news along the pike

SEPTEMBER-OCTOBER 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

VOLUME 7, ISSUE 7

INSIDE . . .

PIKE'S CORNERS . . .

Center, Employees Respond to Terror Attacks

Counter Terrorism Work Skyrockets to CDER's Top Priority

BY NORMAN J. OLIVER

The first therapy for those exposed to a biological warfare agent is often a drug. The Center has been taking an aggressive and proactive approach to getting antibioterrorism treatment information into the labeling of already approved drugs. The first such drug, ciprofloxacin, was approved Aug. 31 last year for treating inhalational anthrax.

The Sept. 11 terrorist attacks and the subsequent anthrax attacks have vaulted this work and other actions to protect public health and safety to top priority. Center Director **Janet Woodcock, M.D.,** declared in her "State of the Center" address Oct. 16 that the Center's antibioterrorism work will trump user fee deadlines.

So far, the Center's immediate response to the anthrax crisis has resulted in:

- Publishing a *Federal Register* notice concerning new labeling information for doxycycline and procaine penicillin in post-exposure management of inhalational anthrax.
- Issuing a public health advisory on the use of doxycycline to treat inhalational anthrax.
- Detailing a medical team leader to the HHS

(Continued on page 10)

PHS Officers Staff 2 Teams Sent to WTC, Deploy Locally

Twenty Center employees who are members of the Public Health Service's Commissioned Corps responded to the Sept. 11 terror attacks. They provided:

- Primary and emergency medical care and mental health care to rescue workers in New York City.
- Specialized pharmacy support for the National Pharmaceutical Stockpile, commonly called "push packs."
- Data entry and forensic dentistry to help confirm identities of the dead in New York.
- Replacement medical care and pharmacy care at the National Naval Medical Center in Bethesda.
- Stand-by primary and emergency care for the Pentagon attack and the Sept. 20 presidential address to Congress.
- Administrative support of the deployments.

Officers involved had previously volunteered to be members of either the Commissioned Corps Readiness Force, the PHS-1 Disaster Medical Assistance Team or both.

The Commissioned Corps Readiness Force began a 12-day deployment to New York on Sept. 21, and the PHS-1 Disaster Medical Assistance Team began its 12-day tour Sept. 22.

(Continued on page 9)

Center Speeds Approvals of Emergency IND, 2 Supplements

BY SHERUNDA LISTER

The Division of Anti-Infective Drug Products approved one "emergency" investigational new drug and expedited approvals of two manufacturing supplements to respond to needs resulting from the Sept. 11 terror attacks. The drug products involved were topical antibiotics used to treat burns.

"FDA really bent over backwards to make this happen," said Harold H. Slevin, Ph.D., president and CEO of Solvay Pharmaceuticals. Solvay's product, silver sulfadiazine/cerium III nitrate cream (Flammacerium), was in Phase III clinical trials at one major New York burn center.

"Following the awful events of the morning of Sept. 11, we received several requests from sites within New York City to use our Flammacerium product," Dr. Slevin said. After trying for several hours to get through the busy telephone circuits, Dr. Slevin was able to leave messages late Tuesday afternoon with the Office of the Center Director and the Division of Anti-Infective Drug Products.

Wednesday morning, **Maureen Dillon-**

(Continued on page 8)

JOE'S NOTEBOOK

Public Health Is National Security

At the Center's first brown bag discussion after the terrorist attacks, some of us of a certain age recalled past fear-inspiring events associated with the Cold War. We remembered huddling under school desks during air-raid drills, the Cuban Missile Crisis or the long-gone Nike air-defense missile sites ringing Washington.

I retired from the Army in 1989 and started working for NIH because I thought peace was breaking out everywhere and that improving the health of Americans would be the wave of the future. Now, of course, it turns out that public health has also become national security.

We know from past threats that we'll learn to understand the new ones, counter them, help and console each other—and get on with our work.

The PHS-DMAT (page 1) returned from its New York deployment to its Gaithersburg warehouse on a bright, sunlit afternoon on Oct. 2. **RADM Kenneth Moritsugu,** the deputy surgeon general, echoed the thoughts of many of us when he welcomed the officers and told them how proud he was of their contributions. (You can see photographs of the arrival on the HTML version of the *Pike* at http://www.fda.gov/cder/pike/septoct2001.htm#photo.)

Several expressed thanks for the support they received from their coworkers here. **LT Craig Ostroff** noted that the Division of Pulmonary and Allergy Drug Products had four people involved in the deployment. In addition to himself, they were **CDR Mary Purucker, CAPT Ching-Long Joseph Sun** and **CAPT Alan Schroeder,** a chemist co-located with the division.

"Our Division's senior management was very supportive toward the endeavor even though we were already short-staffed before the attacks," Ostroff said. "They didn't know how long we would be engaged in these other activities but were willing to pitch in and help out during this temporary strain on staff resources so others in need could be helped."

LT David Diwa mentioned that he and **LCDR Hye-Joo Kim** were glad to lend a hand in such difficult times in their capacities as PHS officers. "We are even more pleased that **CAPT Jerry Phillips** and OPDRA provided the necessary support for the mission," Diwa said. "Since the relief efforts were multi-agency, we received a lot of questions about the Commissioned Corps and FDA. New Yorkers were appreciative of our participation and offered food and recreational services in support of our activities."

Finally, **CDR Lynn Slepski** from the PHS Office of Emergency Preparedness pointed out that other Commissioned Corps missions that didn't involve CDER employees saw officers supporting the Federal Emergency Management Agency where the served as the eyes and ears of HHS and at the Strategic Intelligence Center for the FBI.

