news along the pike

JUNE 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

VOLUME 6, ISSUE 6

INSIDE . . .

PIKE'S CORNERS

New CDER Functions for QA, Small Businesses

Quality Assurance Program Lays Groundwork with Studies

BY MARK GOLDBERGER, M.D., AND JUDY MCINTYRE

The number of recent product withdrawals and the lack of consistency in the way we do things have led to concerns that the Center may not be performing the way we would want to be performing. The Quality Assurance program, launched just over a year ago, has identified several projects that will lay the groundwork for finding ways to help us improve the way we work.

These include a comparison of how action packages are prepared in the five offices of drug evaluation and a "lessons learned" look at the troglitazone (Rezulin) withdrawal. For the latter effort, the QA program will be focusing on processes only, not individuals.

Quality assurance has made important contributions in the private sector and should provide similar benefits to our public health work by improving our consistency and efficiency. Quality control takes place in the day-to-day activities we perform. Quality assurance—a second, independent look at these processes—can't take place until we're clear about what we want to do and how to evaluate it.

Many Center employees participate in the work of coordinating committees, working groups, steering committees and task forces. **Rubynell Jordan,** a project manager from the Division of Medical Imaging and Radiopharma-

(Continued on page 8)

Center Seeks to Keep Small Businesses Well-Informed

BY RON WILSON

Small pharmaceutical businesses with fewer than 500 employees now have a source of help with regulatory issues and information about financial assistance and incentives in CDER. The Small Business Assistance Program, located within the Office of Training and Communications, is an initiative under the 1997 FDA Modernization Act to ensure that stakeholders are well-informed about Agency processes, policies and procedures.

Our initial efforts include launching a Website with extensive information about regulatory issues and financial assistance and incentives for small businesses and creating a two-page brochure for clinical investigators:

- The site (http://www.fda.gov/cder/about/smallbiz) describes the new drug development process, over-the-counter drugs and generic drugs. Information for clinical investigators on the Website was featured in the "From the FDA" column in the June 7 Journal of the American Medical Association by Commissioner Jane E. Henney, M.D.
- The two-page brochure for clinical investigators provides the Web address and identifies the categories of information on the Website. This information targets experienced investigators as well as those who may not be familiar with FDA regulatory requirements, especially those for protection of human subjects.

The Small Business Assistance Program is responsible for the Clinical Investigator Educational and Outreach Program in OTCOM because many clinical investigators are involved with small pharmaceutical businesses in developing new drugs.

While a new function for CDER, FDA has been assisting small businesses for many years. In 1976, the Center for Devices and Radiological Health created the Division of Small Manufacturers Assistance. In addition, FDA regional offices have small business representatives who assist small firms in their areas with all FDA-regulated products.

CDER's program will assist small pharmaceutical companies with fewer than 500 employees that are not a subsidiary of a larger pharmaceutical business. This definition, based on number of employees, is consistent with those used by CDRH, the Prescription Drug User Fee Act and the Small Innovative Re-

(Continued on page 8)

JOE'S NOTEBOOK

Forced to be Helpful

There's been many a time when riding the Parklawn elevator that I've stepped off on the wrong floor because I wasn't watching where I was going. There are other times, when crossing the street, that I failed to notice that the walk sign has given me permission to cross. I've then had to hurry across with "don't walk" flashing furiously.

The obvious answer is for me to get my head out of the clouds and pay attention. The not-so-obvious answer is that accommodations for people with real disabilities can also help normal folks, including those of us who are chronically inattentive.

Elevator and walk signs provide good examples. Some elevators now use a recorded voice to announce the number of the floor at which they are stopping. I was in San Diego earlier this month, and some of their walk signs make a chirping sound when the signal to walk first illuminates. That gave me plenty of time to stop sightseeing and get safely across the street.

All of this brings us to a recent e-mail from Vincent Andolina, a *Pike* reader in AOL Land. He writes: "Thanks for posting *News Along the Pike* in HTML format as well as in Acrobat format. The HTML format is easier to read on screen."

