagliacci." This, of course, was at a time when most other 16-year-olds were bopping to the sounds of Elvis or the Beatles. At the time, Bill knew nothing about opera and was simply curious about the great tenor's near mythical reputation. He didn't even understand the words since it was in Italian. What he found was that the music captivated him, and he's been a lover of opera ever since.

So, if you want to know something about opera, radio broadcasting or pharmacy, if you need some information about the Air Force or Navy, or if some pointers on flying your personally owned F-4 or B-52 are in order, you know who to call—Bill Russell, the one who works at CDER, not the NBA star.

Edward Miracco is a consumer safety officer in the Division of Labeling and Nonpresecription Drug Compliance.

Reviewer Affairs Corner

Your Representatives and Alternates Elected for 1997

By Karen Oliver

Your representative to the Reviewer Affairs Committee (RAC) is your communications link between your division's reviewers and Center Director **Janet Woodcock.** Your representative helps develop recommendations for Dr. Woodcock and her Senior Management Team. In addition, your representative provides feedback on issues referred to the committee by Dr. Woodcock and is responsible for discussing them within your division.

Members of the RAC are non-supervisory professionals in the physical, life and social sciences whose work involves technical expertise in those disciplines and who perform duties such as reviewing drug applications and communicating about drugs. RAC members serve for two years and may run for re-election; however, they cannot serve more than two consecutive two-year terms without a break in service.

Each primary voting member appoints his or her alternate. Alternates have voting privileges when serving in the place of the primary member. The RAC rep is responsible for keeping the alternate fully informed and knowledgeable of the RAC's activities.

Hopefully, you know your RAC rep and alternate rep by name. For the new folks, short-term memory types or those suffering from face recognition associated with "name amnesia," your 1997 RAC reps and alternate reps are listed below. Please clip, save and frequently communicate with your representative. *Karen Oliver is a regulatory health project manager in the Division of Gastrointestinal & Coagulation Drug Products.*

- **Tanya Abbott** (OCD liaison & executive secretary), Office of the Center Director, 594-6779.
- **Karen Lechter, Nancy Ostrove** (A), Division of Drug Marketing, Advertising & Communications, 827-2828.
- **Aisar Atrakchi, Andrea Powell** (A), Division of Neuropharmacologic Drug Products, 594-2850.
- **Karen Johnson, Judy Chiao** (A), Division of Oncologic Drug Products, 594-5724/5766.
- **Lori Paserchia, Nakissa Sadrieh** (A), Division of Medical Imaging & Radiopharmaceutical Drug Products, 443-1560.
- **Harry Geyer,** Division of Anesthetic, Critical Care & Addiction Drug Products, 443-4250.
- **Karen Oliver, Robert Prizont** (A), Division of Gastrointestinal & Coagulation Drug Products, 443-0487/0479.
- **Russ Rutledge,** Division of Manufacturing and Product Quality, 594-0098.
- **Gurston Turner, Mathew Thomas** (A), Office of Compliance Clinical Investigations Branch, 594-1032.
- **Gemma Kuijpers,** Division of Metabolic & Endocrine Drug Products, 443-3510.
- **Harold Silver, Cheryl McDonald** (A), Division of Anti-Infective Drug Products, 827-2188/2120.
- **Javier Avalos, Lynnda Reid** (A), Division of Dermatologic & Ophthalmologic Drug Products, 827-2044/2072.
- **Rudy Widmark, Lissante LoBianco** (A), Division of Anti-Inflammatory, Analgesic & Dental Drug Products, 827-2080/2090.
- **Katharine Freeman, Linda Hu** (A), Division of Over-the-Counter Drug Products, 827-2244/2241.
- **Shannon Williams, Larry Sancilio** (A), Division of Pulmonary Drug Products, 827-1089/1050.
- **Jean Fourcroy, Jeri El-Hage** (A), Division of Reproductive & Urologic Drug Products, 827-4260/4247.
- **Chan Park, Jacqueline White** (A), Division of Labeling & Program Support, 594-0365.
- **Melissa Maust, Naiqui Ya** (A), Division of Chemistry I, 594-0310/1841.
- **Abraham Croitoru, Tracey Rogers** (A), Division of Chemistry II, 594-1300.
- **Nhan Tran, Zakaria Wahba** (A), **Lin-Whei Chuang** (A), Division of Bioequivalence, 594-0350/0345/0355.
- **Japobrata Choudhury,** Division of Biometrics I, 827-1518.
- **Barbara Bono, Kate Meaker** (A), Division of Biometrics II, 827-1088/4259.
- **Abdul Sankoh, Ferrin Harrison** (A), Division of Biometrics III, 827-3090/3118.
- **Nancy Silliman,** Division of Biometrics IV, 827-2212.
- **Beverly Friedman,** Division of Pharmacovigilance & Epidemiology, 827-1519.
- **Paul Stinavage, Patricia Hughes** (A), Office of New Drug Chemistry, 827-1601/1603.
- **Paul Dietze, Liang Zhou** (A), Division of New Drug Chemistry I, 827-1513/5760.
- **Ravi Kasliwal,** Division of New Drug Chemistry II, 443-1560.
- **Janet Higgins** (chair), **David Katague** (A), Division of New Drug Chemistry III, 827-2068/2174.
- **Vijaya Tammara** (vice-chair)**,** Division of Pharmaceutical Evaluation I, 594-0496.
- **Raj Pradhan,** Division of Pharmaceutical Evaluation II, 443-8098.
- **Funmi Ajayi,** Division of Pharmaceutical Evaluation III, 827-2204.