Little did we know that as the sun was brightening the return ceremony anthrax-laced letters had already been placed in the U.S. mail.

Bioterrorism background reading—Some useful Web sites are:

- HHS: http://www.hhs.gov/hottopics/healing/biological.html.
- FDA: http://www.fda.gov/oc/opacom/hottopics/bioterrorism.html.
- CDC: http://www.bt.cdc.gov/.
- Army surgeon general: http://www.nbc-med.org/.
- CDER: http://www.fda.gov/cder/drugprepare/default.html.
- The Johns Hopkins University Center for Civilian Biodefense: http://www.hopkins-biodefense.org.
- The *Journal of the American Medical Association* has made available for free its series of articles on five biological agents that might be used against a civilian population—smallpox, anthrax, plague, botulinum toxin and tularemia: http://www.jama.com.

news along the pike

The Pike is published electronically approximately monthly 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).

Views and opinions expressed are those of the authors and do not necessarily reflect official FDA or CDER policies. All material in the Pike is in the public domain and may be freely copied or printed.

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

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OMBUDSMAN'S CORNER

Tolerance

BY JIM MORRISON

We in CDER are truly blessed to be a part of a multicultural, multiethnic and multidisciplinary staff working together toward a common mission. In this troubling time, as we try to comprehend the enormity of what has happened and what we as a nation should do, we all must keep in mind the vision of America as a land of opportunity and a sanctuary for peoples from around the world.

At critical times in America's history, we have lost sight of that vision. In searching for someone to punish for unprovoked attacks, whether it be Pearl Harbor, the hostages in Tehran or the World Trade Center and the Pentagon, some have lashed out at those whose only connection with the perpetrators was a religion, a skin color or an ethnic ancestry.

We can be assured that our leaders are taking actions that will bring the real perpetrators and their abettors to account. These actions, as the president has made clear, will take time.

In the meantime, we may see acts or hear expressions of religious or ethnic intolerance. Such intolerance stems from ignorance and from a lack of close contact with people in whatever group is being disparaged.

Thinking back to the Oklahoma City bombing a few years ago, when the perpetrators were identified, we did not hear of incidents of intolerance against white males. I believe that was because everyone knew many white men who were good, so that the evilness of the act was associated only with the individuals involved and the fringe organizations that condoned the bombing.

Because we in CDER have daily contact with people of all races and religions and witness their enormous contributions to American society, we tend to forget that many of our fellow citizens do not. Each of us, especially those of us who are not of the Islamic faith or of Middle Eastern ancestry, should accept as a moral imperative to speak out against any intolerance. When we do, we will be paying homage to the victims of the attacks, who are of all races, religions and ethnicities.

I have not heard of any incidents of ethnic or religious intolerance in CDER following the recent attacks, nor would I expect such incidents here. But if anyone has ideas about how CDER can help in combating such intolerance in the larger community, please e-mail me (MORRISONJ).

Jim Morrison is CDER's Ombudsman.

PIKE'S PUZZLER

The Study of . . .

BY TONY CHITE, P.D.

Match a word in column A with a definition in column B. There two more items in column B than in column A.

Column A	Column B
1. Etymology	a. insects
2. Ornithology	b. animals
3. Ichthyology	c. trees
4. Entomology	d. weather
5. Toxicology	e. supernatural occurrences
6. Dendrology	f. fish
7. Meteorology	g. poisons
8. Paleontology	h. aging
9. Gerontology	i. word origins
10. Zoology	j. the nervous system
	k. birds
	l. fossils

Answer key: 1i, 2k, 3f, 4a, 5g, 6c, 7d, 8l, 9h, 10b.

Tony Chite is a pharmacist and CSO in the Division of Information Disclosure Policy.

Contracts Give Access to Prescription Use Data

The Office of Post-Marketing Drug Risk Assessment awarded three contracts that give the Agency access to commercial databases that contain non-patient-identifiable information on the actual use of marketed prescription drugs in adults and children.

The information contained in these large databases will significantly augment FDA's ability to determine the public health significance of the reports it receives through its Adverse Event Reporting System, published information and other data sources.

The recipients of the contracts are AdvancePCS, Premier Inc. and Child Health Corp. of America.

The AdvancePCS database will allow FDA to examine how long non-hospitalized patients stay on prescription medication therapy and to learn which combinations of medications are being prescribed to patients.

The contract awarded to Premier Inc. will provide information on how drugs are used in hospitalized patients.

The Child Health Corp. of America database contains information on the use of prescription drugs in children's hospitals. This information will, among other benefits, support the Center's ongoing initiative to have more prescription drugs labeled for use in children.

FDA's ability to respond expeditiously to the issues arising once drugs are on the market is important to overall public safety. Access to data provided by the contracts will complement and strengthen the usefulness of the passive adverse event reports by providing estimates of the numbers of patients exposed to drugs nationwide in the inpatient setting.

Thus, the data will provide a denominator, or context, for understanding adverse drug event reports, for modeling drug risk based on usage patterns and for calculating discharge-based reporting rates for drugs used in inpatient settings.

By examining actual use of products over time in non-hospitalized patients in relation to recommended labeling, FDA access to these data will also increase the Agency's capability to perform regulatory impact studies and to understand better the usefulness of drug labeling to clinicians.

Finally, real-time access to data will enhance and accelerate the pace of FDA's regulatory decision-making process.

INFORMATION TECHNOLOGY CORNER

Steps You Can Take to Protect CDER from Computer Viruses

BY FRAN WEISS

There are several ways that we get computer viruses—from Internet e-mail attachments, e-mails from outside of CDER, diskettes from home or from others and from dialing into the network using the Remote Access System.

