news along the pike

Center for Drug Evaluation and Research

February 1998

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Pike's Corners . . .

Center Continues High Performance in 1997

Approves 121 NDAs, 39 NMEs, 108 Efficacy Supplements

By Murray Lumpkin, M.D.

In calendar year 1997, CDER achieved the fastest median approval times for new drug applications (NDAs) and approved the second highest total of new molecular entities (NMEs). More than half these NMEs were marketed first to American consumers. Last year, CDER took 235 actions on original new drug applications. Notably, the proportion of total calendar year actions that are approvals during the initial review process has risen steadily from under one-third in 1993, when the PDUFA program started, to more than half in 1997. All Center staff are to be congratulated on an outstanding performance—last year and for the entire PDUFA period to date.

Of the 235 actions on original NDAs, 121 were approvals. This represents a 75 percent increase in the annual number of NDAs approved over the Center's performance level in 1993, the start of the PDUFA program. The median total FDA review time for these products was 12.2 months, 18 percent shorter

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431 Generic Products Approved, 30 First Time Ever

By Ted Sherwood

The Center approved 431 generic products in 1997, including 30 that represent the first time a generic drug was available for the brand name product. Approval times continued a downward trend. Examples of first-time approvals include:

- A histamine H-2 antagonist used in the treatment of ulcers: ranitidine tablets (generic for Zantac, Glaxo Wellcome).
- An antiviral drug used in the treatment of serious viral infections: acyclovir sodium for injection (generic for Zovirax, Glaxo Wellcome).

The approval of generic versions of these two drug products could save the American public and Federal Government hundreds of millions of dollars.

The number of approvals in 1997 represents a substantial increase over 302 approved in 1995 and 351 in 1996. This increase occurred despite a continuing growth in workload over the past three years. From 1991 to 1993, submissions remained relatively stable at approximately 323 applications each year. In

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FDA Public Workshop

Woodcock Gives CDER Perspective on Medication Errors

By Norman Oliver

The FDA held its first public workshop to explore the extent of user errors occurring with regulated products. The one-day workshop held Jan. 8 at NIH featured presentations and panel discussions among the FDA's center directors, academic experts and representatives from lay and professional health groups.

"At least one death every day is attributable to a drug administration error, and 1.3 million people in the United States are injured per year," said Center Director **Janet Woodcock, M.D.** She emphasized that most errors are rarely the result of a specific individual's failure but a breakdown in the complex interactions within the health care system. "Medication mishaps can occur anywhere in the distribution pipeline—prescribing, repackaging, dispensing, administering, monitoring," she said. Examples of the causes of such errors are:

- Poor communication.
- Ambiguities in product names, directions for use, medical abbreviations and hand writing.

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Joe's Notebook

Murphy's Law and the Rocket Men

You may know Murphy's Law as the quaint aphorism that if anything can go wrong it will. You may have even thought it was coined by some wise old Irish sage who once too often went looking for sheep that had wandered out of their pen. Before I explain Murphy's connection to the rocket men, I need to digress a bit about medication errors, the subject of a workshop described on page 1.

I have recently taken a very personal interest in medication errors. How could it happen to me? I work for CDER, I have a wife who is a nurse. Well, perhaps it was the result of my less than totally rewired brain when I was discharged from the hospital last summer. But maybe it was something else.

I was taking three pills a day of the medicine that was going to cure my condition. I even told friends and neighbors of the megadose I was consuming. I had noticed, however, that the pills were a different size and color than the ones I took in the hospital. My wife stopped by the pharmacy and was told the pills come from many different manufacturers and that was the likely reason for the difference.

About a week later, I was reading the label on the bottle and noticed that the strength was printed there. It was one-half the dose I was supposed to be taking. "These aren't the right pills," I told the pharmacist. Sure enough, he took the bottle, examined the label, checked the pills, compared them to the picture in the *PDR* and called up my record on the computer.

"These are the correct pills," he pronounced.

"Well," I said, "let's check the prescription. Perhaps my doctor made a mistake in writing it."

