news along the pike

CENTER FOR DRUG EVALUATION AND RESEARCH

MARCH, APRIL, MAY 2003

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INSIDE . . .

PIKE'S CORNERS

CDER small business grant helps develop oxygen test

Device can measure gas nondestructively in finished products

BY JOHN A. SPENCER, PH.D.

ST. LOUIS—The presence of oxygen even at low levels in some drug products can lead to decomposition of the active ingredient. This can reduce the potency of the drug or, worse, lead to toxic impurities. These are usually injectable drug products in sealed glass containers.

Currently, the only way to assess the level of oxygen in such a drug product is to collect a few production samples and chemically analyze them. This is slow, expensive and uses chemicals that require safe disposal. When the analysis is done, the samples have been destroyed. Additionally, there is always the haunting question of whether the samples tested were representative of the whole batch.

All this may change soon as the result, in part, of two modest Small Business Innovation Research grants from CDER to a Charlottesville, Va., technology startup.

Lighthouse Instruments has developed an instrument that can monitor the amount of oxygen in finished products dispensed in practically any sealed glass container. Because it is unnecessary to unseal the container to make the measurement, the product can be used normally if it passes the test. By retesting some of the containers, the reliability of the seals can be followed over the lifetime of the product.

James Veale, Ph.D., a physicist and president of Lighthouse Instruments, has devised a means to pass the monochromatic light produced by a laser through the neck of a sealed glass vial. By choosing an appropriate wave-

(Continued on page 8)

CDER, ORA hold small business town meeting

BY RON WILSON

In early March, the Center and FDA's field operations co-sponsored a town hall meeting in Philadelphia for 130 representatives from the small pharmaceutical business community. The meeting provided small businesses with the opportunity to dialogue with subject matter experts from CDER and FDA's Office of Regulatory Affairs and gain an understanding of the regulatory requirements for approval and marketing of drug products.

The ORA co-sponsors were the Central Region, located in Philadelphia, and the Philadelphia District Office.

Since this meeting was a first of its kind, FDA planners assumed that the response from the small business community would be modest. However, once we released the meeting announcement, it became quickly apparent that this was not the case. Registrations arrived rapidly—sometimes as many as 10 to 15 per day. The overall reaction to the meeting announcement was so enthusiastic that the previously

(Continued on page 8)

First in new class of HIV drugs gets accelerated approval

In mid-March, FDA granted accelerated approval to enfuvirtide (Fuzeon) for use in combination with other anti-HIV medications to treat advanced HIV-1 infection in adults and children ages 6 years and older.

FDA's accelerated approval of enfuvirtide makes it the first product in a new class of medications called fusion inhibitors to receive marketing approval anywhere in the world. Drugs in this class interfere with the entry of HIV-1 into cells by inhibiting the fusion of viral and cellular membranes. This inhibition blocks the virus' ability to infect certain components of the immune system.

Since HIV must be treated with a combination of medications to be effective, enfuvirtide can be used as part of a medication regimen in patients for whom there are limited options.

Enfuvirtide should only be used in patients who have previously used other anti-HIV medications and have ongoing evidence of viral replication. Enfuvirtide is administered as a subcutaneous injection.

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JOE'S NOTEBOOK

HIV-AIDS update

We have a very, very sad situation in the United States. Each year we continue to see about 40,000 new HIV infections domestically. We have well over 800,000 people living with HIV in our country, but an estimated 200,000 of these people do not know they are infected and, tragically, are not getting appropriate treatment for their HIV infection. This is an intolerable situation in the minds of the public health officials and certainly in the minds of clinicians who are seeing these patients when they're diagnosed late in their course of illness and, again, tragically, have not had the opportunity to benefit from the potentially life-saving treatments that we now have available.