In response to recent computer virus threats, OIT is installing the latest virus protection software on each CDER desktop. Part of the install is a new daily "auto update" feature that will update each PC with new protection files when they become available, making sure to provide the best virus protection.

It is also important for you to do everything you can to help protect the Center's systems from computer viruses. Understanding how viruses enter your PC and taking steps to protect your system are vital to a successful virus protection program. Follow the advice below to protect CDER from computer viruses.

Internet E-Mail

CDER e-mail protection is not available for personal Internet e-mail accounts from providers such as Hotmail, AOL or Erols. ***Access to all external, Internet e-mail is prohibited in CDER.*** This is an important policy to note. If you launch an infected attachment, you risk spreading a virus to your PC and, consequently, to the CDER network.

Advice:

- Don't access any external e-mail accounts from your CDER PC.

CDER E-Mail

We are protected from viruses in Outlook and TeamLinks e-mail because both servers won't allow attachments known to contain viruses.

Advice:

- Don't open attachments if you aren't expecting them, especially from unsolicited sources. Confirm with the sender if you aren't sure.
- Make sure your virus protection software is installed correctly. Look at the lower right corner of the Windows taskbar. Call the Help Desk (7-0911) if you don't see the VirusScan Console or Vshield icons.

- Check your "auto update" feature regularly. Double-click on the VirusScan Console (magnifying glass). If the date is not current, call the Help Desk.

Diskettes

If you have a virus on your home PC or you receive a diskette from another source with a virus and you open documents on it, the virus infects your PC .

Advice:

- Scan diskettes for viruses before opening any documents.
- Keep your virus protection software up-to-date.

Dialing In

If the PC you use at home to connect to RAS has a virus and then dials in and connects to the network, the virus can then infect the network, which in turn can infect all of CDER.

Advice:

- Don't load software from an internet service provider on your CDER PC.
- Don't launch attachments without scanning them first. Contact the Help Desk if you need instruction.
- Keep your virus protection software up-to-date. Home users should go to the OITweb, download to diskette the newest McAfee DAT files, and then install them on their home PC.

Your cooperation will help keep the Center, the Agency, and the Department protected from computer viruses. Consult with the Help Desk and OITweb (http://oitweb) for more information on virus protection.

Fran Weiss is a technician with the CDER OIT Help Desk.

OPDRA's Yaplee Tapped as Mansfield Fellow to Focus on Drug Safety

BY PAIGE COTTINGHAM-STREATER AND MARY-JANE ATWATER

Deborah Yaplee, a senior program management officer in the Office of Post-Marketing Drug Risk Assessment is one of two FDA employees selected for a two-year fellowship by the Mansfield Center for Pacific Affairs.

In September, she began 10 months of full-time Japanese language and area studies training in the Washington area. She will then spend a year in Japan working in a government ministry or agency. Yaplee has a strong career interest in drug safety policy-making. During her year in Japan, she plans to learn about the Japanese regulatory authorities' pre- and post-marketing safety program, their electronic submission of adverse events program and their implementation of the International Conference on Harmonization standards for electronic submission of drug safety reports.

Martin Yahiro, M.D., a medical officer with the Center for Devices and Radiological Health, is the second FDAer among this year's seven fellows. He plans to focus on Japan's pre-market evaluation of medical devices and combination device and biological products, using cutting-edge orthopedic spinal devices as the model.

Established by Congress in 1994, the Mansfield fellowships are building a core group of U.S. government officials who serve as a resource to their agencies on Japan issues because they have proficiency in the Japanese language and experience working inside Japan's government.

The Mansfield Center for Pacific Affairs is a public policy organization committed to promoting understanding and cooperation between the United States and Asia. In honor of the lifelong interest in Asia of Ambassador Mike Mansfield and his wife Maureen, the center seeks to span distances and differences among policy makers, government officials, scholars and the public.

Focusing on new voices and audiences, the center's programs inform, explore the underlying issues that influence policies, and facilitate dialogue among Asians and Americans to enhance policy formation. With offices in Washington; Missoula, Mont.; and Tokyo, the center provides a forum for Asians and Americans to address issues of local, national and international concern.

Paige Cottingham-Streater and Mary-Jane Atwater work in communications for the Mansfield Center.

ORM Office Formed for Pediatric Drugs, Program Initiatives

The Office of Pediatric Drug Development and Program Initiatives in the Office of Review Management officially began operations Oct. 1. Under the direction of **Dianne Murphy, M.D.,** it is responsible for Center activities related to pediatric issues, pregnancy labeling and antibioterrorism.

"Establishment of this office recognizes the important and ever-increasing role that pediatric drug development is playing in our regulatory work," said Center Director **Janet Woodcock, M.D.** "The pediatric exclusivity provisions of FDA Modernization Act have resulted in a tremendous surge of clinical trials in children, while at the same time creating extensive policy and regulatory challenges."

The new office continues the work of the Pediatric Team in providing policy and regulatory support to ORM's review divisions. It will also serve as the Center's liaison to external pediatric advocacy groups.

Additional pediatric activities have focused on the 1998 regulation, which went into effect in December and required all products to address pediatric needs early in their development. Sponsors must either provide the needed studies in the new drug application or have reached an agreement with FDA on why the studies could be deferred or waived.