He hadn't. We both stared at the prescription—written clearly with unmistakable precision. "I don't understand how we gave you the wrong dose," the pharmacist apologized as he handed me a bottle with the correct dose. Fortunately, I am none the worse for the experience. In this case it wasn't "anything" that went wrong. Multiple backup systems failed, those at home and in the pharmacy.

The subtitle to January's workshop on medication errors was "A Systems Approach"—one the real Murphy would appreciate. In my tortured academic career I once took a course in human factors engineering. I haven't used it much other than to advise my co-workers on the correct typing position to avoid carpal tunnel syndrome. The professor was an engineer who got into his profession from a background investigating airplane accidents. In the first half of this century, most airplane accidents were ascribed to "pilot error."

He was fond of reiterating Murphy's story and passing on the formulation that Murphy used for his law:

> *"If there are two or more ways of doing something, and one of them can lead to catastrophe, then someone will do it."*

Murphy, you see, was a Federal employee engaged in scientific work. In 1949, Capt. Edward A. Murphy was part of the Air Force team studying the effects of rapid deceleration on pilots, and his story is recounted by Robert A.J. Matthews in last April's *Scientific American.* Volunteers were strapped to a rocket-powered sled and monitored with a harness that Murphy designed. One day, after a seemingly perfect test, the harness failed to record any data. Every one of its electrodes had been improperly connected.

If all 365 persons estimated to have died last year as a result of medication errors were on a jumbo jet that crashed, we'd recognize it for the catastrophe it truly is. Preventing those medication errors will take rocket science, too.

news along the pike

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

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

Ombudsman's Corner

Plugging in the V-Chip at Work

By Jim Morrison

In a sleepy, up-scale bedroom community outside Los Angeles, a junior high school vice principal calls a faculty meeting. When about half of the teachers have arrived, he pulls out a .45 automatic and opens fire. He then goes around the school looking for teachers who weren't at the meeting. When the shooting ends, five teachers are dead and one is crippled for life.

That was my introduction to violence in the workplace. It occurred at the school I attended, but I wasn't there when the killings happened. I was there 15 years later, when he came up for his first parole hearing. The teachers for whom he searched unsuccessfully were very nervous. They recounted the story with the immediacy of yesterday's news.

Was this another case of a nice, mild-mannered guy who snapped and became a lethal maniac? That stereotype is a myth, perpetuated by news media interviews with neighbors and acquaintances after the fact, according to violence expert Dennis Davis. In his book, *Threats Pending, Fuses Burning: Managing Workplace Violence*, Davis says:

"Human behavior is not organized in such a way that a 'perfectly normal,' hardworking family man wakes up one day and suddenly decides to act out his rage in a manner that leads to the injury or death of others. There are always warning signs."

He explains that after the fact, coworkers and acquaintances are reluctant to say publicly that they knew the guy was weird and suspected that he might act violently. Such statements would beg the question: "Then why didn't you do something?"

It's easy to ignore the threat of violence if one believes that, like tornadoes, it occurs randomly and with little or no warning. There is a natural reluctance to talk about violence in the workplace. We think it won't happen here. After all, there are only about 1,000 workplace homicides a year out of a 100 million workers. And, let's face it, there is the fear factor. The Postal Service now has a rule that bringing a gun to work will mean the worker will be fired on the spot. But should the supervisor fire the worker before or after he is disarmed?

According to Davis, there are plenty of warning signs. They are known and easily recognized. Many of the warning signs are the types of lesser violence that are reported over a 100,000 times a year. There are many more that are not reported. When one includes that number, we are dealing with at least one incident per year per 1,000 workers. Based on averages, that would mean about nine reported incidents per year for FDA. We experienced a tragic episode a few years ago, when an FDA employee killed three people, but not at work.