You're welcome, of course, Vincent; but it wasn't exactly generosity of heart that led me to create an HTML version in addition to the PDF one. You may have also noticed the *CDER 1999 Report to the Nation* was published in both Adobe PDF versions and HTML versions.

When challenged on this issue in the past, I've acknowledged that the PDF versions of the *Report* and the *Pike* might be less than optimum for people with visual impairment. I thought, however, that it was a pretty good compromise.

It turns out—correctly—that others, including the Congress, disagreed. In 1998, they amended the Rehabilitation Act and strengthened its provisions covering access to information in the Federal sector for people with disabilities. As amended, Section 508 of the Rehabilitation Act requires access to the Federal government's electronic and information technology. The law applies to all Federal agencies when they develop, procure, maintain or use electronic and information technology. Federal agencies must ensure that this technology is accessible to employees and the public. There's a Website about this issue at http://www.section508.gov.

Access for publications like the *Pike* and the *Report* means making sure they are available in HTML format. The deadline for accessibility is Aug. 7, so I'm getting a head start. If you need to read the *Pike* on line, have poor eyesight, are using a small monitor or need to use a text-to-voice converter, by all means use the HTML version. If you want to send it to one of those fancy wireless phones, use the HTML version. If you're going to be making a printout and you have normal eyesight, use the PDF. You'll save lots of trees!

CDER's Spring Honor Awards Ceremony: Normally, we would have had a story about the June 16 event in this issue. Unfortunately, a bad combination of out-of-town meetings and vacations is going to delay the story until the next issue.

Corrections: Credit for authoring last month's Page 1 story on how CDER's laboratories earned accreditation from the Association for Assessment and Accretion of Laboratory Animals International should have gone to **Patricia E. Long-Bradley.** In the same story, **Joseph Hanig, Ph.D.,** should have been included in the list of members of the Institutional Animal Care and Use Committee who lent their support and expertise to the effort to gain accreditation.

news along the pike

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

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

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

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

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OMBUDSMAN'S CORNER

Now, If Only We Could Float an IPO

BY JIM MORRISON

An ancient Chinese blessing says: "May you live in interesting times." Well, we are blessed. We are privileged to witness the beginning of a new age, the Information Age, which is fast replacing the Industrial Age.

The Information Revolution is being fueled by computer, Internet and wireless technologies, just as the Industrial Revolution was fueled by steam and electric power, the assembly line, the telegraph, the telephone and better transportation technology.

When the telegraph was invented, people said: "It will change our world, and it will transform the way we live." In my view, the Internet has a greater potential to change our world than the telegraph ever had. Who can say if the new economy can sustain the multibillion-dollar capitalization of IPOs (initial public offerings) that have made a lot of people rich? But the hype has provided an unprecedented bankroll for venture capitalists to play with and to feed progress.

When venture capitalists decide to fund infotech startups, they ask several questions:

- Does the company have unique information that businesses or the public want or need?
- Does the company have a catchy dot-com name or can it develop name recognition?
- Can the startup sustain a buzz that will keep its name in the public consciousness?
- Can the firm manage and sustain growth?
- Does it have the technological savvy to stay at the cutting edge?

Since all organizations, not just startups, need to assess how they will meet the challenges of the Information Revolution, lets look at how CDER would fare in a venture capitalist driven world. First, we certainly have unique information that people want and need. Secondly, we have an Internet identity that attracts Web traffic, and FDA is a household name that is kept in public view daily by news media reports of our activities. Our growth is limited by the budget, but we have shown we can manage growth to improve performance dramatically. Do we have cutting edge information technology? Well, four out of five isn't bad. In fact, if we were a private enterprise, venture capitalists would be beating down our door. Now, if only we could float an IPO . . .

About now, you are probably asking yourself: "Any moron knows CDER can't sell stock, so what is his point?"

Good question. My point is that regulatory agencies, like the rest of society, are greatly affected by paradigm shifts. The FDA was created in the Industrial Age, when the focus of enterprise was on producing goods. The FDA was created to act like a funnel with a filter. All drugs would pass through the funnel before reaching the consumer. In the Information Age, when people in Peoria are hardwired to Paris, Potsdam and Beijing, the funnel is developing leaks.