—Julie Gerberding, M.D., MPH
April 17, 2003

While our Center's approval of the first in a new class of HIV therapies is encouraging (page 1), these sobering words from the director of the Centers for Disease Control and Prevention remind us of the infection's cruel burden on our nation's health—a burden that has already claimed almost half a million American lives. Shortly before the approval of enfuvirtide, **Anthony Fauci, M.D.,** presented a CDER scientific seminar on the progress and challenges in the areas of HIV and AIDS. Dr. Fauci is the director of the National Institute of Allergy and Infectious Diseases at the NIH. He noted that when he and the rest of us learned of HIV in the early 1980s, none of us would expect that two decades later we would be facing a global pandemic.

Worldwide, there are 42 million people living with HIV and AIDS. Last year there were 5 million new infections, with 10,000 per day in sub-Saharan Africa. Also in 2002, 3.1 million people died from AIDS. HIV now eclipses malaria and tuberculosis as the leading cause of death from microbial infection. The next wave of infection, according to CIA estimates, will take place in Nigeria, Ethiopia, Russia, India and China. The devastation of HIV in Asia has the potential of being worse than in Africa. In the United States, the rate of infection has plateaued at about 40,000 infections per year for the last dozen years. That means when the rate of infection goes down in some groups, it goes up in others. HIV is no longer primarily a disease of young, mostly white, gay men. Fully half of all new U.S. infections are among African-Americans, and another 20 percent are among Hispanics.

Dr. Fauci noted that the life cycle of the AIDS virus—from fusing with the cell surface and integrating with the cell's DNA to spawning a new virus—offers multiple targets for therapeutic intervention. "The fundamental issue with HIV," Dr. Fauci said, "is that the immune system controls but does not eradicate the virus."

Highly active antiretroviral therapy has transformed the epidemic in the United States, reducing deaths from about 50,000 per year to about 15,000 per year. The two classes of therapeutics today are the reverse transcriptase inhibitors, which interfere with conversion of the viral RNA into DNA, and the protease inhibitors, which interfere with the budding off of a new virus from an infected cell. The recently approved enfuvirtide belongs to a class of drugs known as fusion inhibitors that block entry of the virus into the cell. Other drugs under development include integrase inhibitors that attempt to block the integration with the cell's DNA.

Sadly, current therapies won't eliminate the disease from its hiding places in the body, so the immediate goals are to develop better drugs that can be used longer and better tolerated. With better treatment comes suppression of the viral load in individual patients and a reduced rate of transmission.

news along the pike

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

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FDA issues report, launches Web site on Phase IV commitments

On May 22, FDA announced two measures to inform the public about the status of manufacturers' commitments to carry out postmarket studies after FDA has approved certain drugs and biological products:

- FDA published its first annual *Federal Register* report on these postmarketing studies, which covers FDA-required and voluntary commitments. The report is mandated by the 1997 FDA Modernization Act.
- In addition, FDA is posting a searchable database with most of the same information. The database can be found at http://www.fda.gov/cder/pmc/.

In its announcement, FDA noted "considerable room for improvement, by manufacturers as well as the FDA," in making sure that:

- Postmarketing study commitments are completed in a timely manner.
- Important new data from the studies are promptly incorporated into product labeling.

The Center is continuing to implement new internal procedures to ensure better tracking and follow-up of postmarketing commitments and to make certain that the final study reports are reviewed and acted upon in timely manner.

CDER has initiated new procedures to ensure that new postmarketing commitments clearly describe the nature of the study and the specific timelines for submission of the study protocol, initiation of the study and submission of the final study report.

The database includes open postmarketing study commitments that have been made with CDER and the Center for Biologics Evaluation and Research since Jan. 1, 1991.

Both the FR notice and the Web site list study commitments addressing clinical safety, clinical efficacy, clinical pharmacology and nonclinical toxicology. Not included are certain other postmarketing commitments, such as those concerning chemistry and manufacturing and controls, and there is no listing of proprietary information.

Manufacturers are required to submit annual status reports on postmarketing study commitments for approved drugs, and for certain licensed biological products. Each report must include, among other information, a description of the postmarketing study commitment, a schedule for its completion, and a characterization and brief description of its current status. The schedule is expected to include the projected dates for the initiation and the completion of the study, and for the submission of the final study report to FDA. Manufacturers are also required to categorize the current status of the commitment using a defined set of terms.