So what are the warning signs, and what should organizations do to prevent violence in the workplace? Fortunately for us, Davis teaches a course on violence in the workplace for the Parklawn Training Center (PTC). The CDER EEO Staff, PTC and I are arranging for him to give a one-hour presentation as part of a regular CDER staff meeting in March. It will cover such subjects as spotting the warning signs and identifying preventative measures. As usual, it will be held in Parklawn and videoconferenced to WOC II and Corporate sites. I encourage everyone who has not already taken the PTC course to attend, especially supervisors and managers.

If we educate ourselves about the nature of violence, we stand a better chance of filtering it out of the workplace, just as the V-chip will one day filter out violent programming on TV sets in the home.

Jim Morrison is the Center's Ombudsman.

OM's James Allen Earns HHS Employee of Month Award

By Jackie Barber

CDER Office of Management's **James R. Allen** received December's HHS Employee of the Month Award from Center Director Janet Woodcock, M.D., in a Parklawn ceremony Feb. 12. Allen is being recognized for his leadership role in the time reporting project. Allen joined CDER in 1992 and is currently an operations research analyst in the Division of Planning Evaluation and Resource Management. The citation read:

"Richard has demonstrated initiative, persistence, tolerance and stamina as the team leader for the time reporting project. He is committed to the CDER mission and values the CDER community. His leadership has enabled the team to overcome many obstacles that otherwise would have delayed the project. Because of his dedication the project is successfully completed."

The HHS award recognizes those whose talent and daily activities show the dedication and exemplary acts and services that have made the FDA and the Department a success. The opportunity to make the award rotates through each major organization in HHS on a 14-month cycle. December was CDER's opportunity. Nominees for the award must have provided overall excellent services to a center or office in FDA enabling its efficient operation as well as demonstrated initiative, persistence and adaptability in performing their duties or demonstrated ability to work as a team member.

(If you're reading this electronically, click on the blue text to view a photograph of the ceremony.)

Jackie Barber is CDER's awards officer.

Communications Corner

Try Some Short Reports

Here's a plan for good short reports:

- Prepare a single statement telling what the report is about.
- Identify two or three main points.
- Highlight each main point. Use statistics, brief examples or a one sentence explanation.

Source: Denys J. Gary, Williamsport, Pa., in *communications briefings* vol. 16, no. 4.

Reviewer Affairs Corner

RAC Provides Summary Report on 1997 Survey

By Harold Silver

Last year the Reviewer Affairs Committee (RAC) determined that a second survey of primary reviewers, consumer safety officers and project managers would be appropriate. The first survey was conducted in 1995. I chaired a survey task force consisting of: **Javier Avalos, Beverly Friedman, Harry Geyer, Janet Higgins** (last year's RAC chair), **Karen Lechter, Karen Oliver, Norman See, Matthew Thomas, Rudolph Widmark** and a special guest member, **Bonnie Dunn.**

The task force discussed and agreed upon the following goals:

- To identify primary reviewers' needs and issues of concern.
- To review areas that needed the most and least improvement.
- To compare both positive and negative changes since the first RAC survey.

The task force developed and conducted the survey, after which a RAC survey analysis team analyzed the raw responses. The survey analysis team consisted of: **Japo Choudhury, Karen Lechter, Kate Meaker** and myself. Throughout the 1997 RAC survey and report process, a technical support team of **Tanya Abbott, Shane Griffith,** and **Jamie Metz** provided much assistance.

Survey Design

We designed a set of 49 questions to reflect the degree that an issue needed improvement and whether that issue had changed in a positive or negative direction since the first survey. All survey responses were anonymous. A cover letter on the front of the survey described the RAC and the survey's purpose. At the beginning of the questionnaire, the reviewer entered his or her discipline and number of years as a reviewer. Space at the bottom of each main section allowed reviewers to provide written comments. These were collected in a single document, and some were incorporated into the text of the main survey report.

The final report on the survey was first presented to the RAC for review and to be voted on for distribution and then to Dr. Woodcock and the CDER Senior Management Team. The final report is intended to help:

- Inform, enhance and further CDER's vision and mission.
- Develop a better sense of community among reviewers and all of CDER.
- Set the agenda for the RAC's activities.