Reviewers' Corner

Virtual Journal Is Coming to a Screen Near You

By Zan Fleming and Nancy Smith

Much has happened since the first article about CDER's *Virtual Journal (vJ)* hit the *Pike* in November's issue. First, the official title, *The Virtual Journal of the Center for Drug Evaluation and Research*, has been chosen. But don't worry about saying that mouthful. *Virtual Journal* or *vJ* will do it. The title is also likely to evolve as other centers join us.

So, what else has been happening?

The *vJ's* executive and editorial boards have met frequently over the past several months to resolve the many logistical, policy and stylistic issues that face the production of any conventional publication. The *vJ* has presented additional challenges due to its electronic format and the unique role of its publisher, CDER. One of the most gratifying aspects of these efforts is the enthusiastic involvement of people from every part of CDER. Members of both the editorial boards and the executive committee were selected to encompass the wide variety of skills needed for producing the *vJ* and to reflect the diverse audience for which it is intended. Others have since come forward on their own initiative to fill critical roles. Examples include: **Diana Clark,** pharmacologist in Division of Oncologic Drug Products, who is the associate page editor; **Lori Frederick,** medical writer in Division of Communications Management, who serves as manuscript editor; and **Belle Burkhart,** Medical Library, who is the graphics designer.

The actual (should we say virtual?) form of the *vJ* is taking shape. The designs of the graphics, layout and linkages are nearly complete. Some nifty features will be built in, such as the option to pull up the authors' biographical sketch and picture. Data files and other appendices can be embedded in the text for easy access by the interested reader. References in some cases can be linked to actual articles or abstracts. An informal part of the *vJ*, called the "Workroom," allows for direct communication between the author and reader. This provides a source of feedback that can help authors polish up ideas or manuscripts into finished articles. We are finding that this electronic medium is in many ways more powerful than Gutenberg's approach.

How will this help me, the reviewer?

The *vJ* is designed to capture important information, useful approaches, accumulated experience and ideas that are generated in the drug evaluation and regulatory processes and make them all easily retrievable. We hope that the *vJ* will eventually form a comprehensive commentary on virtually every aspect of drug evaluation. More than just a conventional encyclopedia, the *vJ's* dynamic nature provides knowledge in "real time."

When will we see something? What can I do to help?

