news along the pike

JULY-AUGUST 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

VOLUME 7, ISSUE 6

INSIDE . . .

PIKE'S CORNERS

Medical Gas Mix-Up Working Group Uses Leveraging

7 Deaths, 15 Injuries Spur Agency's Risk Management Effort

BY NANCY DERR

The last thing you want to be worrying about as you drift off before surgery is whether the oxygen system being used will be feeding you oxygen—and not nitrogen or argon. Yet this continues to be a concern.

In April, CDER issued a public health advisory guidance alerting hospitals, nursing homes and other health care facilities to the hazards of medical gas mix-ups (http://www.fda.gov/cder/guidance/4341fnl.htm).

On July 20, the Center for Devices and Radiological Health issued a public health advisory on the same issue (http://www.fda.gov/cdrh/safety/medical-gas-misconnect.html).

Both actions are part of Agencywide efforts to help manage the risks from medical product use. In the case of medical gas mix-ups, the Agency is using a creative approach (see page 10) to the problem that relies heavily on leveraging and partnering.

Medical oxygen is a prescription drug, and from 1996 to 2000, FDA received reports of

(Continued on page 10)

DTD Launches Gender Differences Course on Internet

CDER reviewers can sign up for a free, online course on gender differences in clinical drug development. The course will help them meet two recommendations of a recent Government Accounting Office report to:

- Consistently and systematically discuss gender differences in their written reviews.
- Determine industry compliance with regulations that mandate presentation of data for women in new drug applications and annual reports for investigational new drugs.

The Women's Health Subcommittee and the Division of Training and Development are offering this new course online over the Internet. CDER's physicians and pharmacists can earn continuing education credit by completing the final exam and course evaluation.

The course developers would like Center reviewers to pilot the course before making it available publicly. After Sept. 17, persons outside FDA will be able to take the course, but CE credit will be unavailable for them.

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State of Center Address Set for Sept. 12 at Shady Grove

BY KAREN ZAWALICK

The Committee for Advanced Scientific Education kicks off the fall semester with the State of the Center address and a rousing game of CDER Jeopardy.

Center Director **Janet Woodcock, M.D.,** will give her annual talk, restricted this year to an internal audience, in the auditorium at the University of Maryland Shady Grove campus, Sept. 12, 1:30 p.m. to 3:30 p.m. Light refreshments are planned prior to the presentation. Continuing education credit will not be offered.

The following week, we welcome John Anderson, Ph.D., research adviser from Eli Lilly, who will present a seminar, "Portfolio Management in the Pharmaceutical Industry: The Eli Lilly Experience." Dr. Anderson will talk at the Corporate and Parklawn locations. See the weekly calendar for details.

The fall semester would be incomplete without our own CDER Jeopardy. Watch office directors and review staff match wits Sept. 26, 1:30 p.m. to 3:30 p.m., in Parklawn Conference Rooms D and E. Due to its interactive nature, this event won't be videoconferenced, and continuing education credit won't be offered.

Seminars and rounds will take place on alternate Wednesdays in Parklawn with videoconferencing to Woodmont II, Corporate Boulevard and Metro Park North II. Watch the weekly calendar of events for upcoming programs or visit the Division of Training and Development's site on CDERnet at http://cdernet/dtd/index.htm.

Karen Zawalick is an educational specialist in DTD and CASE executive secretary.

JOE'S NOTEBOOK

Drug Use Studied in Physician Survey

When Americans visited their doctors' offices in 1999, 66 percent received at least one medication, and nearly 4 percent received one or more of the 104 new molecular entities CDER approved between 1997 and 1999. The data come from a survey of physicians conducted by the National Center for Health Statistics, a part of the Centers for Disease Control and Prevention.

In 1999, an estimated 756.7 million visits were made to doctors' offices in the United States, an overall rate of 278.5 visits per 100 persons. The annual number of visits increased by 19 percent since 1985, but the population-based visit rates have not changed significantly, varying between 270 and 310 visits per 100 persons. About one-half of the visits were to physicians in the primary care specialties of family practice, internal medicine and pediatrics.