Overall Results

A total of 714 surveys were distributed, and 311 were completed and returned. This was a response rate of 44 percent, compared with a response rate of 33 percent for the first RAC survey.

The seven items overall needing the *most improvement* were:

- Proposal to increase PDUFA time reporting requirements from quarterly to daily.
- Current awards and bonus system.
- Potential for career advancement.
- Potential for management promotion within your discipline.
- Availability of cross-training between divisions.
- Workplace morale.
- Obtaining manuscript clearance.

The five items overall needing the *least improvement* were:

- Core hours.
- Availability of maxiflex.
- Access to the Internet.
- Do-it-yourself time and attendance recording.
- Effectiveness of your RAC representative.

The seven items overall showing the *most positive change* since the 1995 survey were*:*

- Access to the Internet.
- Your familiarity with RAC.
- Concept of master reviewer (now called the CDER Reviewer Career Path).
- Do-it-yourself time and attendance recording.
- Availability of maxiflex.
- Availability of computer hardware and software.
- Communication flow from RAC to you.

The five items overall showing the *most negative change* were:

- Proposal to increase PDUFA time reporting requirements from quarterly to daily.
- Opportunities to travel.
- Availability of overtime.
- Workplace morale.
- Ability to attend external training.

Subgroup Analysis

Respondents were classified into three categories in terms of time served as a primary reviewer—those with less than one year of experience, those with one to five years experience, and those with more than five years of experience.

Primary reviewers in CDER for less than one year (19 percent of respondents).

They rated the four items needing the *most improvement* as follows:

- Availability of flexiplace.
- Maxiflex 24-hour accumulation limit.
- Availability of compensatory time.
- Availability of overtime.

This group was not asked about positive and negative changes in CDER.

Primary reviewers in CDER for one to five years (43 percent of respondents).

This group ranked as needing *improvement* the following two items that were not among the top 10 overall:

- Anonymous ways to make suggestions.
- Processing of paperwork for travel.

This group found the most *positive change* in the following five items:

- Access to the Internet.

(Continued on page 5)

Reviewers' Corner

CDER Reviewer Career Path Launched, Applications Due

By Nancy Smith

The CDER Reviewer Career Path (CRCP), formerly known as the Master Reviewer Program, has launched as a pilot program. The CRCP provides a career path that is professionally satisfying and scientifically meaningful for outstanding CDER Reviewers.

The CRCP recognizes outstanding reviewers who possess a breadth of scientific and regulatory expertise in a broad range of areas. The CRCP provides four levels of career advancement: associate reviewer, reviewer, senior reviewer and master reviewer. Applications for senior reviewer will be accepted for the first time beginning Feb. 17 and for master reviewer beginning March 16.

To view CRCP information, go into the CDERnet, click on the Disciplines and Subjects button and then click on the CDER Reviewer Career Path button. The six links are:

- *CRCP Program Description* contains requirements for each level, the committees and procedures for application.
- *CRCP Implementation Notes* gives the history of the CRCP, grandfathering, time requirements, individual development plans, core competencies, good review practices, team leaders and confidentiality of committee discussions.
- *The FDA Personnel Guide* provides written grade-level criteria at the GS-14 and 15 levels for the evaluation of CDER's regulatory review scientists and establishes the responsibilities and procedures for a peer-review classification system.
- *Procedure MaPPs and Forms* contains draft MaPPs delineating the application procedures for senior and master reviewer candidates and their supervisors.
- *Committee Structure and Procedures* contains a list of committee chairs and project officers. MaPPs for committee operations will be added shortly.
- *CDERstaff Slides* contains the slides presented at January's CDER staff meeting.

Jack Pevenstein, Gail Chotoff, Stacy Nichols and **Bill Woodard** assisted in getting the Web site up and running.

Nancy Smith is Director, Office of Training and Communications. The CRCP was her CDER Leadership Fellows project.

Reviewer Survey Identifies Needs, Issues of Concern

(Continued from page 4)

- The master reviewer concept.
- Availability of maxiflex.
- Do-it-yourself time and attendance recording.
- Current proposal for the master reviewer track.