The first edition of the *vJ* will be out in the next four to six weeks and will be available through CDER's intranet, CDERNET. The first edition is just about closed, but the real challenge of developing a steady stream of useful, high-quality articles on a continuous basis is just beginning. Each of us can contribute to this stream by maintaining a mind prepared for discovery and then taking the time to put these discoveries into writing. We also need a large pool of peer reviewers who can ensure that high scientific and editorial standards are maintained. Ultimately, the *vJ*'s success depends on a devoted but critical readership. Your constructive criticism, not only of the articles but also of the journal's format and function, is essential for achieving this forum's full potential. To inform us of your interest in volunteering, please e-mail Nancy Smith, SMITHN, Zan Fleming, FLEMINGG, or the *Virtual Journal's* e-mail account, VJ.

Zan Fleming is a group leader in the Division of Metabolic and Endocrine Drug Products, and Nancy Smith is Director of the Division of Biometrics III.

EEO Corner: February Marks Black History Month

By Diane Smith

The observance of Black History Month began 71 years ago as a means of commemorating the contributions of Black Americans. The Association of Afro American Life and History, organized by Carter G. Woodson in 1915, established this annual celebration in 1926 as "Negro History Week."

Initially, the observance took place in February between the birthdays of Frederick Douglass and Abraham Lincoln. Linking the accomplishments of prominent African Americans to established historical figures served as a symbol to Woodson of the potential that the future held. Beginning with the Bicentennial in 1976, the observance was extended from one week to the entire month of February.

It was not Woodson's goal to rewrite history through "Black History Month," but to explode the myth that African Americans had no part to play in the framing of our nation's history.

In 1988 (CDER's baseline year), African American employees held 156 or 14.3 percent of the 1,095 full-time permanent positions in the Center. Their occupations included analysts, scientists, statisticians and medical officers; yet none held top-level managerial positions. Today, there are 200 African American employees, an increase of 44, representing 13 percent of the total workforce. Three, two division directors (one in the Senior Executive Service) and one deputy office director, have reached senior level managerial positions during this period. Others hold staff and team leader positions.

Be sure to visit the Center's Black History Month exhibit, "Women of Hope: African Americans Who Made A Difference" located in the lobby of Woodmont II.

Diane Smith is a member of the Center's EEO Staff.

Leadership Fellows' Corner

Taking Another Look at Organizational Assessment Survey

By Karen Lechter

Do you remember the organizational assessment survey CDER conducted last spring? If you're like many of us, you may have forgotten all about it. As part of my project in the Center's Leadership Fellows Program, I will be working on further analyses of the survey results over the next few months. These will be macro analyses that apply to the Center as a whole and won't pinpoint individual divisions or offices.

As you may recall, the survey revealed a number of areas in which we all want to improve. But knowing that we want to improve an area and identifying the specific actions to accomplish those improvements are two different things. In the course of my project, I will suggest actions that can be taken to improve some of the areas found by the survey to be weak. In addition, I will make suggestions for future surveys, emphasizing CDER-specific areas of inquiry.

As part of my project, I have conducted a series of interviews with the Center's office directors. They demonstrated an interest in examining the results for their specific organizations, which could provide the basis for follow-up actions. Many were interested in seeing the results broken out by discipline and by other factors that may indicate where further attention should be directed. Most had not yet had an opportunity to plan corrective actions for areas they wanted to improve.

The areas that the survey identified for improvement in CDER are generally those that we all want to see improved, including communication issues, intergroup coordination, decision-making processes, supervisory skills and employment climate. Further analyses will be conducted before recommendations on how to improve these areas of the organizational climate are implemented and before decisions are made about what should be asked in future surveys.

The organizational assessment survey provided a "snapshot" of CDER at the time it was done. It will be supplemented by future CDER-wide efforts, such as the 360-degree competency evaluations that are now ongoing that will evaluate supervisors and some non-supervisors. If future surveys are conducted, they will allow us to see how we are doing over time. Joining me in my project are **Linda Brophy,** Associate Director of the Office of Training and Communications, and **Richard Allen** from the Division of Management and Budget. To find out more about CDER's Leadership Fellows program, read **Jim Morrison's** Ombudsman's column in this issue of the Pike.