Summary of postmarketing commitments to CDER
(as of 9/30/02)
Federal Register, May 21, 2003, Vol. 68, No. 98, p. 27823

	NDAs/ANDAs (% of total)
Applicants with open postmarketing commitments	126
Number of open postmarketing commitments	1,339
Status of open postmarketing commitments	
• Pending	820 (61%)
• Ongoing	285 (21%)
• Delayed	25 (2%)
• Terminated	8 (1%)
• Submitted	201 (15%)
Concluded studies	349
• Commitment met	240 (69%)
• Commitment not met	0 (0%)
• Study no longer needed or feasible	109 (31%)
Open postmarketing commitments with annual report due but not received	289 (22%)

Pike's Puzzler: General medical quiz

BY TONY CHITE

1. This highly contagious skin infection caused primarily by *Staphylococcus aureus* or *Streptococcus pyogenes* occurs most often in children living under conditions of poor hygiene is:

a. scurvy
b. scarlet fever
c. impetigo
d. Lyme disease
e. St. Anthony's fire

2. The Centers for Disease Control and Prevention is located in:

a. Gloversville, N.Y.
b. Atlanta, Ga.
c. Salt Lake City, Utah
d. Des Moines, Iowa
e. New Port Ritchey, Fla.

3. A dark green mucilaginous material in the intestine of the full-term fetus, being a mixture of the secretions of the liver, intestinal glands, and some amniotic fluid is called:

a. meconium
b. viridin
c. fluorocyte
d. chitin
e. phlegm

4. The tough white outer coat of the eyeball, covering approximately five-sixths of its surface is called the:

a. choroid
b. cornea
c. sclera
d. retina
e. macula

5. A word describing a condition or thing that is short lived or transient is:

a. surreal
b. ephemeral
c. apoptosis
d. kyphotic
e. stalagom

Key: 1c; 2b; 3a; 4c; 5b.

Tony Chite is a consumer safety officer for the Division of Information Disclosure Policy.

Data backup; Windows 2000 update; New tools for searching

BY TRACY MARTIN

There are three locations to which you can back up the information stored on your hard drive:

- A shared network drive.
- A CD/RW drive.
- An external connection.

You can use a shared network drive as a repository for your backup files. If you are already connected to the network, this is the easiest method to use for backups. Because the shared drives are regularly backed up by the network administrators, the files you copy to the shared drive will be included in these regular network backups.

You should create a folder on your shared drive to be used explicitly for your backup files. You can then use Windows Explorer to copy the files to that folder. For subsequent backups, you can copy new or updated files to the same folder.

Similarly, you can use a CD read-write drive to backup files from your computer to a CD. If you have a drive already connected to your computer, either externally or internally, and a blank CD, you can copy the files and folders directly to the CD using the utility that came with the drive or your computer. For subsequent backups, you can copy new or updated files to the same CD.

Finally, if you have an external connection to your computer such as a Zip drive or a peer-to-peer connection, you can use that as a means by which to backup the files and folders on your computer.

Windows 2000 Professional Update

BY GURMINDERS J KHALSA

The Windows 2000 Professional project is complete. So what happens for those of you who are still running Windows 95 or Windows 98? You are not forgotten!

The Center has purchased new desktops and laptops configured to run Windows 2000. All office and home systems still running Windows 95/98 will be replaced with one of these new desktops or laptops. This was a more cost-effective and customer-friendly solution compared with the option of upgrading these older systems for Windows 2000 and then replacing the machine with a newer model a short time later.

How quickly will you get your replacement desktop or laptop?

As you are aware, CDER was trying to meet a mandated deadline for installing Secure Remote Access Services on all desktops and laptops by March 31. Meeting this deadline required virtually all of our desktop resources. OIT thanks you for your patience and understanding during the deployment of the new desktops and laptops. Machines that required SRAS had to take priority over other desktop installations.

We are currently deploying the new desktops and laptops as fast as we can. We ask for your help. When we contact you to schedule your upgrade, please make sure your current machine is available.

New Search Tool Available Soon

BY HELEN MITCHELL

Many of you have been waiting for the opportunity to do full content searches on DFS, the review document management system.