All but the last of these items were among the top five for the sample as a whole.

The five items showing the most *negative change* for this group were the same as those for the overall sample:

- Proposal to increase PDUFA time reporting requirements from quarterly to daily.
- Opportunities to travel.
- Availability of overtime.
- Workplace morale.
- Ability to attend external training.

Primary reviewers who have been at CDER for more than five years (37 percent of respondents).

This group believed the following two items needed *improvement* more than did the overall sample:

- Concept of the master reviewer.
- Current proposal for the master reviewer Track.

This group rated the following six items as having more *positive change* than did those who were primary reviewers for one to five years:

- Availability of alternate work schedules.
- Effectiveness of your RAC representative.
- Availability of computer hardware and software.
- Clarity of policies regarding the use of the Internet.
- Ease of communication from you to the RAC.
- Timeliness of meeting notifications.

They believed the following two items demonstrated more *negative change* than did the primary reviewers who had been on the job for one to five years:

- Obtaining approval for external presentations.
- Intradivisional communications.

Written Comments

The written remarks of respondents provided insight into some of the issues that appeared of most concern to the most vocal respondents. These comments provided details of problems that, in some cases, were specific to individual divisions or disciplines and, in other cases, that were widespread. The written comments appeared to reflect the perception among those who were the most outspoken of an increased workload with inadequate compensation and inadequate opportunities for training, travel or advancement. These may be major factors contributing to morale problems.

Some of the areas and issues of concern are affected by the availability of funds and workload burdens. The RAC hopes that the others can be addressed and resolved administratively.

You can find more data on the X:drive in the folder \coorcomm\rac\news\survey or contact any member of the survey task force. To view a copy of the 1997 RAC survey report (racrept.pdf) and reviewers' written comments (raccomm.pdf), click on the blue text to open copies, if you are reading this electronically. If you are in TeamLinks or on the Internet, you must have simultaneous access to CDER's intranet.

Harold Silver is a microbiologist in the Division of Anti-Infective Drug Products.

EEO Corner

Black History Month Profile: Banks Johnson Credits Mentors

By Gloria Marquez Sundaresan

To celebrate February as Black History Month, CDER is cosponsoring a one-hour program to be held 10 a.m. Feb. 26 in the Parklawn Conference Center. The keynote speaker will be Dr. Dorothy Height, formerly of the National Council of Negro Women. Cosponsors are the other centers and FDA's EEO and Civil Rights Office.

Pictures of notable African-American employees in CDER are on display on the first floor lobby in the Woodmont II building. Among those pictured is the Office of Management's **Banks Johnson**, appointed last month as Associate Director of Management for Administrative Services.

Johnson attributes the steady rise in his professional career to a number of things. "For success in one's career, education is a basic foundation," he said. "There is no escape from this. It is a passport to achieve almost anything one wants in life. Networking is also very important—plus, of course, being at the right place at the right time. Right now I'm happy where I am in my career."

In his new position, Johnson directs a team responsible for administrative services such as:

- International and domestic travel, including training, quarterly reports, audits of travel documents as well as researching and developing MAPPs on travel matters.
- Approval of outside activities.
- Update of the Federal Staff Directory.
- Responsibility for CDER's computerized budget system.

Johnson also represents the Center on the FDA committee that is working on the new computerized time and attendance system.

"I like this new job," Johnson said. "It's the challenge of working in all these areas. Most importantly, this job helps prepare the Center to be ready for the coming millennium."

Following graduation from high school in Mobile, Ala., Johnson joined the Air Force and served during the Vietnam War. After about 10 years in the military, he left as a disabled Vietnam veteran. He first worked as a police officer on Capitol Hill and then returned to school to earn a bachelor's degree in accounting from the University of Maryland in 1982.

He received an internship with the Department of the Army. There he underwent training and worked conscientiously for the next three years. The internship eventually led to jobs as an auditor and later as a systems accountant for the Army.