Karen Lechter is a participant in the CDER Leadership Fellows Program and a social science analyst and attorney in the Division of Drug Marketing, Advertising and Communications.

FDA Launches Outreach To Protect Children From Tobacco

On Feb. 11, the Food and Drug Administration launched a nationwide outreach effort to retailers, parents and community leaders about the provisions of the FDA rule to protect children from tobacco products. The first provisions of the rule—making 18 the age for the purchase of tobacco products nationwide and requiring photo IDs for anyone under 27—become effective Feb. 28.

As President Clinton said in his State of the Union address: "It's critical to protect our children by standing firm in our determination to ban the advertising and marketing of cigarettes that endanger their lives."

As part of the announcement, the FDA said it planned 10 regional outreach meetings around the country over the following three weeks and one televised national outreach meeting. The Agency has mailed information to more than 400,000 retailers about the provisions of the new FDA rule. In addition, informational brochures for retailers and consumers will be distributed nationwide, and a toll-free telephone number (1-888-FDA-4KIDS) has been established for retailers to obtain further information.

> "Nicotine addiction begins as a pediatric disease."
>
> —David Kessler

In addition to the public education campaign, FDA will enforce the new rule by working with state and local officials in conducting spot checks of retail outlets. The nationwide toll- free telephone number has also been designed so that anyone can report potential violations. Retailers can be subject to penalties of $250 or more for selling tobacco products to minors.

"We are going to work with store owners to make sure they understand their responsibility not to sell tobacco products to anyone under 18," said Health and Human Services Secretary **Donna E. Shalala.**

"Our kids deserve a life free from the deadly disease that comes with using tobacco."

Nearly 3,000 young people become regular smokers each day, and nearly 1,000 of these children and adolescents will die early from their use of tobacco products.

"Nicotine addiction begins as a pediatric disease," said FDA Commissioner **David A. Kessler, M.D.** "We will be vigorous in our enforcement efforts: Our children deserve that."

The regional meetings will be held between Feb. 11 and Feb. 27 in Atlanta, Baltimore, Boston, Boulder, Chicago, Detroit, Houston, Los Angeles, Miami and Seattle. On Feb. 18, the national teleconference will be televised in an additional 25 cities around the country.

Government Industry Partnership

Easy-to-Read Prescription Information Program Launched

HHS Secretary **Donna E. Shalala** on Jan. 14 launched a cooperative public-private plan designed to provide consumers with better and easy-to-read information about their prescription drugs. The plan will help people correctly adhere to medical regimens and prevent misuse of prescription drugs. Hospitalizations caused by improper use of prescription drugs cost an estimated $20 billion per year.

The plan puts on track an effort that has long been high on the agenda of Federal public health officials, according to **Louis Morris** of the Center's Division of Drug Marketing, Advertising and Communications. The concept, he said, dates to the 1968-69 Health, Education and Welfare Task Force on Prescription Drugs. Today's computer technology was the key that unlocked a practical method for implementing the plan, Morris said. While the idea enjoyed strong support from public health and consumer groups, industry and pharmacists balked at the notion of maintaining an inventory of thousands of consumer leaflets in each corner drug store across the country. Now computer equipment available in most pharmacies can print out the patient information sheets when the prescription is filled and preclude the need to store large quantities of preprinted sheets. Under the plan, useful drug information must reach 75 percent of patients by the year 2000 and virtually all patients (95 percent) by 2006.

The plan was developed by a 34-member steering committee representing the pharmaceutical industry, pharmacists, physicians, consumer and patient advocacy groups, patient drug information database companies and other interested groups.