Persons 75 years of age and older had the highest rate of physician office visits, 678.7 visits per 100 persons. Trend data from 1985 through 1999 show that the visit rate increased by 22 percent for persons 65 years of age and older, but declined by 19 percent for persons 15–24 years of age.

Medication was the most commonly mentioned therapeutic service in 1999, reported at 500.6 million office visits or 66.2 percent of the total visits. As you might expect given the prevalence of heart disease, the most frequently mentioned medicines were cardiovascular and renal drugs (15.6 percent). These were followed by drugs for pain relief (10.8 percent), respiratory tract drugs (10.4 percent), hormones and agents affecting hormonal mechanisms (9.9 percent), antimicrobials (9.3 percent), central nervous system drugs (8.8 percent), metabolic and nutrient agents (6.6 percent) and skin/mucous membrane drugs (5.7 percent).

Prescription rates didn't vary by sex or race. Diagnoses least likely to result in a drug prescription were routine infant or child health check, normal pregnancy, general medical examination and potential health hazards. Diagnoses most likely to result in the prescription of three or more medicines were hypertension, diabetes mellitus, sinusitis, cardiac dysrhythmias and asthma.

While NMEs accounted for 3.7 percent of all drug mentions in 1999, the percent varied by physician specialty and patient age. There was a positive linear trend between a patent's age and the likelihood of having an NME prescribed. Patients 65 and older were 13 percent more likely than children 15 and younger to have any drug prescribed, 72.0 percent vs. 63.8 percent; but the older patients were 558 percent more likely to have an NME prescribed.

The report notes that dissemination of new drugs may occur for several reasons. These include the prevalence of the disease the drug is intended to treat, dissemination of new information to physicians, changes in patients' care seeking behaviors and the attention given to drugs because of advertising. More than 80 percent of NMEs that were heavily marketed in 1999 were in the top 20 percent ranked by usage. On the other hand, 10 percent of the NMEs that weren't heavily marketed were also in the top 20 percent. Furthermore, the report examined one blockbuster NME that was heavily marketed to consumers and found—unexpectedly—that the trend for patients seeking care for the condition remained unchanged after the drug's introduction. This suggests physicians were turning to the NME in place of older therapies.

The report, *National Ambulatory Medical Care Survey: 1999 Summary*, and other data are available at http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.htm. A neat feature at the site allows you to use a drug's brand or generic name to search the survey database for how frequently it was used.

Correction: Rajeshwari Sridhara, Ph.D., had his name misspelled in the awards story in some early copies of the last issue.

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).

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

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OMBUDSMAN'S CORNER

Reserve Disdain for Supermarket Checkout

BY JIM MORRISON

About the only enjoyment I get from shopping at the supermarket anymore is reading the headlines of the tabloids while waiting at the checkout counter. It's the only way I can catch up on the latest Elvis sightings and the mating habits of extraterrestrials. It's amusing, because the stories are so over the top that they don't threaten my smug comfort in my own knowledge base.

Reading serious scientific publications, on the other hand, can be an unsettling experience. Every new issue of *Scientific American* pokes a few more holes in my intellectual armor, which by now has more patches than the Mir space station before it burned up in the atmosphere.

We like to think that we are enlightened and open to new ideas. After all, that is the essence of science. We in CDER frequently express our openness to and nurturing of new concepts in drug development. But on an individual level, when new ideas clash with our personal concepts of reality, problems can arise.

It's easy to understand why we are loath to abandon old ideas for new ones. A lot of our inner tranquility and peace of mind comes from a confidence that we know certain things about how the world works. Then someone comes along and pulls a loose thread in the fabric of our knowledge. We see our protective clothing start to unravel, and we react defensively. This phenomenon is universal. Consider, for example, how long the Australian researcher, Barry Marshall, had to struggle to get the international medical community to accept his proof that *H. pylori* causes most ulcers.