In the near future, OIT will be rolling out a new Web application called Enterprise Search which will be available to all CDER staff.

This new search tool will allow you to do full content searches on DFS documents, if you have a DFS account. The new tool will also allow you to search many types of "digital assets" in Word, PDF, XML, text, HTML and scanned images within the CDER network. This includes CDER guidances, Office of Generic Drugs division files and several Web sites.

It will also replace the current E-DocQuery (RetrievalWare) search tool for access to Drug Master File reviews, Adverse Event Reporting System individual safety reports (images only), Biopharm division files (prior to entry in DFS) and approved final printed labels (1994-2000). Security has been put in

(Continued on page 5)

June OIT Training

Monday	Tuesday	Wednesday	Thursday	Friday
2	3 Office XP Hands-On Course 9 - 4 (C)	4 Office XP Hands-On Course 9 - 4 (C)	5	6 Office XP Hands-On Course 9 - 4 (P)
9 Office XP Hands-On Course 9 - 4 (C)	10 NEST 9-12 (C) NEDAT 1-4 (C)	11 Office XP Hands-On Course 9 - 4 (P)	12 Office XP Hands-On Course 9 - 4 (C)	13
16 Office XP Hands-On Course 9 - 4 (C)	17 JMP (Session I) 1-4(C) (Session II 6/24) (Outlook Email & Calendar Cancelled)	18 Office XP Hands-On Course 9 - 4 (C)	19 DSS 9-12 (C) DFS 1-4 (C) File Management 1-4 (P)	20 Office XP Hands-On Course 9 - 4 (P)
23	24 JMP (Session II) 1-4 (C) Office XP Hands-On Course 9 - 4 (P)	25 Office XP Hands-On Course 9 - 4 (P)	26 Office XP Hands-On Course 9 - 4 (C)	27

Key: Corporate Blvd (C), Park Building (P)
Go to http://OITWeb to access training registration and resources.

FDA, firm to collaborate on developing tools for safety data mining

FDA established a Cooperative Research and Development Agreement with Lincoln Technologies Inc. to use data mining—a promising new technology—to enhance FDA's post-market monitoring of the safety of drugs, biologics and vaccines.

Data mining is a technique for extracting meaningful, organized information from large complex databases. The CRADA involves data that FDA already collects about adverse events involving approved drugs, biologics and vaccines. The specific data set used for data mining purposes excludes patient names, addresses, social security numbers or similar information.

Data collected from suspected drug-related adverse event reports and other electronic medical information could aid in identifying signals of adverse events and the patterns in which they occur.

For example, more effective data mining might allow the Agency to identify a pattern of adverse events in a specific population of patients taking a drug or in patients who take a certain combination of drugs,

The Agency could then communicate this knowledge sooner to medical professionals and patients—preventing more adverse events.

"Preventing adverse events associated with medical products is one of FDA's top priorities," said the FDA Commissioner **Mark B. McClellan, M.D., Ph.D.** "By making greater use of state-of-the-art statistical tools coupled with 21st-century medical information systems, we can act more quickly and effectively to prevent adverse events."

The CRADA is expected to improve the utility of safety data mining technology. CDER and the Center for Biologics Evaluation and Research will work with the firm to develop new and innovative ways for extracting information related to drug safety and risk assessment.

"Further development of this tool holds great promise as a way to optimize our evaluation resources and enhance our ability to identify drug-related safety concerns," said **Paul J. Seligman, M.D.,** the Center's principal investigator for the CRADA and director of the Office of Pharmacoepidemiology and Statistical Science.

"Through the use of enhanced data mining techniques we hope to improve upon our current ability to identify adverse event patterns in post-market safety databases. Application of improved data mining tools has the potential for even earlier detection of safety signals associated with marketed products, especially adverse events from drug-drug interactions."

CBER's principal investigator for the project, **M. Miles Braun M.D.**, added: "This CRADA is intended to use modern computing and state-of-the-art statistical algorithms to sift through millions of suspected reaction reports and thousands of products to look for potential safety signals needing further scrutiny. The tools developed are expected to be highly useful aids to safety evaluators and reviewers."