In addition to himself, Morris said that Center officials who helped bring the plan to fruition were **Nancy Ostrove** from DDMAC and Associate Center Director for Medical Policy **Robert Temple.** Morris stressed the plan was jointly supported by the Center and the FDA, and key Agency officials included **William Hubbard, Thomas McGinnis** and **Ilisa Bernstein.**

FDA Commissioner **David A. Kessler** said: "When patients get prescription drugs, they deserve the same kind of easy-to-read and easy-to-understand information they get when buying a box of cereal with the Food Label. That's what this is about." The plan, which was developed under a 1996 law, parallels the requirements of a proposal made by FDA in 1995 for the development and distribution of medication guides that are easily understood, non-promotional in tone and content and scientifically accurate. Following publication of the FDA proposal, Congress directed the HHS Secretary to convene a committee of diverse interest groups to develop a long-range, comprehensive action plan to voluntarily improve oral and written communication to patients about their prescription medicines.

The plan fulfills the Congressional mandate by addressing the following requirements:

- Encouraging health care professionals to improve their communications with consumers about prescription medicines.
- Identifying mechanisms and incentives to ensure voluntary efforts to meet the distribution targets for the years 2000 and 2006.
- Establishing criteria for the development and distribution of written leaflets with drug information for patients.
- Encouraging activities to increase consumer understanding of the benefits of such information.
- Developing mechanisms for periodic evaluation of the voluntary program.
- Promoting consistency with relevant state board regulations.

Director's Annual Report on OTCOM's Progress & Promise

By Lucy Rose

A little over one year ago, CDER created the Office of Training and Communications (OTCOM), charged with the dual responsibility of facilitating the professional development of all members of our community to their greatest potential and enhancing communications, both within CDER and with all of our outside constituents. This the first of what will become an annual OTCOM report to CDER. Here are some of the highlights of OTCOM's first-year contributions and successes:

- Responded to more than 48,000 phone inquiries from constituents in 1996.
- Replied to approximately 20,000 Freedom of Information requests in 1996.
- Fulfilled approximately 2,500 requests for publications in 1996.
- Answered requests for information other than for publications with 1,900 letters in 1996.
- Implemented Fax-on-Demand and provided information to our customers over 15,000 times via this medium in 1996.
- Opened a branch library in our Corporate Boulevard location.
- Began renovating the main Medical Library.
- Created and maintained the CDER WWW Internet site with huge Center and FDA participation.
- Created CDERnet, our Intranet site, again with help.
- Led the development of the Meetings Management MAPP.
- Brought videoconferencing to the three primary CDER buildings.
- Designed and implemented a highly successful orientation program for new CDER employees.
- Worked with the GRP Track XI Training subcommittee to

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Center's First Report to Industry Highlights Progress

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under control.

- Implementing guidances from the International Conference on Harmonization.
- Finishing Good Review Practice documents.
- Implementing further electronic submissions, including adverse event reports.

According to Division of Communications Management's **Kevin Ropp,** who edited the report, the key individuals who helped collect and review the data for the calendar year report included: **Jane Axelrad, Debra Bowen, Wanda Clabaugh, Rosemary Cook, Elaine Frost, Betty Jones, Murray Lumpkin, Nancy Maizel, Khyati Roberts, Lucy Rose, Ted Sherwood, Doug Sporn, Roger Williams** and **Helen Winkle.**

OTCOM was able to obtain a limited print order based on the intended audience of the publication: chief executive officers of pharmaceutical companies that have submitted applications to CDER for review.

A small number of copies have been provided to the Agency's Office of External Affairs to help with their outreach efforts.

Within CDER, office and division directors are being provided an individual copy for their organizations. Other members of the CDER staff who need copies for their own work should download them from the Internet. CDER staff who are meeting with their industry counterparts and feel copies would be appropriate should call OTCOM to see if any additional copies can be made available for their meetings. Call OTCOM's Division of Communications Management at 827-1243 for assistance.

OTCOM Reports on Ist Year Highlights

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design and implement the New Reviewer's Training Program.

- Designed and implemented the highly successful secretarial training course and soon-to-be-implemented secretarial certificate program.
- Wrote and disseminated CDER's first *Report to Industry* (see page 1 of this issue of the *Pike*).
- Provided scientific training during the Staff College's '95-'96 academic year for more than 800 people in 20 courses.
- Designed and implemented CDER's Leadership Skills educational series.
- Coordinated the CDER New Reviewers Mentoring Program.
- Provided the coordination for CDER's organizational assessment survey.
- Served as the internal partner for CDER's Leadership Fellows Program.
- Produced *News Along the Pike.*
- Designed and will soon implement the new CDER Informational Brown Bag Series.