This increase in pediatric trials has highlighted the many scientific areas in pediatric drug development that have been neglected and are requiring attention. Because children cannot legally provide consent, the enrollment of children into clinical trials has always carried an additional burden of responsibility to ensure the safe conduct and oversight of such trials. This area has received considerable recent attention. FDA has been addressing these thorny ethical issues by bringing them forward for public discussion at advisory committee meetings.

Under special initiatives, the new office is the center's focal point for antibioterrorism. The Center has taken an increasingly proactive role in addressing the unique aspects of developing information appropriate for labeling or use of products that would be used in the event of a bioterrorist act involving chemicals or infectious agents.

The new office will also work on CDER initiatives related to the study and labeling of drugs used in pregnancy.

The office will initially be located in Corporate Boulevard facility, and no one's address or telephone number will change.

Mark Goldberger, M.D., will be acting director of ODE IV, and **Renata Albrecht, M.D.,** will be acting director of the Division of Special Pathogen and Immunologic Drug Products.

FDA Funds Research on Prescription Drugs Used by Pregnant Women

FDA in partnership with the HHS Office of Women's Health announced on Sept. 28 the award of two contracts to labetalol and atenolol, two drugs used by pregnant women to treat their high blood pressure. The contracts are the first in a series to assess treatments commonly used by pregnant women.

The awards were made to the University of Illinois at Chicago to determine the appropriate doses and effects of labetolol for treating hypertension in pregnant women and the University of Washington for similar studies of atentolol in pregnant women.

FDA is funding the research to identify the doses that will provide the greatest benefit and least risk for the mother and her baby. The studies will evaluate the medications already being used by the pregnant women in the study.

Pregnant women with high blood pressure commonly use both of these drugs, even though little clinical data is currently available on this patient population.

A study conducted in l994 by FDA found that the average number of prescriptions during pregnancy was three for each patient, excluding prenatal vitamins, iron preparations and medications at the time of delivery. The number of prescriptions increased with age. Pregnant women older than 35 were taking an average of five prescriptions. Information needed to guide drug dosing in pregnant women is rarely collected.

Both of the study centers involved are members of the HHS National Centers of Excellence in Women's Health. These centers were established by the Public Health Service's Office of Women's Health in l996 as models for health care for women.

The centers provide a direct mechanism for HHS agencies to fund women's health research at premier academic institutions.

FDA Approves 1st Nucleotide Analog for HIV-1 Infection

FDA announced Oct. 29 that it had approved tenofovir disoproxil fumarate (Viread), a new antiviral drug indicated for treatment of HIV-1 infection in combination with other antiretroviral medicines.

Tenofovir disoproxil fumarate is the first nucleotide analog approved for HIV-1 treatment. Nucleotides are similar to nucleoside analogs, and block HIV replication in the same manner.

The introduction of potent antiviral drugs and the combined use of these drugs has markedly reduced replication of HIV in many patients and has improved survival rates. Yet because HIV mutates rapidly, resistance to one or more of these potent drugs may develop over time, necessitating the development of new drugs to treat these resistant virus strains.

FDA based its approval of tenofovir disoproxil fumarate on two clinical studies involving more than 700 patients who had previously been treated with antiretroviral agents, but showed signs of continued HIV replication despite drug therapy.

Viread, the brand name for tenofovir disoproxil fumarate, is marketed by Gilead Sciences Inc. of Foster City, Calif.

MEDICAL LIBRARY CORNER

PC Desktop Gives You Access to Full-Text Journal Articles

BY KATHY KRUSE, MLS

Have you ever conducted a literature search or perused a bibliography in your office, identifying a journal article you would like to read on the spot?

Have you ever needed to consult an article when the print copy isn't at hand?

The Medical Library has a solution.

From your desktop, you can now access the electronic full-text versions of articles from a growing number of journals.

The Library Electronic Reference Network on the Web, called WebLERN, is the starting point for accessing full-text titles from your desktop. To reach it, type http://weblern.cder.fda.gov in the address field of your browser or click on WebLERN button on the bottom of the CDERnet home page.

There are three sources for full-text journals listed in the e-journals category of the WebLERN opening page:

- The Medical Library's Full-Text Journals Online.
- ScienceDirect.
- The International Digital Electronic Access Library, or IDEAL.

The first resource is a Web page created by the library's staff. The other two are commercial Web sites accessible through license agreements between the publishers and the Library.

WebLERN: E-Journals Category

The Medical Library's Full-Text Journals Online is a list of library-subscribed journals available electronically in full-text. This list includes subscribed titles, which are present in IDEAL and ScienceDirect, as well as those from other individual publishers. Among the publishers currently included the American Chemical Society, Annual Reviews and Lippincott Williams and Wilkins.

Clicking on a title on the list takes you to the site for the journal. If there are specific instructions for reaching the full-text, such as a user ID and password, this information is placed next to the title on the list.

ScienceDirect gives you access to the more than 1,200 Elsevier Science journals, primarily from 1995 to the present. These journals cover the life, physical, medical, technical and social sciences. All titles are available in full-text, including those for which we don't have paper subscriptions.

The method for viewing the text of unsubscribed titles is to choose the personal login option from the ScienceDirect home page, rather than the "group-wide login." The first time you choose personal login, you will need to create a personal profile including a password. After completing the profile, you will receive a user name. You must enter your user name and password to view unsubscribed titles on subsequent visits to ScienceDirect.

Over 350 Harcourt journals are available full-text in IDEAL. Academic Press, Churchill Livingstone, Mosby and W.B. Saunders are some of the well-known scientific, technical and medical publishers that are Harcourt companies. You have access to a number of the journals included in IDEAL. To see the list of specific titles which are available, with full-text for 2000 and 2001 and abstracts for prior years, click on My Profile from the IDEAL Home page. Under Check Access, click on View a list of your licenses. From this list, click on Show Journals next to Subscription to U.S. Food and Drug Administration Collection.