OIT develops new tool to conduct full content searches on DFS documents

(Continued from page 4)

place, so you will only be able to view those collections of documents you've been granted permission to access.

We look forward to being able to present this new tool to you and to get your feedback as to what additional collections of documents you'd like to be able to search through this interface as well as what suggestions you have to make this tool more useful.

Also, training classes will be offered to cover such topics as:

- Logging on to the system.
- Changing passwords.
- Choosing which libraries to search.
- Query using wildcards, date ranges, Boolean operators and exact phrases.
- Launching documents in their native format, such as PDF or Word.
- Saving queries and resubmitting them later.
- Refining a search within the original group of returned documents.

My Portal

BY BOBBYE UNDERWOOD

OIT's Portal will be here before you know it. Many CDER users have been asking when it's going to be available, and it's soon.

We are currently making as many improvements as possible before the initial rollout based on recent focus groups we held to get your final feedback.

The Portal is going to be packed with easy-to-find information, including:

- Useful links.
- Single sign-on to a number of CDER applications.
- Training registration with automatic e-mail confirmations.
- Full content searching of DFS and other CDER document repositories.
- One-stop-shopping for technical answers that are on OIT's intranet.

It's going to be a great tool, so stay tuned.

FTC, FDA Crackdown on Internet SARS Products

The Federal Trade Commission and FDA sent warnings to Web site operators, manufacturers and distributors who suggested that their products would protect against, treat or even cure Severe Acute Respiratory Syndrome. The agencies told firms that the government is unaware of any scientific proof for such claims and that the Web site operators must remove any misleading or deceptive claims from the Internet.

The warning campaign is based on information gathered through an Internet surf that the FTC coordinated with the help of the FDA and the Ontario Ministry of Consumer and Business Services.

Included in the review were Web sites that promised consumers would be protected from SARS if they purchased such items as personal air purifiers, disinfectant sprays and wipes, respirator masks, latex gloves, dietary supplements like colloidal silver and oregano oil, and SARS "prevention kits."

Concept papers on risk management set stage for public workshop

By Patrick E. Clarke

FDA held a three-day public workshop to discuss risk-management activities for drug and biologic products in April. The purpose of the workshop was to present FDA's current thoughts on risk management and to solicit views from the public.

Before the workshop, FDA had issued three concept papers in draft format for discussion:

- "Premarketing Risk Assessment," was developed by a working group chaired by **Robert J. Meyer, M.D.,** director of the Office of Drug Evaluation II.
- "Risk Management Programs," was developed by a working group chaired by **Anne Trontell, M.D.,** deputy director of the Office of Drug Safety.
- "Risk Assessment of Observational Data: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment" was developed by a working group chaired by **Julie Beitz, M.D.,** deputy director of the Office of Drug Evaluation III.

"These concept papers and workshops offered an important opportunity to engage the public in tackling many of the difficult issues and challenges associated with optimizing the assessment and management of risk associated with drug and biologic products," said **Paul Seligman, M.D.,** director of the Office of Pharmacoepidemiology and Statistical Sciences. "The papers were very well received and stimulated the discussion we were hoping to have. CDER and CBER staff did an outstanding job."

The concept papers, presentations and transcripts of the workshops are available on CDER's Web site at http://www.fda.gov/cder/meeting/riskManagement.htm.

The first day of the workshop was moderated by **Deborah Henderson,** director of the Office of Executive Programs; the second by Dr. Seligman; and the final day by **Steven Galson, M.D.,** the Center's deputy director.

Premarket assessment

The premarketing concept paper focuses on risk assessment during clinical development, particularly in Phase III studies. Some of the topics presented in the paper include:

- The appropriate size of the premarketing safety database.
- Characteristics of an ideal safety database.
- Detecting unanticipated interactions as a part of a safety assessment.
- Some special considerations for optimal risk assessment during product development.
- Minimizing medication errors.
- Safety aspects of products that should be addressed in all development programs.
- Considerations for data analysis and presentation.