This is just a sampling of the programs OTCOM has brought to you in the last year. OTCOM also provides internal consultants on communications issues, as well as consultants on numerous CDER organizational development projects. While working hard to serve you, we have also undertaken an intensive look at our own internal processes and worked to improve their efficiency as well. An example is the barcoding project recently completed by our FOI staff, which has enabled them to log and track all incoming and outgoing correspondence more efficiently.

Looking forward, OTCOM has an aggressive plan for the coming year aligned with CDER's 1997 priorities. For instance, the Division of Training and Development (DTD) is working on identifying the core competencies and skills necessary to be successful in each of CDER's job series. They are also in the midst of conducting 360-degree competency evaluations on every CDER supervisor. This developmental tool will provide supervisors with input from their supervisors, peers and subordinates. The results of these two programs will help us determine what training is necessary for our employees and aid CDER in designing programs specific to the Center's needs.

DTD is also working with the Committee for the Advancement of Scientific Education (CASE) to evaluate all of our scientific courses and their current relevance and applicability and to revise them where necessary. These groups are also working to improve the quality and attendance for both the Wednesday Seminar Series as well as the Scientific Rounds.

The Division of Communications Management (DCM) also has a full plate. They are working to implement more effective ways to disseminate our messages to our constituents and hear from them through such programs as: a live monthly videoconference with industry, roundtable discussions with constituent groups, and improved communications with FDA public affairs specialists in the district offices. To improve internal CDER communications, they are working on such projects as the new Brown Bag Informational Series, weekly video messages via CDERnet from the Center Director and management "walking rounds" through all CDER organizations.

The Medical Library is working hard to complete their renovation and to improve their on-line services. All of their improvements are being made with better service to their customers the primary goal.

Our 1997 goals provide a snapshot of some of the major projects OTCOM will complete. However, the most important aspect to us is that these projects have a positive impact on you, our internal customers, as well as our external customers. Therefore, we will design program evaluations that not only measure our results but also the impact on such performance attributes as customer satisfaction. We will modify our programs based on the results. We look forward to working with you to provide you an even higher level of service in the coming year. *Lucy Rose is Director of OTCOM.*

OGD Approves 33 First-Ever Generics

1996 Policy Initiatives Target Streamlining Review Process

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annual market value. American consumers can expect health care cost savings since generics sell for 30 percent to 70 percent of their brand-name equivalents and competition also helps hold the line on costs.

Drug Shortages

The Office helped resolve several drug shortages. One example, in August, involved hydroxocobalamin injection. OGD made arrangements for a generic drug company to ship limited supplies of the product to patients as requested. The shortage was finally resolved by cooperative efforts between OGD, the Office of Regulatory Affairs and the drug firm. The product is used in rare disorders of children, methylmalonic aciduria and homocystinuria, reportedly affecting about 100 patients.

Guidance Documents for Industry

To facilitate the review process and impart uniform policy to the industry, OGD provides guidance on bioequivalence studies, an approval requirement for many drug products. On Nov. 15, OGD issued one such guidance "Clozapine Tablets *In Vivo* Bioequivalence and *In Vitro* Dissolution Testing." Clozapine is indicated for the management of schizophrenic patients who fail to respond adequately to standard antipsychotic drug treatment. The document is on CDER's Web site at:

http://www.fda.gov/cder/guidance/clozbio.pdf

On July 26, the Office implemented a policy on "Substitution of an Alternate Source of the New Drug Substance in Unapproved Abbreviated Applications." Previously, if a generic drug application was otherwise approvable with the exception of an unsatisfactory current good manufacturing practice (cGMP) inspection for the primary new drug substance (NDS) supplier used to manufacture the exhibit/bioequivalence batch, it would not be approved until those cGMP issues were resolved. In order to qualify an acceptable alternate source, a new exhibit batch based on the alternate source would be needed. Additionally, a bioequivalence study would be required (depending on dosage form) to support use of the alternate source.