"Looking back," Johnson said, "I fondly remember four African-Americans who gave me extra the help and attention that helped me master my job and life in general. The extra knowledge that I learned from John L. Leflore, Lionel Johnson, Ed Walton and Mary Wyles did make a difference in my career. I'm certainly grateful to all of them."

His knowledge and experience served him and earned hem a job as a systems accountant in the Office of the Commissioner. In 1996, Johnson took a detail as a budget supervisor in the Office of Management. Subsequently, Johnson became the special assistant to Office of Management's Director **Russ Abbott,** the job he held just before accepting his new position.

Gloria Marquez Sundaresan is an equal employment specialist in CDER's EEO staff.

FDA Announces Financial Disclosure Rules for Clinical Investigators

The FDA issued a final rule Feb. 2 on requirements for sponsors of drug, device and biologics marketing applications to disclose whether clinical investigators have financial interests that could affect the reliability of submissions for approval. The rule addresses concerns that clinical data submitted in support of an application might be influenced by financial considerations undisclosed to FDA.

"Although some have argued that there is nothing inherently wrong with scientists in the private sector and academia having financial interest in the products they study, FDA must be aware of these relationships as it evaluates the clinical data from those trials," said Lead Deputy Commissioner **Michael A. Friedman, M.D.** "This regulation will help assure that the process is thoroughly open and above-board."

The final rule, which goes into effect in one year, requires firms applying for drug, biological product or medical device marketing approval to either disclose, or certify to the absence of, the following types of financial interests and arrangements:

- Compensation made to the clinical investigator whose value could be affected by the study outcome.
- Proprietary interest—such as a patent—held by the investigator in the tested product.
- Significant equity interest in the sponsor of the study held by the investigator in the tested product.
- Significant payment by the sponsor of other sorts, such as a grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria.

FDA may refuse to file applications without the disclosure or a certification that no such financial arrangement exists.

FDA Reaffirms Generic Equivalence

In a letter to state pharmacy boards and other health organizations, Associate Commissioner for Health Affairs **Stuart Nightingale, M.D.,** has reaffirmed FDA's position that generic drugs meet the same specifications for identity, strength, quality, purity and potency and are interchangeable with their brand-name equivalent. The letter addresses concerns raised about "narrow therapeutic index drug products."

A copy of the letter is available at: http://www.fda.gov/cder/news/nightgenlett.htm.

Introducing Nancy Smith, OTCOM's New Director

"I want CDER to be recognized as an outstanding institution for scientific training and communications," said Nancy Smith, Ph.D., the newly appointed Director, Office of Training and Communications (OTCOM). "I want to continue the great things I've seen come out of OTCOM, expand on some of them and work with internal communications so we can all appreciate what everyone else in the organization is doing."

Smith said that OTCOM will be offering enhanced programs to improve the quality of life for scientists at CDER. "Scientists keep sharp by reading journals, attending seminars and talking with other scientists in their field. We need to bring in more outstanding speakers to give seminars and short courses, to offer opportunities for CDER scientists to interact with scientists at NIH and other institutions and to encourage them to publish."

OTCOM helps CDER scientists publish by offering the *virtual Journal* and has plans to offer courses in scientific writing. "We want to improve the writing in reviews, also," Smith said. "With the Electronic Freedom of Information, reviews are technically publications. We are offered the challenge and the opportunity of improving them. I think of publishing as helping industry do a better job and helping other scientists in our fields understand what we do at the FDA."

Smith was a Biometrics Division Director and has been with CDER for more than 10 years. She developed and taught the basic statistics course for CDER Staff College from 1991 through 1996, making it one of the Center's most popular courses. Smith has been active with the Good Review Practices Initiative, serving as chair of the New Reviewer Subcommittee from 1995 to 1996 and is co-chair of Track 2, Innovations in Drug Review. Her work with Track 2 includes serving as the executive editor of the CDER *virtual Journal* and coordinating the CDER Reviewer Career Path Program (see page 5). Smith has been a member of the FDA Science Awards Committee since 1995, assuming its chair in 1997. She graduated with the first class of CDER Leadership Fellows last year. Smith earned her bachelor's degree in mathematics from Hendrix College and a master's in mathematics from Virginia Tech. She was initially a high school teacher. After her daughter entered kindergarten, she returned to graduate school to earn a master's and Ph.D. in applied mathematics from the University of Maryland.