Rather than being dismayed that we cannot create a funnel large enough to encompass the whole world, we should recognize that we are in an excellent position to thrive in the new Information Age. Although we don't have cutting edge information technology, that's OK. The Information Revolution is propelled by technology, but it is really about content, about developing relationships among far-flung strangers with common interests and about communicating information instantaneously and globally.

Hardly a day passes that I don't get e-mail from consumers and health professionals complaining about being spammed or about seeing Internet sites for fraudulent products or for prescription drugs obtainable without actually seeing a physician. With over a million Web sites being created annually and a 150,000 new Internet users added daily, the world is drowning in information about diseases and treatments, much of which is of dubious veracity.

When people are bewildered by the glut of contradictory information about drugs and health, they look to the Websites of organizations they trust. That is why venture capitalists put so much value on name recognition and ongoing publicity about startups. The FDA has that already, and we can do a lot of good if we understand how to communicate what we know about drugs.

That isn't to say we should abandon our traditional role of filtering and regulating. There will always be pharmaceutical development and production, just as agriculture is still an important enterprise long after society stopped being predominately agrarian. All of us need to keep doing what we are doing now while devoting thought and resources to adapting CDER to the Information Age. We have vital information to communicate. We need to do it more effectively.

Jim Morrison is the Center's ombudsman.

Draft Guidance on Adverse Reaction Labeling Aims at Consistency

FDA issued a draft guidance for the development of the adverse reactions section of labeling for human prescription drugs and biologics. The document, which was published in the *Federal Register* on June 21, is the first in a series of guidances for industry that are intended to make the labeling more consistent and helpful to prescribers and patients.

The draft guidance emphasizes the need to focus the label's adverse reactions section on drug safety information that is important to prescribing decisions and to convey it in a format that is clear, easy to find and consistent across different drugs and drug classes. The common format provided by the guidance divides the labeling into two subsections:

- An overview subsection that highlights the adverse reactions that are most serious, most commonly occurring and most frequently resulting in clinical interventions.
- A discussion subsection that deals in greater detail with the significance of adverse reaction data obtained from the clinical trials.

The document is available on CDER's Website in HTML at http://www.fda.gov/cder/guidance/1888dft.htm and in PDF.

Protect Your CDER Home PC from E-Mail Viruses

While the automated McAfee virus shield procedure protects CDER office computers, PCs at home remain vulnerable to attack until the latest software is installed. All authorized home PCs need to have the latest version of antivirus software installed as soon as possible.

Follow one of these steps to protect your home PC:

- *Diskette installation:* The Web page for the disk creation instructions and links (http://oitweb) has been simplified to make all instructions and links accessible from one start page. Go to the link from the OIT homepage and print the complete instructions in PDF format before creating the diskettes.
- *CD-ROM installation:* If your authorized home-use PC has a CD-ROM drive, OIT has CDs available that have the home-load version of McAfee. Contact your division IT focal point to arrange to borrow a copy of the CD for your home installation. The CD is for loan only and must be returned after you have successfully installed the McAfee upgrade.

If neither of these solutions is successful, please bring your authorized PC in from home and the Helpdesk (HELP) can assist with this important upgrade.

Help Desk FAQ

How do I find out who in the pharmaceutical industry is using secure e-mail with CDER?

All the companies and individuals in the pharmaceutical industry who have successfully tested secure e-mail with CDER are listed on the OIT intranet site. Go to the "Notices" section at http://oitweb/ and click on "participating companies."

The list is divided into two parts. The first shows the companies that have server-based security in which all e-mail to the address, regardless of the username, is encrypted. The second part shows the list of individual mail accounts. Encryption is only done for these specific e-mail addresses in those companies. Other mail sent to the company with a different user name is not encrypted.

> "All the companies and individuals in the pharmaceutical industry who have successfully tested secure e-mail with CDER are listed on the OIT intranet site."

The OIT point of contact is **Greg Brolund** (BROLUND)

RetrievalWare Coming Soon

RetrievalWare will replace Excalibur's Electronic File System software by the end of this summer. RetrievalWare is Excalibur's new, improved, upgraded and enhanced Web-based software for the search and retrieval of electronic documents and data. This phase of the RetrievalWare rollout will replace the current EFS file rooms, which include adverse event reports, Drug Master File reviews, Biopharm division files and approved package inserts.