For unapproved applications, OGD now allows substitution of an alternate source of the NDS. This substitution can be based on assurance that the specifications and test data are essentially the same as those of the original source used in the exhibit batch (and bioequivalence study, if required) that would have been acceptable except for cGMP issues. Generally, a new *in vivo* bioequivalence study will not be required for the alternate exhibit batch, but it will be necessary to provide comparative dissolution data depending on the dosage form of the proposed product. This new policy is identical to the existing policy regarding post-approval changes that provide for alternate sources of the NDS and should reduce approval times in certain situations.

On Aug. 23, the Office issued a MAPP entitled: "Procedure for Public Release of Bioequivalence Protocols and Reviews." When firms submit proposed bioequivalence protocols, they are frequently duplicates of already submitted and reviewed protocols. In order to decrease the burden of reviewing several protocols for the same drug product, OGD is now making available copies of acceptable protocols and related review comments. OGD believes that, by utilizing completed review comments, firms will need to submit fewer protocols. This will free time for reviewer evaluation of applications. The MAPP is available at:

http://www.fda.gov/cder/mapp/5210-1.pdf

Also, OGD initiated a procedure to contact applicants that undergo two or more major deficiency cycles during the review process. Applicants are requested to contact OGD for discussion or clarification regarding the deficiencies. If OGD is not contacted, the Office will call the applicant within 30 days to see if any further discussion, or perhaps a meeting, is necessary. This should prevent additional major deficiency cycles and shorten total time to approval.

Streamling and Communications Initiatives

On Dec. 24, OGD issued a letter to all generic drug applicants describing streamlining and communication initiatives that affect the chemistry, bioequivalence and labeling review processes. Initiatives discussed range from phone consultations and electronic submission of bioequivalence data to *in vivo* study requirements for review of cytotoxic drugs.

In order to decrease the burden of reviewing several protocols for the same drug product, OGD is now making available copies of acceptable protocols and related review comments.

In addition, OGD and the Office of Pharmaceutical Science issued two letters to the new drug and generic drug industries in April. The first provided clarification on applications using CDER's guidance entitled: "Immediate Release Solid Oral Dosage Forms; Scale-up and Postapproval Changes." The second provided information on *in vivo* bioequivalence studies for clozapine. The first letter is available at:

http://www.fda.gov/cder/guidance/cmc5.pdf

The Office held two successful meetings with the three generic drug trade associations, the Generic Pharmaceutical Industry Association (GPIA), the National Association of Pharmaceutical Manufacturers (NAPM) and the National Pharmaceutical Association (NPA). OGD discussed initiatives for streamlining the review process and consequently reducing overall approval times. In addition, OGD participated in the Office of Pharmaceutical Science's three meetings with the pharmaceutical and generic drug trade associations that discussed the International Conference on Harmonization, initiatives on scale-up and post-approval changes and other topics of general interest.

Ted Sherwood is a management analyst in OGD.

CDER '96: Improved Performance Builds Strong Foundation

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decreased significantly. The "FDA review time" represents the time we took to review the applications, and the "total time to approval" represents FDA review time plus the time industry took to respond to questions we raised in approvable and non-approvable letters. For the 131 new drugs approved in 1996, the median FDA review time was 14.8 months, down 3 percent from 1995, and the median total time to approval was 15.4 months, down 7 percent from 1995.

Of these 131 new drug approvals, 53 were new molecular entities (NMEs). This represented, by far and away, the highest number of NMEs approved in a calendar year since the 1962 efficacy amendments to the FD&C Act. In comparison to the 28 NMEs approved in 1995, the 1996 total was an 89 percent increase. Again, even though the total numbers of NMEs increased markedly, the median FDA review time and the median total time to approval for these 53 applications were down significantly from the times for the 1995 approvals: median FDA review time was 12.0 months, down 21 percent from 1995, and the median total time to approval was 14.3 months, down 10 percent from 1995 and down almost 50 percent from the pre-PDUFA era.