Risk-management programs

The second concept paper discusses risk-management programs. It begins by defining risk management as the overall and continuing process of minimizing risks throughout a product's life cycle to optimize its benefit-risk balance.

> "The papers were very well received and stimulated the discussion we were hoping to have."
>
> —Paul Seligman, M.D.

The paper points out that traditional risk-management planning consists of professional product labeling and postmarketing surveillance but notes that more may be needed in some cases.

The concept paper proposes that sponsors for some drugs or biologics should submit a risk-management program. This is defined as a strategic safety program to decrease product risk by using one or more interventions or tools beyond the package insert. Examples include:

- Specialized educational material for health care practitioners or patients.
- Processes or forms to increase compliance with reduced-risk prescribing and use.
- Systems that modify conventional prescribing, dispensing, and use of the product to minimize specific risks.

The paper discusses risk management tools as well as how and when risk management programs can be evaluated.

The desired elements of a risk-management program submission as spelled out in the concept paper are:

- The background of the overall risk reduction goals and rationale for the planned approach.
- The targeted goals, objectives and "level" of the intervention.
- One or more proposed tools with a rationale and implementation plan for each.
- An evaluation plan for component tools and the overall objectives or goals detailing the analyses that will be conducted and the plan for reporting the evaluation results to FDA.

Postmarket assessment

The third concept paper addresses good pharmacovigilance practices and pharmacoepidemiologic assessment. It offers this distinction between a pharmacovigilance plan and an risk-management program: "While a pharmacovigilance plan might be a component of a larger RMP, its sole focus would be to assist in detecting new signals and/or evaluating already identified safety signals."

FDA envisions that sponsors would propose a pharmacovigilance plan for the ongoing evaluation of identified safety signals or for the monitoring of at-risk patient populations, which had not been adequately studied before approval.

The paper discusses safety signals, characteristics of good case reports and appropriate methodologies for pharmacoepidemiologic studies, including patient registries. The need to safeguard confidentiality when conducting pharmacoepidemiologic studies is stressed, with the recommendation that sponsors use informed consents and consult with Institutional Review Boards as appropriate.

The paper reviews factors to be considered in assessing causality between use of a product and reported adverse events. If the safety signal relates to a medication error, FDA would expect the sponsor to evaluate each event to identify the root causal factors that led to the event or possible event. The paper says that FDA has found that development of pharmacovigilance plans is useful at the time of product launch or when a safety signal is identified.

Patrick Clarke is a public affairs specialist in the Division of Public Affairs in the Office of Training and Communications.

Center launches campaign on safe use of daily aspirin therapy

By Mandy Eisemann

CDER released an educational campaign for the general public on the safe use of aspirin for preventing a heart attack and stroke. The campaign materials include:

- A black-and-white print public service announcement.
- A double-sided fact sheet.
- A six-panel color brochure.

The campaign informs consumers of the risks and benefits of daily aspirin therapy and the need for professional guidance before beginning such a regimen.

Each piece is designed to reach people where they are most likely to see it:

- The full-page black-and-white print public service announcement will be sent to nearly 100 popular magazines.
- The fact sheets and brochures will be disseminated at the Center's exhibit programs.

We are exploring co-sponsorships with pharmacy chains and consumer groups to provide additional avenues for dissemination.

All three products are posted on CDER's Consumer Education page: http://www.fda.gov/cder/consumerinfo/DPAdefault.htm. Beginning this summer, consumers will be able to order a free copy of the brochure from the Federal Citizen Information Center in Pueblo, Colo., (http://www.pueblo.gsa.gov/).

In recent years, direct-to-consumer advertising has promoted aspirin's ability to reduce the risk of a heart attack and stroke in certain people who are living with specific cardiovascular disease.

The Center's campaign reminds consumers that the most commonly known and used medicine—aspirin—is not without risk. A decision to use aspirin to prevent a heart attack or stroke is safest when made in consultation with a medical professional. A health professional has the experience and the training to help the individual with evaluating the risks and deciding if aspirin is the appropriate treatment.

No drug is completely safe, and some consumers may be surprised to learn that aspirin has undesirable side effects that may cause injuries.