CDER Approves First OTC Drug for Relief of Mild to Moderate Migraine Pain

FDA has approved Excedrin Migraine—the first OTC medicine approved for treating mild to moderate pain associated with migraine headaches. Although migraine headaches can include significant signs or symptoms other than pain, this product is indicated only for treating pain associated with migraines. The product contains 250 mg of acetaminophen, 250 mg of aspirin and 65 mg of caffeine per tablet. Caffeine, which is included in some approved combination prescription medicines for migraine, appears to act primarily as an analgesic adjuvant in relieving pain. Three U.S. clinical studies involving more than 1,300 patients with acute migraine headaches demonstrated the effectiveness of Excedrin Migraine for alleviating pain associated with migraine attacks within two to four hours of taking the medicine.

Excedrin Migraine is recommended in a two-tablet dosage every six-hours, as needed, for two days. Although this combination of ingredients is the same as the currently marketed Excedrin Extra Strength product, Excedrin Migraine labeling contains different, important instructions and warnings for its specific use in treating the pain of migraine headache.

Consumers are advised to consult with their doctor before use of the new Excedrin product if:

- The headache is so severe as to require bed rest, is the worst headache ever, is accompanied by vomiting, fever, or stiff neck, or begins after head injury or exertion.
- They experienced a first headache after the age of 50.
- They have asthma, liver disease, kidney disease, stomach problems, or bleeding problems.
- They are taking a prescription drug for anticoagulation, diabetes, gout or arthritis.

Patients with migraine headaches not helped by this product may need prescription drugs to control symptoms or signs.

Woodcock Stresses Systems Approach to Medication Errors, Preapproal Checks

(Continued from page 1)

- Poor procedures or techniques.
- Patient misuse because of poor understanding.

"Since January 1992, CDER has received some 6,000 reports of actual or potential errors," Woodcock reported. "Approximately 50 percent, or 3,000, of these reports were attributable to the labeling, packaging or design of the product. The total number of serious errors represent 1,273 reports, with 326 deaths, 441 cases resulting in hospitalization, 235 life-threatening cases, 206 that needed medical intervention and 65 cases that resulted in permanent disability."

CDER's responsibilities go beyond ensuring safety and efficacy but also include helping ensure safe use by identifying potential problems in a drug's name, labeling or package design. The Center's current approach to medication errors includes:

- Reviewing proposed proprietary names before a drug is approved. As of last December, review by the Labeling and Nomenclature Committee is mandatory.
- Monitoring reports of medication errors after approval and taking action as appropriate through the efforts of the Medication Errors Committee.
- Educating and providing feedback to health care professionals about medication errors through the *FDA Medical Bulletin* and the *FDA Consumer*.
- Sharing information with outside organizations involved in preventing medication errors.

CDER Approves 121 NDAs, 39 NMEs, 108 Efficacy Supplements

(Continued from page 1)

than the year before. The median total FDA review time for these applications fell 41 percent from the performance level at the beginning of the PDUFA program.

In addition, the median total time to approval (total FDA review time plus industry response time to previous Agency "approvable" or "not approvable" letters) was 14.4 months, 6 percent shorter than the 15.4 months for those products approved in calendar year 1996. The median total time to approval fell 40 percent from the performance level at the beginning of the PDUFA program.

New Molecular Entity Approvals: Of the 121 NDAs approved in calendar year 1997, 39 were new molecular entities (NMEs)—products that contain an active substance that has not been previously marketed as a drug in the United States. This represents a 56 percent increase in the annual number of NMEs approved compared with the Center's performance level at the beginning of the PDUFA program. In the 1960s, the average number of NMEs approved each year was 13.7. In the 1970s, that went up to 17.3. In the 1980s, the average was 21.7. In the first half of the 1990s, it stood at 25.6. Often these products represent new therapies or improved therapies for various diseases. Most importantly, the Center accomplished this without creating a backlog of applications.