OIT has been working with current EFS users to demonstrate the RetrievalWare application, gather requirements and address any concerns. The feedback has been terrific, and users describe RetrievalWare as "much easier to use than EFS." Two different interfaces, an "easy" interface for the occasional user and an "expert" interface for the power user, are a definite advantage.

Training sessions are scheduled for August and September. Based on feedback from the users, the half-day training sessions will be broken out by areas of interest. An announcement regarding training session dates and times will be coming soon via e-mail.

The OIT point of contact is **Linda Sigg** (SIGGL).

July IT Training

Monday	Tuesday	Wednesday	Thursday	Friday
3	**4**	**5**	**6**	**7**
10	**11**	**12** **DFS** 9:00-12:00 **Excel 97 Intro** 1:00-4:00	**13** **PowerPoint 97 Intro** 9:00-12:00	**14** **PowerPoint Charts** 9:00-12:00
17	**18**	**19** **NEST** 9:00-12:00 **Creating PDF Documents** 1:00-4:00	**20** **DFS** 9:00-12:00	**21**
24	**25**	**26**	**27**	**28**

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

Meta IP in CDER

Meta IP is CDER's new IP address management software. It is used to assign and manage IP addresses automatically in the Center and helps to prevent address conflicts. An IP (Internet protocol) address is a necessary identification that allows your computer to access the CDER network. If there are problems with your IP address, you may not be able to log on to the network, retrieve e-mail and important files or access the Web.

The main purpose of switching to the new system is to speed up and simplify IP address assignments. Because it's an automatic procedure, it also makes OIT staff available to provide additional support to CDER users.

Initial installation was used to assign addresses to Metro Park North I in March. With a few exceptions, the change from the previous system went smoothly. As of the end of May, all CDER locations are using the Meta IP system.

Please contact the Help Desk (HELP) for more information on IP addresses or if you are having trouble connecting to the network.

First Academics to CDER Educational Activity Launched

BY ARZU SELEN, PH.D. AND DALE F. WILCOX

The new Academics to CDER Program uses the capacity and skills of local academic institutions to enhance and increase the opportunities for scientific education in the Center. The program's first activity, "Pharmacokinetics and Pharmacodynamics for CDER Reviewers," was developed jointly by the Center and Georgetown University's Center for Drug Development Science.

This course, held in six half-day sessions from Feb. 17 to March 23, was attended by 112 scientists and medical officers from CDER, CBER and CVM, as well as 17 Georgetown fellows.

The instruction consisted of lectures, breakout sessions to examine case studies and a panel discussion. The course focused on fundamental pharmacokinetic and pharmacodynamic concepts and illustrated how they applied to regulatory decision-making. Scientists from academia, industry, CDER's Office of Clinical Pharmacology and Biopharmaceutics and CBER developed the lectures. The examples for the breakout sessions were selected from reviews conducted in OCPB. These examples were prepared by the Office of Training and Communications, OCPB and the Quantitative Research Methods Staff from the Office of Biostatistics.

The diverse background of the lecturers and the faculty facilitated an in-depth overview of fundamental concepts, critical factors that influence study outcomes and decision-making during drug candidate selection, development and review.

The applications of the scientific principles in guidance documents was presented in the lectures, panel discussion and illustrated by examples in the breakout sessions. The examples demonstrated the impact of pharmacokinetic and pharmacodynamic studies on drug development and patient care as reflected in optimized dosing recommendations in drug labels. The occasional difficulties encountered in these studies were also recognized and presented. The course discussed how effective use of these tools will contribute to optimized drug development programs and individualized therapy.

The course curriculum was developed in response to an OTCOM core competencies assessment conducted last year that identified the knowledge and skills reviewers need.