The FDA-approved over-the-counter labeling for aspirin covers temporary self-treatment of pain, swelling and fevers. Using aspirin without following directions on the OTC label or without receiving guidance from a medical professional could increase the risk of other kinds of strokes, stomach bleeding and more.

Mandy Eisemann is a public affairs specialist in the Division of Public Affairs in the Office of Training and Communications.

Botanical Review Team consolidates expertise for growing workload

By Patrick E. Clarke

A three-member Botanical Review Team consolidates scientific and regulatory expertise in botanical drug products for CDER's Office of New Drugs.

Formed in February, the team is located in the Office of Drug Evaluation V and serves as an OND resource in the review of all botanical drug products at all stages of the review process.

Currently, there are 139 botanical investigational new drug applications filed with the Center, but there are no approved or pending new drug applications.

"Our mission in CDER is to facilitate botanical drug development and the review of new drug investigations under INDs and later as NDAs," said **Shaw T. Chen, M.D., Ph.D.,** the team's leader and associate director for special product review in ODE V.

A botanical drug product contains one or more active ingredients derived from one or more plants, algae or macroscopic fungi and their combinations.

The Center doesn't consider as botanical drugs those that have highly purified or chemically modified active ingredients derived from natural sources, such as the anticancer drug paclitaxel, which was first isolated from the Pacific yew tree, *Taxus brevifolia.*

"There are still many technical difficulties to developing these types of products that the industry is working hard to resolve," Dr. Chen said.

"In addition, for old products already on the market as dietary supplements, there may be little incentive for the sponsor to study them up. Furthermore, an IND for a marketed dietary supplement can be very useful for promotion, and the sponsor may not feel the need of actually conducting the proposed study."

The other team members are **Jin Hui Dou, Ph.D.,** the pharmacognosy reviewer, and **Leslie Vaccari, BSN, RAC,** the project manager. There are other reviewers identified in CDER to assist the team when needed. They are three chemistry reviewers **Rajiv Agarwal, Ph.D., Yung Ao Hsieh, Ph.D.,** and **Sue-Ching Lin, M.S., R.Ph.; Kuei-Meng Wu, Ph.D.,** a pharmacology-toxicology reviewer; and **John Z. Duan, Ph.D.,** a clinical pharmacology reviewer.

The team responds to a steady level of requests for consultation. In an average month, they consult on one to two pre-INDs and one-to-two new original INDs. They also respond to multiple requests from the Center for Food Safety and Nutrition as well as the National Center for Complementary and Alternative Medicine and the National Cancer Institute.

Dr. Dou brings to the team specialized knowledge of traditional Chinese medicine, which uses herbal preparations as therapy, and the Western science of pharmacognosy, which focuses on the biology of medicinal plants, their pharmacological activity and their history of therapeutic use in humans.

Dr. Dou was on the faculty at Beijing Traditional Chinese Medicine University as an instructor and has a doctorate in pharmacognosy from University of Mississippi.

"Pharmacognosists study herbal preparations, from the raw material in the field to the products as we see them in the bottle," Dr. Dou said.

"In the United States in the past several decades, generally speaking, pharmacognosy has been focused on searching for single-molecule drug candidates. New botanical drug products may finally fall between the two ends of the development spectrum with a resulting product that has a well-defined safety and efficacy profile but without being purified as single molecules."

Small business grant helps develop rapid test for oxygen in vials

(Continued from page 1)

length of the light, gaseous oxygen can be measured quantitatively in the space above the liquid inside the container, often called the "headspace."

Because the laser light beam is in the near infrared part of the spectrum, the product is not harmed. The instrument can measure down to 0.5 percent oxygen and is extremely rapid. In an analytical laboratory, a result can be obtained in as little as 1 second. The firm has demonstrated a version of its instrument that can be used on production lines. This instrument can provide 100 percent product testing for residual oxygen.