Linking from PubMed, Embase

The Library's licensing of ScienceDirect and IDEAL offers a real bonus to users of the PubMed (MEDLINE) and Embase bibliographic databases, two other information resources available from the Biomedical Information category of WebLERN.

From specific references retrieved in searches of PubMed and Embase, you are now able to link directly to the full-text articles in ScienceDirect and IDEAL. Either the LinkOut or Abstract option for displaying retrieved references in PubMed, will link you to the full-text. From the abstract display, look for the buttons labeled "ELSEVIER SCIENCE" or "IDEAL." In Embase, look for one of the following hyperlinked phrases when a reference is displayed in either its short or full form: "Go to Science Direct and get the full text" or "Go to Ideal and get the full text."

The Library's access to ScienceDirect and IDEAL is by Internet Protocol (IP) address, so you will not be able to use these products from your home unless you are connecting to the CDER or an FDA network using Remote Access Software.

Other Specialty Resources

A final WebLERN resource for obtaining full-text journal articles is DialogSelect, found in the Other Specialty Resources category. By searching this database, you can obtain copies of articles from nearly 100 medical journals, with some covered back as far as 1982. American Journal of Diseases of Children, American Journal of Drug and Alcohol Abuse, Drug Topics, Journal of Family Practice, and Medical Letter on Drugs and Therapeutics are among the titles included.

The advantage of using DialogSelect, is the availability of titles with retrospective full-text coverage before 1995; however, one disadvantage is the absence of pictures, tables and graphs accompanying the text. From the DialogSelect opening page, click on Medical Journals Fulltext; beneath this link, there is another to the full list of titles covered. The fill-in-the-blank search screen lets you enter any of the following pieces of information: journal name, words in the article title or text, author, and publication date.

Full-Text Journal Caveats

As this discussion has pointed out, there a number of valuable resources for electronic journals. Even so, there are misconceptions regarding the full-text availability of journals on the Web. Not every journal has a Web presence, and, even if it does, table of contents from individual issues or article abstracts may be all that are provided.

Just because a library has a subscription to a specific title does not automatically give it electronic access to the full-text. Costs added on to the subscription fee or licensing requirements that cannot be fulfilled may prevent acquisition. Even with these limitations, however, members of the Library's Information Resources and Infrastructure Management Team and of the FDA Libraries Consortium will

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Two New Technical Writing Skills Seminars Offered

The Division of Training and Development is pleased to announce two new Technical Writing Skills seminars scheduled for this fall. If the two pilot seminars are well received, DTD will offer additional seminars next year.

The first new seminar, "English as a Second Language", is a one-day seminar to help CDER's foreign-born staff for whom English is a second language. Participants learn proven techniques to organize paragraphs, avoid idioms, simplify grammar and improve correctness. Also, the instructor explains the six most troublesome parts of American English:

- Articles.
- Pronouns.
- Prepositions.
- Verb tenses.
- Modifiers.
- Punctuation.

ESL is limited to 20 and is scheduled for Oct. 17 from 9 a.m. to 4 p.m.

The second one-day seminar, Grammar Refresher, will help participants improve grammar skills by reviewing parts of speech, sentence structure and punctuation. Participants will also learn to identify and use parts of speech correctly, write complete and clear sentences and avoid common sentence faults. In addition, participants learn how to use punctuation marks accurately and recognize common punctuation errors.

The seminar is limited to 20 and is scheduled for Nov. 8.

Reviewers, non-reviewers and support staff may register for the seminars.

Register for these seminars online at http://cdernet.cder.fda.gov/dtd/index.htm. Click on Registration, then click on CDERnet Registration Form. Complete and submit the registration form

If you have questions, e-mail Jack Morin (MORINJ).

CDER's 2001-2002 Training Catalog Features 20 New Programs

Twenty new educational programs are in the 2001-2002 Training Catalog that was distributed to all employees. The Center's training and development programs are designed to enhance our scientific, regulatory and administrative capabilities. In addition to course-related information, the catalog provides useful career development information for reviewers and non-reviewers.

You should review the catalog with your supervisor and select training opportunities for your career, personal growth, and development. CDER's Training Catalog is also a useful tool to help you prepare your individual development plan.

Consult the online course schedule at http://CDERnet/DTD/index.htm for specific details about the fall 2001 semester. Registration information is also included in the on-line schedule.

The new educational and career-related programs include:

- CDER Mentoring Program.
- CDER Support Staff Semi-Annual Workshop.
- CDER Facilitation Program.
- CDER's Training and Development Program.
- Recommended Epidemiologist Competencies and Learning Pathway.

> "The Center's training and development programs are designed to enhance our scientific, regulatory and administrative capabilities."

- Recommended Safety Evaluator Competencies and Learning Pathway.
- Recommended DTD Competencies and Learning Pathway for Instructional Systems Specialists.
- In Search of Solutions.
- Introduction to IMS Health Information.
- QT Prolongation and Drug Development.
- Special Topics in Pharmacoepidemiology—Drug-Induced Disease.
- Coaching and Effective Feedback.
- Group Decision-Making Techniques.
- Leading Effective Meetings.
- Facilitation Program.
- Leadership Seminar Series Online.
- CDER Neighborhood Leaders' Program.
- Creating Web pages using MS FrontPage.
- EMBASE.com.
- *Federal Register* and *Code of Federal Regulations* Resource.