OCPB Director **Larry Lesko, Ph.D.,** and Georgetown's Carl Peck, M.D., led the planning committee that included Georgetown's Charles Grudzinskas, Ph.D., and, from CDER, **John Senior, M.D., Shiew-Mei Huang, Ph.D., Stella Machado, Ph.D.,** and **Daniel Shames, M.D.,** and the course coordinators, **Peter Lee, Ph.D.,** and **Arzu Selen, Ph.D.,** both from OCPB, and **Dale Wilcox** from the Division of Training and Development.

Future plans include identifying other opportunities for collaboration with academia. An additional component of the Academics to CDER Program will be a visiting professor lecture series scheduled to begin in September.

Arzu Selen is a supervisory pharmacologist in OCPB, and Dale Wilcox is Deputy Director in DTD.

Teaching = CME Credit

BY KAREN ZAWALICK

CDER medical officers and invited speakers can now earn Category 1 continuing medical education credit for lecturing at an accredited CDER educational activity such as a training course, scientific rounds and scientific seminar.

As a result of a December decision by the American Medical Association, an approved provider of CME such as CDER may now award up to two Category 1 credits for every one hour of lecture up to a maximum of 10 hours per year. The learning activity must be designated for Category 1 CME. A copy of the course or seminar announcement will be accepted as proof of participation.

Please contact me (ZAWALICKK) for more information.

Karen Zawalick is an education specialist in the Division of Training and Development.

Pike's Puzzler: Test Your Knowledge of FDA History

BY TONY CHITE

1. Congress passed the Prescription Drug User Fee Act, which authorized user fees from drug companies to hire more scientists to review new drugs in:

a. 1989 b. 1991 c. 1992 d. 1993

2. Congress reauthorized PDUFA and passed the Food and Drug Administration Modernization Act. FDAMA codified a number of practices that had become common in the Agency, such as, expanding the use of "accelerated approval" mechanisms for drugs for life-threatening conditions and using surrogate endpoints in clinical trials. It also included a number of mechanisms for speeding FDA review and changed the legal standard for new drug approval to a single clinical trial (instead of two). These actions took place in:

a. 1995 b. 1997 c. 1998 d. 1996

3. Who *did not* serve as a Commissioner of Food and Drugs:

a. C. Everett Koop, M.D. b. Harvey Wiley, M.D. c. Frank E. Young, M.D., Ph.D. d. Arthur Hull Hayes, M.D. e. Jane E. Henney, M.D.

4. In 1930, under an agricultural appropriations act, the name of the Food and Drug Administration was shortened from:

a. Food, Drug and Narcotic Administration b. Food, Drug and Cosmetic Administration c. Food, Drug and Device Administration d. Food, Drug and Insecticide Administration

5. In 1862, President Lincoln appointed Charles M. Wetherill to serve in the new Department of Agriculture. This was the beginning of the Bureau of Chemistry, which was the predecessor of the:

a. Food and Drug Administration; b. National Institutes of Health; c. Drug Enforcement Administration; d. Bureau of Alcohol, Tobacco and Firearms

Answers: 1c; 2b; 3a; 4d; 5a.

Tony Chite is a CSO in CDER's Freedom of Information Division.

FDA Approves New Cancer Drug, Postpones Sunscreen Rule

FDA approved a new drug, gemtuzumab ozogomicin, on May 18, for the treatment of CD33 positive acute myeloid leukemia. The drug is approved for patients 60 years or older who have relapsed for the first time and are poor candidates for cytotoxic therapy. Mylotarg was approved as an orphan drug, a drug intended for the treatment of rare diseases or conditions.

This new treatment is given in IV form as a 2-hour infusion in two doses given 14 days apart. Standard chemotherapy is given in the hospital for seven days and requires patients to be hospitalized for an extended period of time.

Myeloid leukemia is characterized by a rapid accumulation of abnormal white blood cells in the blood and bone marrow, resulting in severe anemia, infection and hemorrhage during the course of the disease.

Three clinical studies with Mylotarg involved 142 patients with surrogate markers based on rates of complete remission. A total of 80 patients were age 60 or older. Side effects included liver toxicity. During the clinical trials 14 percent to 24 percent of patients showed elevations in liver enzymes leading to clinical liver disease and jaundice.