Because laser diodes can be fabricated to produce many different wavelengths of light, the Lighthouse instrument is not limited to analyzing for oxygen alone. Residual moisture can be a problem in freeze-dried products. By switching to a wavelength where water vapor absorbs light, the moisture level can be checked before releasing the lot. Furthermore, the characteristics of water-vapor absorption vary with the internal pressure of the vial. Lighthouse has capitalized on this feature to offer both bench-top and in-line pressure monitors for vials.

Internet resources

- More information about Small Business Innovation Research grants can be found on CDER's small business assistance Web site at http://www.fda.gov/cder/about/smallbiz/Econonic.htm.
- FDA's small business guide is at http://www.fda.gov/ora/fed_state/Small_Business/sb_guide/default.htm.

Bench-top and in-line monitors are presently used to qualify final products for release. Development in consort with several pharmaceutical manufacturers is now underway to produce and test instruments that can be incorporated into the process control system. Manufacturers could then detect and correct process problems before they can affect the product. That makes this technology a tool to be added to those that can further the Center's Process Analytical Technology initiative.

Dr. Veale will describe the development and implementation of these instruments in a seminar entitled "Nondestructive Headspace Gas Analysis for Monitoring Oxygen, Moisture and Vacuum Levels in Parenteral Containers" on June 18, 1:30 p.m., in Parklawn Conference Room C. More information on Lighthouse Instruments is available at http://www.lighthouseinstruments.com.

John Spencer is a chemist in the Office of Testing and Research's Division of Pharmaceutical Analysis in St. Louis.

CDER, ORA hold small business town meeting for 130 in Philadelphia

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scheduled room had to be changed to accommodate the growing numbers of attendees. Ultimately, a cut-off limit had to be put in place.

In addition, companies from across the country attended. A participant from Oregon commented that the trip was "worth it." Others braved uncertain weather to make the trip. One attendee traveled from Canada in the midst of a snowstorm.

Topics and presenters included:

- *OTC Monographs and Labeling:* **David Hilfiker,** a supervisory consumer safety officer in the Division of Over-the-Counter Drug Products in the Office of New Drugs.
- *The Meetings Process and Communication with the FDA:* **Judit Milstein,** a regulatory health project manager in the Division of Anti-Infective Drug Products in OND.
- *Navigating the FDA Web Site:* **Marie Falcone,** Central Region small business representative.
- *Imports and Exports:* **Ada Irizarry,** a consumer safety officer in the Division of New Drugs and Labeling Compliance in the Office of Compliance.
- *Registration and Listing System:* **Kathy Smith,** a management analyst and **David Mazyck**, a contractor, both from the Division of Data Management and Services in the Office of Information Technology.
- *Financial Assistance and Incentives:* **Ron Wilson.**

Participant evaluations were solidly supportive, confirming that this town meeting met a high priority Agency goal in its successful outreach to an important constituency, the small pharmaceutical business community.

With such obvious interest, additional town meetings may be held in the future if funding can be obtained. If you would like to provide additional comments regarding this meeting or suggestions for an upcoming small business meetings, please contact myself (wilsonr@cder.fda.gov) or one of the other members of meeting planning committee:

- **Marie Falcone,** Central Region, mfalcon@ora.fda.gov.
- **John Friel,** deputy director, OTCOM, frielj@cder.fda.gov.
- **Debbie Kallgren,** OTCOM, kallgrend@cder.fda.gov.

Ron Wilson is CDER's small business representative in the Office of Training and Communications.

First in new class of HIV drugs approved for kids, adults

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FDA based its accelerated approval of enfuvirtide on an analysis of six months of data from two ongoing clinical studies of enfuvirtide involving approximately 1,000 patients. The data from this analysis showed that the addition of enfuvirtide to a combination of other anti-HIV medications reduced the level of HIV infection in the blood more than the use of the combination of anti-HIV medications alone. The long-term effects of enfuvirtide are not known at this time, but are being evaluated by the ongoing clinical studies.

The approved labeling for enfuvirtide warns physicians to carefully monitor patients for signs and symptoms of pneumonia. Although bacterial pneumonia was uncommon in clinical study participants, more patients treated with enfuvirtide developed bacterial pneumonia than did patients who did not receive enfuvirtide.