Questions related to the catalog's contents or course schedule should be referred to any DTD staff member listed in the front of the catalog or by calling 7-4580.

PC Desktop Gives You Access to Growing Number of Full-Text Articles

(Continued from page 6)

continue to research, pilot test, and negotiate licenses for a variety of full-text journal products from publishers, subscription agents, and other sources.

Watch your E-mail for future announcements of additional full-text services for FDA staff.

If you would like more information on any of these products or if you would like more detailed individual instruction, please contact the Library's Reference Desk at 7-5703. You can also send an e-mail to MEDLIB. For group instruction, please contact Nancy Muir (7-5686, MUIRN), who heads the Instructional Services Team.

To suggest that the Library consider the acquisition of specific resources for full-text articles, you can complete the form called "Recommendation for Purchase/Evaluation of Library Materials," available from the Library's home page.

Click on the Library Publications button on the home page and choose the recommendation form from the "Request Forms" page. You can also contact Karen Kapust (7-5530, KAPUSTK), who heads the library's Information Resources and Infrastructure Management Team.

CDER Speeds Approvals of Emergency IND, 2 Supplements

(Continued from page 1)

Parker, a project manager in the division, contacted Dr. Slevin and explained what needed to be done to receive FDA permission to ship the drug. Working with Dillon-Parker and **David Bostwick,** a medical reviewer in the division, Solvay obtained approval of the new protocol and, by late Wednesday afternoon, shipped the product to New York.

Jennifer Sustack, a Solvay employee and a nurse who was volunteering at a burn unit in New York, reported that the drug was put to good use.

"As the increased number of burn patients came in, supplies began to run low," she said. "The hospital staff are very grateful for the immediate delivery of Flammacerium."

CDER's quick work didn't end with that one drug. Mafenide acetate (Sulfamylon for 5% Topical Solution) and silver sulfadiazine (Silvadene Cream 1%) are two other drugs used to treat burn victims that received expedited approval. These involved manufacturing supplements that are approved by the Center's chemists.

On Sept. 12, Mylan Pharmaceuticals Inc. requested expedited approval of its supplement for mafenide acetate. Because of a request from the Federal Emergency Management Agency, Mylan had donated 6,000 pouches of the drug, resulting in a shortage.

"Based on the immediate need for continued availability of the drug product for this public health need, an expedited review was granted," said **Bonnie Dunn, Ph.D.,** deputy director of the Division of New Drug Chemistry III. The approval letter was issued Sept. 17. **David B. Katague, Ph.D.,** chemistry team leader, Dillon-Parker and **Milton J. Sloan, Ph.D.,** chemistry reviewer, received a note of thanks from Mylan on behalf of the burn victims and their families.

On Sept. 17, CDER received a supplement from King Pharmaceuticals Inc. requesting a site transfer for the manufacturing and testing of its silver sulfadiazine product. The Army had asked the company that there be a supply of the drug available in case of war, and the existing supply was below the Army's requested level.

The action needed the Office of Compliance to coordinate an establishment evaluation by FDA's Office of Regulatory Affairs. Again, based on continued availability of the drug product for this public health need, an expedited review was granted. An approval was issued Sept. 27.

Drs. Katague and Sloan expedited the chemistry review, and Dillon-Parker expedited the drafting of the approval letter. **Patricia Alcock,** a supervisory consumer safety officer in OC's Division of Manufacturing and Product Quality, pushed the approval of the establishment evaluation request through in two days. **Tony Abel** and **Richard Debo,** both in ORA, expedited the preapproval inspection request.

Sherunda Lister is a public affairs specialist in OTCOM.

DRUGS IN THE NEWS

$33M Fine for False Records; Contraceptive Ring, Crohn's Treatment OK'd

The Department of Justice and FDA announced Oct. 19 that the French drug firm, Roussel Uclaf S.A., pleaded guilty to felony charges of conspiracy and defrauding FDA. Under a plea agreement, Aventis, Pharma A.G., the successor corporation to Roussel Uclaf, will pay criminal and civil penalties of more than $33 million, among the largest monetary penalties ever imposed in a criminal pharmaceutical prosecution.

The case involved Roussel Uclaf's manufacture of the antibiotic cefaclor in 1995 and 1996 through a wholly-owned subsidiary in Italy. **Eric P. Duffy, Ph.D,** then a chemistry reviewer in the Office of Generic Drugs and reviewing the firm's cefaclor ANDA, suspected fraud. "The process they were claiming to use looked impractical and unable to produce cefaclor the way they claimed," said Dr. Duffy, now director of the Division of New Drug Chemistry II.

In or about May of 1996, FDA inspectors sent to Italy at Dr. Duffy's request were provided false cefaclor batch records. Also, the firm kept a set of false records regarding the manufacturing facilities involved, such as raw material log books, a double software application and work orders. In fact, other facilities in Italy, France and also in Romania were involved in the manufacture of the drug shipped to the United States and these facilities had not been disclosed to the FDA. More information is at http://www.usdoj.gov/usao/md/press01/rousselfinal.htm.

FDA approved a vaginal contraceptive ring containing a combination of estrogen and progestin hormones released from a flexible polymer ring. The product, etonogestrel and ethinyl estradiol ring (NuvaRing), consists of a flexible, transparent, colorless vaginal ring about 2.1 inches in diameter containing the hormones etonogestrel and ethinyl estradiol, which are similar to the active ingredients in some oral contraceptives. After the ring is inserted, it releases a continuous low dose of the hormones. A new ring is used each month for continuous contraception. AstraZeneca LP of Wilmington, Del. is the sponsor.