The drug is manufactured under the trade name Mylotarg by Wyeth Ayerst of Philadelphia.

FDA announced June 8 that it will extend until Dec. 31, 2002, implementation of a comprehensive final sunscreen monograph. This announcement reflects the Agency's Oct. 1 decision in a citizen's-petition response to allow additional time for the completion of a comprehensive sunscreen monograph that is expected to include standards for both ultraviolet A and ultraviolet B radiation.

To comply with the FDA Modernization Act of 1997, the Agency had published a final OTC monograph for sunscreen products in the *Federal Register* of May 21, 1999. The monograph did not, however, address certain issues involving active ingredients, labeling and test methods for products intended to provide UVA coverage.

FDA is amending the date the sunscreen monograph takes effect to accommodate the final completion of standards for UVA formulation ingredients, labeling and testing. The completed monograph may also address issues associated with the testing and labeling of sun protection factor values above SPF 30.

FDA will also consider ways to integrate UVA and UVB indications. As a result of the amendment to the effective date, sunscreen products are not required to comply with the general OTC labeling rule until Dec. 31, 2002.

HHS Announces Steps to Strengthen Protection of Research Subjects

HHS Secretary Donna E. Shalala announced on May 23 several new initiatives to further strengthen protections of human research subjects in clinical trials. The department's actions are designed to heighten government oversight of biomedical research and to reinforce to research institutions their responsibility to oversee their clinical researchers and institutional review boards.

"In the last few years, we've seen dramatic advances in the effort to find new therapies for cancer and other diseases, and we've taken new steps to protect the safety of patients in clinical trials," Shalala said. "But the explosion in biomedical research has also brought new challenges, as more researchers are becoming involved in commercial ventures that may create new ethical dilemmas."

The HHS actions focus on:

- Expanding education and training for all clinical investigators and IRB members and staff.
- Enhancing the informed consent process and ensuring more vigilant monitoring and oversight.
- Ensuring that researchers understand and comply with federal conflict of interest regulations.
- Pursuing efforts to provide FDA with additional enforcement tools to enhance its oversight role.

Shalala also stressed the responsibility of the leaders of universities and academic medical centers to oversee IRBs.

HHS will undertake an aggressive effort to improve the education and training of clinical investigators, IRB members and associated IRB and institutional staff.

NIH, FDA and the new HHS-level Office for Human Research Protections will work closely together to ensure that all clinical investigators, research administrators, IRB members and IRB staff receive appropriate research bioethics training and human subjects research training.

Such training will be a requirement of all clinical investigators receiving NIH funds and will be a condition of the NIH grant award process.

NIH and FDA will issue specific guidance on informed consent, clarifying that research institutions and sponsors are expected to audit records for evidence of compliance with informed consent requirements. For particularly risky or complex clinical trials, IRBs will be expected to take additional measures, which, for example, could include third-party observation of the informed consent process. The guidance will also reassert the obligation of investigators to reconfirm informed consent of participants upon the occurrence of any significant trial-related event that may affect a subject's willingness to participate in the trial.

NIH will now require investigators conducting smaller-scale early clinical trials (Phase I and Phase II) to submit clinical trial monitoring plans to the NIH at the time of grant application and will expect investigators to share these plans with IRBs. The NIH already requires investigators to have such plans and they also require large-scale (Phase III) trials to have Data and Safety Monitoring Boards. For research on medical products intended to be marketed, FDA will also issue guidance

(Continued on page 7)

REVIEWER AFFAIRS CORNER

RAC Abolished, Plans for Unfinished Business Outlined

BY THE RAC REPRESENTATIVES

Dear Colleagues,

It is with great regret that we announce that, as of May 31, the Reviewer Affairs Committee has officially been disbanded.

The committee conducted a survey asking CDER reviewers their opinion on the utility of keeping the committee. We had an overwhelming response in favor of retaining the RAC and conducting business in the same democratic way we always have. Eighty-nine percent of responses were in favor of continuation, with a fair number of those stating that it was important for the RAC representatives to continue to be appointed by CDER's primary reviewers. The survey also revealed that reviewers desired that the RAC represent all primary reviewers, both bargaining unit members and non-bargaining unit members such as Commissioned Corps officers and visiting scientists.