When we come upon a new therapeutic entity, it's only natural to try to fit it into the fabric of our previous experience. It's unrealistic to expect that we can deduce the mechanism of action of such a new entity, but we all try. We try despite knowing that many drugs make it all the way through development to approval and marketing, and we still don't have a clue about their mechanisms of action.

Clearly, an investigational new drug should not be put on clinical hold simply because the reviewing division finds the drug's postulated mechanism of action implausible. However, it wouldn't be totally irrational to argue that if a proposed remedy cannot possibly work, and if it carries any risk, then it is unreasonable to allow patients to be exposed to it. But if the assessment that it cannot work is erroneous, then it is unreasonable not to allow patient exposure to it for clinical studies.

Thus, the difference between a drug regulator being a heroic public protector or a dangerous obstruction to the public health can be the quality of his or her knowledge. Unfortunately, it is one of life's persistent truths that we all know substantially less than we think we know.

There is a lot of room for judgment in drawing regulatory lines and in weighing benefits and risks. In using our judgment, we inevitably involve our own values and biases. We can't eliminate them, but we can be aware of them and keep them from exerting an inappropriate influence on our decision making.

We must be careful that our own views and biases about a new drug don't color risk-benefit decisions, not only in initial Phase I trials, but throughout the drug review and regulatory processes as well.

Jim Morrison is the Center's ombudsman.

Thompson Says Safety Problems Make Drug Reimportation Unfeasible

HHS Secretary **Tommy G. Thompson** told Congress on July 10 that the safety of prescription drugs could not be adequately guaranteed if drug reimportation were allowed under the Medicine Equity and Drug Safety Act. In a letter to Sen. James Jeffords of Vermont, Thompson said the law enacted last year cannot be implemented because of safety concerns.

A provision of the law required the HHS secretary to determine that adequate safety could be maintained and that costs would indeed be expected to be reduced significantly. Thompson's finding concluded that neither condition could be adequately assured.

A copy of the letter and the two detailed analyses of risks and costs are available at http://www.fda.gov/oc/po/thompson/medsact.html.

Moving from the current "closed" distribution system with relatively few importers to an "open-border" distribution system would significantly increase the risk that counterfeit, misbranded and adulterated drugs would show up on U.S. drug store shelves and in American homes.

It would not be possible to maintain the same level of drug supply protections in place today even with the law's requirements for chain-of-sales documentation, drug product sampling and product testing.

"I believe very strongly that seniors should have access to affordable prescription drugs," Secretary Thompson said in his letter. "However, I do not believe we should sacrifice public safety for uncertain and speculative cost savings."

Reimportation of prescription drugs by pharmacies and drug wholesalers would remove products from the thorough safety and effectiveness monitoring overseen by FDA, Thompson found.

"Opening our borders as required under this program would increase the likelihood that the shelves of pharmacies in towns and communities across the nation would include counterfeit drugs, cheap foreign copies of FDA-approved drugs, expired drugs, contaminated drugs and drugs stored under inappropriate and unsafe conditions," he said in the letter.

The law would allow prescription drugs manufactured in the United States and exported to certain foreign countries to be reimported from those countries for sale to American consumers.

The law was based on the hope that lower pricing of drugs by those countries would be passed on to American consumers for drugs that were manufactured in the United States and, therefore, had met strict FDA safety and effectiveness standards.

EQUAL OPPORTUNITY CORNERS

My Struggles, Joys in Starting a New Life in America

This article is adapted from a speech that received the Best Speaker Award at the Aug. 14 meeting of the Parklawn Toastmasters Club.

BY SU YANG, R.N., MSN

I would like to share my struggles and joys experienced as a first generation immigrant in the land of opportunity. My family, which consisted of my husband and my two toddler children, immigrated into this country in early '70s from South Korea. Some of the reasons we came here were to have a better life, to give our children a better opportunity and to see another part of the world.

Having lived in a small homogenous country like Korea, I found America to be an eye opener. The country was so big and beautiful. It was very interesting to me to see all kinds of people—black, white, native Americans and people from all over the world.