FDA approved budesonide capsules (Entocort EC) for the treatment of mild to moderate active Crohn's disease involving certain sections of the small and large intestines. Budesonide is an orally administered steroid that is released in the intestine, where it works locally and topically to decrease inflammation.

Crohn's disease is a chronic inflammatory bowel disease that causes patients to develop diarrhea, at times profuse, abdominal pain or cramping, fever, fatigue, anorexia and weight loss. The causes of Crohn's Disease are unknown.

In clinical trials, patients taking budesonide experience fewer of the typical side effects associated with other steroids used to treat Crohn's disease, such as prednisone or prednisolone tablets, because most of budesonide is not absorbed into the body. AstraZeneca LP of Wilmington, Del., is the sponsor.

20 Commissioned Corps Officers in CDER Respond to Attacks

(Continued from page 1)

"We joined a variety of DMATs from around the country," said **CAPT Paul Seligman,** a physician in the Office of Post-Marketing Drug Risk Assessment. "We staffed five around-the-clock medical centers set up around the perimeter of the rubble pile."

Both 44-person teams used equipment and supplies already in place and worked eight- to 12-hour shifts followed by 20 to 24 hours off. "There were boxes and boxes of supplies," Seligman said. "The whole country opened up to help. We had everything one could imagine, including hot, fresh food donated by some of New York's finest restaurants."

When the teams arrived, the operation was still in rescue mode, and some of the firefighters and construction workers had been on the site almost non-stop. Seligman described the site as dangerous with surface temperatures up to 200 degrees and core temperatures about 600 degrees. When debris was removed, oxygen entering would cause new fires.

The medical teams treated everything from cuts, scrapes, burns, foot blisters, dehydration and foreign objects lodged in eyes to emergency care for chest pain and seizures as well as mental health services.

LT Sean K. Bradley, a pharmacist in the Office of Drug Evaluation I and a member of the CCRF team, provided pharmaceutical and first-aid care to the rescue workers in addition to other various duties.

CCRF members also assisted in the identification efforts in New York. **LCDR Mark Scheper,** who works in the Office of Regulatory Policy and has specialized training in forensic dentistry, worked with one of the disaster mortuary assistance teams in New York in identifying remains.

LT David Diwa and **LCDR Hye-Joo Kim,** both pharmacists in OPDRA, assisted in the entry of more than 5,400 interviews into a software program that will be used to help confirm identities.

CDER members of the PHS-1 DMAT who deployed to New York were **CAPT Timothy Ames,** a pharmacist from the Office of Generic Drugs; **CDR Jose Cintron,** a pharmacist from the ODE IV; and **CAPT Eugene Herman,** a scientist from the Office of Testing and Research.

Providing administrative support to the PHS-1 DMAT from Rockville were **CAPT Alan Schroeder,** a chemist from the Office of New Drug Chemistry; **CAPT Ching-Long Joseph Sun,** a pharmacologist from ODE II; and Hess. During their deployment, the PHS-1 DMAT provided care for a total of 672 patients.

Local Deployments

Earlier, the PHS-1 DMAT was deployed locally Sept. 11 and 12 when Pentagon was hit. It was also deployed Sept. 20 to 21 for President Bush's address to the nation in case there had been a terrorist attack during his speech.

It was unnecessary to move the team closer to the Pentagon once it became clear that local government response was adequate. CDER members of the Pentagon activation were Ames; Cintron; **LCDR Andrew Haffer,** a pharmacist from the Office of Medical Policy; Herman; Hess; **CDR Lydia Velazquez Kieffer,** a pharmacist from the Office of Clinical Pharmacology and Biopharmaceutics; **LT Craig Ostroff,** a pharmacist from ODE II; and **LCDR James Rogers,** a pharmacist from OMP.

CDER employees who deployed for the presidential address were Cintron, Herman, Hess, Kieffer, Ostroff and Rogers.

CCRF members deployed locally as well. One physician and three pharmacists from the Office of Review Management supported the National Naval Medical Center in Bethesda when the hospital ship, the USNS Comfort, first sailed to New York City. They were **CDR Mary Purucker,** a physician from ODE II; **LT Sean Belouin,** a pharmacist from ODE IV; Bradley; and Cintron.

The National Pharmaceutical Stockpile consists of strategically deployed caches of drugs and medical supplies. Each push pack can be loaded on a wide body cargo airplane, such as a 757 or a 767, and can be used to treat 300,000 to 1 million persons under chemical or biological terrorism conditions. Two CDER pharmacists who have received special training to assist local governments in using the push packs are deployed. They are **CDR Matthew Tarosky** from OMP and **LCDR Koung Lee** from OGD.

CCRF

"The CCRF is a cadre of officers uniquely qualified by education and skills who can be rapidly mobilized," said **CDR Lynn Slepski,** a nurse who is the CCRF's response coordinator in the PHS Office of Emergency Preparedness. "They can be activated by order of the surgeon general on the request of any organization that can demonstrate a public health challenge that exceeds local or state capabilities."

There are 752 officers on one of seven on-call rosters from a database of about 1,800. Officers are on the on-call roster one month and on a back-up roster for the following month. They can predict their schedules for the five years. CCRF has about 200 pending applications, Slepski said.

PHS-1 DMAT

The PHS-1 DMAT is one of 72 nationwide. "We began as two prototype DMATs in the 1980s and merged in 1993," said **CAPT William Hess,** a pharmacist in the Office of Information Technology and the team's administrative officer. There are 120 members on the PHS-1 DMAT's roster, and about 85 percent are Commissioned Corps officers. The rest are Civil Service employees or civilians. For each mission, the Office of Emergency Preparedness specifies an ideal configuration of specialties, and the team is tailored to the specific mission.