The RAC presented the survey results to the Center's management. In return, they presented the NTEU with the data generated from the survey and expressed CDER's desire that the RAC continue in the way it had in the past. However, the NTEU feels very strongly that they should appoint all bargaining unit members to the RAC and decide which non-bargaining unit members can participate. Because this position is incompatible with the expressed desires of the reviewers and the RAC's current charter doesn't support continuing the committee in the manner in which the NTEU is proposing, Center Director **Janet Woodcock, M.D.,** stated that the best alternative would be for the RAC not to be reconvened.

A final meeting between Dr. Woodcock and RAC representatives was held on May 31. RAC representatives asked Dr. Woodcock how the "unfinished business" such as the evaluation of the CDER Reviewer Career Path and comparable pay issues for review disciplines would be competed.

Dr. Woodcock said the Center would evaluate the career path program and publish the results. She will discuss with OTCOM and OM to determine the most appropriate organizational location for the program. She said the Center had proposed a pay comparability plan for pharmacokineticists and biostatisticians. Other centers have concerns about the impact of the proposal on their organizations, which will have to be addressed

A business case was made that included compelling data on drastic attrition rates directly related to the disparity between current federal salaries with those in the private sector for clinical pharmacologists. If CDER is successful in obtaining approval of this plan, it will look at other review disciplines to see if a business case can be made for additional requests.

The RAC was established to provide a forum for all CDER primary reviewers to improve communication among reviewers and to represent the needs and concerns of primary reviewers directly to Center management. The RAC carried out its mission with distinction over the past six years, and those who have served on the committee should be very proud of their many accomplishments. We hope the union will pick up where the RAC left off and continue with many of the efforts for which the RAC has laid the groundwork because these projects were the desires and concerns of CDER reviewers.

All the RAC representatives joined collectively to write this farewell article to CDER reviewers.

Heightened Government Oversight of Biomedical Research Foreseen

(Continued from page 6)

for DSMBs that will delineate the relationship between DSMBs and IRBs and define when DSMBs should be required, when they should be independent, their responsibilities, confidentiality issues, operational issues and qualified membership.

NIH will issue additional guidance to clarify its regulations regarding conflict of interest, which will apply to all NIH-funded research. HHS will also hold public discussions this summer to find new ways to manage conflicts of interest so that research subjects are appropriately informed and to further ensure that research results are analyzed and presented objectively.

In addition, these public discussions also will focus on clarifying and enhancing the informed consent process. Based on these public forums, NIH and FDA will work together to develop new policies for the broader biomedical research community, which will require, for example, that any researchers' financial interest in a clinical trial be disclosed to potential participants.

HHS will pursue legislation to enable FDA to levy civil monetary penalties for violations of informed consent and other important research practices—up to $250,000 per clinical investigator and up to $1 million per research institution. While FDA can currently issue warning letters or impose regulatory sanctions that halt research until problems are rectified, financial penalties will give the Agency additional tools to sanction research institutions, sponsors and researchers who do not follow federal guidelines.

Office for Human Research Protections Created

A new HHS-level office will lead efforts for protecting human subjects in biomedical and behavioral research, the department announced on June 6.

The new office will be located in the office of the Assistant Secretary for Health. It replaces the Office for Protection from Research Risks, which was part of the NIH and had authority over NIH-funded research. The new office will also provide leadership for all 17 federal agencies which carry out research involving human subjects under a regulation known as the Common Rule.

HHS will also charter a new National Human Research Protections Advisory Committee, to provide broad-based counsel on patient protection and research needs.

Quality Assurance Program Seeks Better Ways for Center to Work

(Continued from page 1)

ceutical Drug Products, on a 120-day detail to the QA Program, will be compiling an inventory of all such groups. This will include information about each project, including its sponsor, purpose, goals, participants, estimated duration, expected output products, current status and criteria for assessment. The inventory will also outline areas of possible overlap.