Several of these NMEs were approved in a total time to approval of six months or less. These products included Division of Anti-Viral Drug Products' ritonavir, indinavir, and nevirapine for treating patients with HIV infection; Division of Anti-Infective Drug Products' albendazole for neurocystercercosis; Division of Metabolic & Endocrine Drug Products' atorvastatin for treating hypercholesterolemia and mixed dyslipidemia; and Division of Oncologic Drug Products' irinotecan for the treatment of refractory colorectal cancer and topotecan for the treatment of refractory metastatic carcinoma of the ovary.

Some of the other products included in the 53 NMEs were treatments for advanced breast cancer, cancer of the pancreas, cancer of the prostate, a new class of drugs to treat asthma, a second treatment for Alzheimer's disease, a treatment for relapsing-remitting multiple sclerosis and a drug to prevent poison ivy, oak and sumac allergic reactions.

Efficacy Supplements

Of the 196 actions taken on efficacy supplements, 118 were approvals. This represented a 146 percent increase over our performance at the beginning of the PDUFA program and a 300 percent increase over our performance in 1990 when only 30 efficacy supplements were approved. While the median total time to approval for the 30 efficacy supplements approved in 1990 was 28.5 months, the median total time to approval for the 118 approved in 1996 was 13.9 months, a greater than 50 percent decrease.

Manufacturing Supplements

In addition, the chemists, the project managers, the Division of Scientific Investigations and the field inspectors all deserve a tremendous accolade for their performance with manufacturing supplements. In 1996, 1,651 manufacturing supplement actions were taken, of which 1,339 were approvals. The median total time to approval for these 1,339 supplements was 5.3 months.

Reasons for Improved Performance

Some people have questioned whether our improved performance is due to fewer applications. This is just not the case. Since 1993, our original NDA applications have risen 36 percent from 84 in FY93 to 114 in FY96; our efficacy supplements have risen 10 percent from 92 in FY93 to 101 in FY96; and our manufacturing supplements have risen 17 percent from 1,045 in FY93 to 1,220 in FY96.

Some people have questioned whether our improved performance is due to our refusing to file (RTF) more applications and thus using RTF as a "clock management tool." This is just not the case. Of the 119 applications submitted in FY96, we refused to file only five, 4 percent of the submission cohort. In FY93 and in the years preceding the PDUFA program, we refused to file between 25 percent to 30 percent of a submission cohort.

Some people have questioned whether our improved performance is due to our applications getting less complex. This also is just not true. From FY93 through FY96, we have maintained approximately 18 percent of our filed original NDAs as priority applications and approximately 36 percent of our filed applications as NMEs. Interestingly, for the FY96 cohort of filed original NDAs, 44 percent were NMEs.

Finally, some people have questioned whether our improved performance is due to ignoring the backlog. Again, this is just not true. At the end of January 1997, of the 81 NDAs pending review, only 2 were overdue; of the 27 resubmissions pending review, none were overdue; of the 82 efficacy supplements pending review, none were overdue; and of the 305 manufacturing supplements pending review, only 8 were overdue. While it would, of course, be nice to have no applications overdue, the few we have represent under 2 percent of our total workload. For the first time in recent history, we are basically working on a current account without having the albatross of the backlog hanging over us.

We were able to achieve our performance record as a result of the human and infrastructure resources we received under the PDUFA program, the increased emphasis on project managing the review process, the new emphasis on accountability and predictability, and the superb dedication and professionalism of the reviewers at CDER and all those whose work facilitates the review activities of the Center. To each and every one of you goes a tremendous debt of gratitude and thanks for a job exceedingly well done.

We as an Agency, the pharmaceutical industry and the American people have benefited greatly from the PDUFA program. To date, the goals of this program, established back in 1992, have continued not only to be met but also exceeded by CDER staff. As we head into further discussions about the future of the PDUFA program, we are able to build on this strong foundation of dedication and performance.