DMATs deploy to federally declared disaster sites with adequate supplies and equipment to support themselves for a period of 72 hours while providing medical care at a fixed or temporary medical site.

"Our team offers unique benefits compared to other DMATs," Hess said. "In addition to physicians, nurses, and paramedics we also have assets for mental health, preventive medicine and laboratory science. We are also very strong on pharmacists."

Initially, DMATs didn't have pharmacists, Hess explained. Hurricane Andrew in 1992 changed that. "Local doctors could write prescriptions, but there were no pharmacies left standing where patients could get them filled," he said.

—Norman J. Oliver

CDER's Counter Terrorism Agenda Becomes Top Priority

(Continued from page 1)

emergency operations office to facilitate its access to timely and reliable expertise from CDER.

- Making available its Commissioned Corps pharmacists to dispense antibiotics to congressional and postal workers in the Washington area.
- Coordinating within FDA and with other agencies to halt the importation of unapproved ciprofloxacin.
- Posting information on antibiotic use for anthrax on the Internet.

Ongoing and long-term antibioterrorism work includes:

- Coordinating with the Defense Department to develop an appropriate animal model to study the treatment of pneumonic plague.
- Cooperating with the National Institutes of Health, Centers for Disease Control and Prevention and DOD to facilitate an IND for antivirals to treat smallpox.
- Working to expand labeling to cover drug therapies for other biological and chemical warfare agents.
- Expediting work on a final regulation that would allow FDA to rely on animal studies and supporting data to approve drugs for bioterrorism agents when clinical studies in humans would be unethical.
- Developing a "streamlined IND" for drug therapies that may need to be used "off-label" in a mass casualty situation.
- Developing a drug preparedness and bioterrorism response Internet site.
- Preparing intranet resources on the bioterrorism medical literature, Center security and response and recovery.
- Working with NIH and CDC to enhance the Medical Library's collection and services and build an HHS-wide library consortium.
- Assisting the CDC in managing the National Pharmaceutical Stockpile.
- Coordinating with FDA field inspectors and manufacturers to help evaluate and resolve any GMP or manufacturing concerns that might arise during emergency production.
- Expediting reviews and inspections for manufacturing supplements that may be required for expanded drug production.
- Working with the CDC and DOD to implement a shelf-life extension program for stockpiled drugs for civilian and military use.
- Gathering and maintaining information on drugs that might be effective in an attack, including data on manufacturers, bulk suppliers, inventories, and lead times for production.
- Providing expertise to decision-makers at DOD and within HHS and its agencies.

The Ciprofloxacin Story

"FDA recognized several years ago that there was nothing specifically labeled for inhalational anthrax," said **Dianne Murphy, M.D.,** director of the new Office of Pediatric Drug Development and Program Initiatives, located in the Office of Review Management (page 5). The office is the Center's focal point for antibioterrorism work.

The Agency's decision to work on ciprofloxacin first was based on expert assessment that anthrax was the most likely biological agent to be used in an attack and the fear that anthrax might be modified to be resistant to older antibiotics that already had an anthrax indication.

An FDA working group examined the available research; the world literature; pathology reports from the accidental release of anthrax in the former Soviet Union; and data from Army experiments in rhesus monkeys exposed to inhalational anthrax and treated with ciprofloxacin, doxycycline, procaine penicillin, anthrax vaccine or a combination of drug and vaccine. Ciprofloxacin had an enormous safety database with more than 100 million patients in the United States having received the drug, including 4 million pediatric patients despite the fact it isn't labeled for use in children.

"We knew we could get similar drug levels in humans to the blood levels in the monkeys that the Army had exposed to anthrax," Dr. Murphy said. "FDA initiated the identification and collection of the necessary data, and the sponsor submitted a supplemental application."

Regulatory Issues

Federal medical officers are permitted to dispense drugs in mass casualty situations only for FDA-approved indications. The medical literature supports "off-label" use of some drugs against biological agents. However, traditional clinical studies to demonstrate these uses are safe and effective may not be feasible or ethical. It would be unethical to expose healthy volunteers to such agents.

Drugs can be dispensed under an IND; however, obtaining informed consent in an emergency mass casualty situation is far from ideal.

To address these issues, FDA published in the *Federal Register* on Oct. 5, 1999, a proposed rule that would create a new mechanism for approving drugs to treat people exposed to bioterrorism agents when safety in humans has been established and results in well-controlled animal trials establish efficacy.

The proposal, commonly called "the animal efficacy rule," would permit FDA to rely on animal evidence when the agent's mechanism of toxicity is well understood; the endpoints in the animal trials are clearly related to benefit in humans; the drug's effect is demonstrated in a species expected to react similarly to humans; and data allow selection of an effective human dose.

Such approvals could include possible postmarketing studies when feasible and ethical, possible restrictions on distribution and a requirement that information about the basis of approval be provided to patients.

The rule is not yet final. For some scenarios, public health officials may still need to recommend administering a drug that remains investigational for that use.

"We are working with CDC to make sure that if an investigational product is needed in a mass casualty situation, we could facilitate access to it," Dr. Murphy said. "We want to make sure that it would be dispensed ethically and that people understand their risks. We've put a lot of work into what we are calling our 'streamlined IND.' We want people to have enough information to make a reasoned judgment but not be encumbered by a lot of paperwork." Such streamlined INDs could apply to products that may be more modern and more accessible.