Jordan will also be examining—perhaps in conjunction with an existing working group—how each of the ODEs prepares an action package on an NDA, looking for the best practices and identifying significant differences. One of the goals of a quality assurance program is an improvement in consistency. There will initially be differences in our processes stemming from the variety of the drugs and the diseases for which an ODE has responsibility. Differences that don't appear to have a basis in the above areas are potential targets for improved consistency.

Brian Pendleton, a lawyer with the Regulatory Policy Staff, will join the QA Program on a 120-day detail beginning in mid-July to look at issues involving the Center's use of and interactions with its advisory committees. This is another area targeted for improved consistency.

We have had a positive response from individuals who will devote approximately half their time to details looking at specific issues from a quality assurance point of view: These individuals and the titles of their projects are:

- **Ruthanna Davi, M.S.,** and **Susan Molchan, M.D.,** Recruitment and Retention.
- **Robin Huff, Ph.D.,** Tools for Learning Discipline-Specific Review at CDER.
- **Ekopimo Ibia, M.D.,** Use of Foreign Data in the CDER Drug Approval Process.
- **Linda Ng, Ph.D.,** CMC Review Process for NDAs.
- **Leslie Wheelock, M.S., R.N.,** Guidance and MAPP Implementation.

Output from these projects will include an assessment of the current process and, if needed, a proposal for improvement. The projects should be completed and presented to CDER management in the fall.

Mark Goldberger the Director of the Division of Special Pathogens and Immunologic Drug Products, is on detail leading the Center's QA Program. He recently headed CDER's survey of the pharmaceutical industry for Y2K transition readiness. Judy McIntyre is the QA Program's full-time project manager.

Small Business Financial Assistance, Incentives Outlined on Website

(Continued from page 1)

search Program. The Small Business Administration, however, uses slightly different numbers that range from fewer than 100 employees for wholesalers to fewer than 750 employees for finished pharmaceuticals.

Small pharmaceutical companies have voiced concerns that they are frequently unaware of and don't know how to use federal programs that provide economic assistance and incentives for developing new drugs. The Center's Small Business Assistance Website currently has information on programs that provide economic assistance during the preapproval process and incentives postapproval.

Preapproval information covers orphan drugs, charging for investigational drugs, the Small Innovative Research Program and funding opportunities at the national Institutes of Health. Postapproval information highlights new drug product exclusivity, pediatric exclusivity, patent term restoration and orphan drugs.

Currently, information on some of the programs is inadequate or unavailable. We will be posting more, in question-and-answer format, on patent term restoration, new drug product exclusivity, charging for investigational drugs, PDUFA and the Small Business Innovative Research Program. Information on expediting a new drug approval and expanding access to investigational drugs is in development. We also plan on having definitions, links to guidances and explanations of terms such as accelerated approval, expedited review and open-label protocols.

The brochure that identifies our information for clinical investigators is being distributed to major research institutions and medical schools. We have established a working relationship with the NIH and The Johns Hopkins University to provide more information about FDA regulatory processes to their investigators. As a result of our relationship with NIH, we have been invited to participate in their annual general clinical research conference. This event brings together clinical investigators and medical students from the 99 major medical research centers that receive NIH research grants. These centers employ more than 9,000 clinical investigators.

> "Small pharmaceutical companies have voiced concerns that they are frequently unaware of and don't know how to use federal programs that provide economic assistance and incentives for developing new drugs."

CDER and the Food and Drug Law Institute will co-sponsor two audio conferences for small businesses. The first, on Oct. 25, will address economic assistance during the preapproval phase of development. The second, on Nov. 8, will highlight postapproval economic incentives.

We plan to provide a system for small businesses to sign up for e-mail updates on timely new information targeted to their needs. In the meantime, you can receive daily or weekly updates on all new information posted to the CDER Website by clicking on the Stay Informed button on the Center's homepage.

Please e-mail your comments or suggestions for additional information that would be helpful to small pharmaceutical businesses directly to me at wilsonr@cder.fda.gov.

Ron Wilson is director of the Small Business Assistance Staff. Previously, he directed the Health Assessment Policy Staff in the Office of the Commissioner where he was responsible for several programs including patent term restoration, institutional review board education and disqualification of clinical investigators.