American consumers were the first in the world to have access to more than half of these NMEs, according to data from the Pharmaceutical Research and Manufacturers of America. Of the 39 NMEs approved in 1997, three had only been approved in the United States as of Dec. 31, and 17 were first marketed in the United States. Also, an additional seven of the NMEs were first marketed in another country or countries only within 1997. In 1996, 17 of the 53 NMEs approved that year were first marketed in the United States. An additional eight of those NMEs were first marketed elsewhere only within 1996.

The median total FDA review time for the 39 NMEs approved in 1997 was 12.8 months, 38 percent faster than the Center's performance level at the start of the PDUFA program. In addition, the median total time to approval for these 39 NMEs was 13.4 months, 6 percent faster than in 1996 and 42 percent faster than the performance level at the beginning of the PDUFA program.

Nine of the NMEs were priority review drugs, because they represent a major advance in medical treatment. Viracept, a new protease inhibitor for treatment of HIV infection, was reviewed and approved in 2.6 months. Evista, which is indicated for prevention of osteoporosis in postmenopausal women, and Rezulin and Prandin, both for treatment of patients with type II diabetes, were reviewed and approved in six months or less.

Other important priority drugs approved last year were Rescriptor, a combination therapy for HIV; Plavix, for the prevention of second stroke in patients with hardening of the arteries; Sclerosol, for the prevention of malignant secretions from the lung membrane; Agrylin, a blood thinner for patients with thrombosis; and PYtest, a breath test for the detection of *Helicobacter pylori.* Noteworthy drug approvals in 1997 also included Tobi, the first inhaled antibiotic for patients with cystic fibrosis and Meridia, for the management of obesity.

Efficacy Supplement Approvals: In calendar year 1997, the Center took action on 189 efficacy supplements, of which 108 were approvals. Efficacy supplements are new uses for already approved drugs and often represent important new treatment options for American patients. The 1997 performance represents a 125 percent increase in the annual number of approved efficacy supplements over the Center's performance level at the beginning of PDUFA.

The median total FDA review time for these applications was 11.9 months, a 35 percent drop from the Center's performance level at the start of the PDUFA program. In addition, the median total time to approval, also 11.9 months, fell 37 percent from the performance level at the beginning of the PDUFA program.

Manufacturing Supplement Approvals: In fiscal year 1997, the Center took action on 1,647 manufacturing supplements, of which 1,178 were approvals. Manufacturing supplements are only tracked on a fiscal year basis. The chemists, project managers, the Division of Scientific Investigations and the field inspectors all deserve congratulations for their performance with manufacturing supplements. The approvals in 1997 are a 39 percent increase in the annual number of approved manufacturing supplements compared with the performance level at the beginning of PDUFA. The median total time to approval for these applications fell 38 percent from the Center's performance level at the start of the PDUFA program.

Murray Lumpkin is Deputy Center Director (Review Management).

431 Generic Drugs Approved

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each of the three years since, there has been an increase in submissions: 411 in 1995, 453 in 1996 and 464 in 1997.

During the past couple of years, CDER has undertaken several initiatives to make the generic drug review process more efficient. Some of these include:

- Faxing deficiency letters to applicants.
- Increasing communications with firms receiving major deficiency letters to help minimize review cycles.
- Making acceptable bioequivalence study protocols publicly available.
- Resolving simple refuse-to-file issues by telephone.
- Providing copies of currently approved labeling to applicants, thereby eliminating the lengthy delay in obtaining this information through the Freedom of Information process.

Several other initiatives to streamline the review process—such as accepting the electronic submissions of bioequivalence data as well as chemistry, manufacturing and controls data—are being implemented or nearing implementation.

Ted Sherwood is a management analyst in OGD.