After the first honeymoon period was over, I started to experience a reality shock—a culture shock. Even though my husband and I had a college education back home and read and write some English, we spoke very limited English. Like the majority of the first-generation immigrants, especially with the lack of language skills, we didn't have much choice in the job market. Consequently, my husband started to work at a construction site. I stayed home to take care of my children.

As my children approached school age, I was going through a soul-searching process as to what I should do for the rest of my life. I was so naïve. I thought that my shyness and fear of speaking would go away by coming to this country. Instead, the problem was more intense due to the language barrier.

One day, I took my children to the local library to check out children's books. Strangely, Norman Vincent Peale's book, *The Power of Positive Thinking,* which I had never heard about, came to my attention. I checked the book out and started to read it the same day. Even though I was not deeply religious, the book inspired me so much. It gave me the courage to jumpstart my life again.

After much consideration and prayer, I decided to become a nurse. I had to start from scratch. I needed to have a high school diploma from this country to get into nursing school. The Montgomery County adult education classes helped me pass the examination.

It seemed that I had solved one problem and faced another even bigger and tougher. I entered nursing school but was unable to understand half the lectures. The classes were very intense. At that point the idea came to me that I should tape the lectures. I listened and relistened to the tapes at home, in the kitchen, in the bathroom and in the car.

The Parklawn Toastmasters Club meets Tuesdays at noon in Conference Room C. The club provides a mutually supportive and positive learning environment. Every member has the opportunity to develop communication and leadership skills, which in turn foster self-confidence and personal growth.

I began to understand the lectures and loved to learn about our bodies and minds. I became a registered nurse, obtained a bachelor of science in nursing and eventually a master of science in nursing.

I took care of patients with all kinds of conditions such as cancer, stroke, diabetes, AIDS, heart disease and eye problems. Along with nitty-gritty chores in nursing, I gave instructions to patients about their treatments, medication regimens and the prevention of diseases through a healthy lifestyle. I've enjoyed working as a nurse especially helping people to get better.

After 20 years of nursing including 14 years at the National Institutes of Health and an Excellence in Patient Care Award from the NIH Nursing Department, I felt I had paid my dues. I wanted to experience something else.

I began working in CDER last year as a regulatory health project manager, and I love the job so much. I like to learn new things especially the new drug development and review process even though it's challenging to learn all kinds of drug laws and regulations.

All my children completed college and are now working as productive citizens. My son got married. My husband and I will have our 33-year wedding anniversary this year. I love my adopted country. I thank God and the American people, especially for those who worked hard to establish this great nation of immigrants.

Su Yang works in the Division of Metabolic and Endocrine Drug Products.

Students with Disabilities Join CDER Workforce for 4th Summer

BY GLORIA MARQUEZ SUNDARESAN

For the fourth consecutive year, CDER has successfully participated in the High School/High Tech summer program. This year, like the previous years, we are able to place all three students assigned to CDER by Cerebral Palsy Inc.:

- **David Coleman,** Office of Generic Drugs.
- **Carl Joyce,** Advisory and Consultants Staff.
- **Steven Reinwall,** Division of Training and Development.

CDER directors who participated this year were **Gary Buehler,** OGD, **Janice Newcomb**, DTD, and **John Treacy**, ACS.

The volunteers who supervised and mentored the students were:

- OGD—**Robert L. West, John F. Grace, James T. Barlow, Angela Payne, Debra M. Catterson,** and **Charles V. Hoppes**.
- OTCOM—**Jennifer Snellings, Amy B. Mason, Elizabeth McCarthy** and **Chris Nguyen**.
- ACS—**Igor Cerny, Donna Anderson** and **John B. Schupp.**

The EEO Staff is grateful to all for helping make this year's program successful.

In addition, hiring HS/HT students helps count toward the number of persons with disabilities CDER must hire to comply with an executive order on hiring persons with disabilities.

When we started the program, it took me many months to convince managers

(Continued on page 5)

INFORMATION TECHNOLOGY CORNER

Outlook Calendar Coming to CDER

OIT has received many queries concerning the use of the Outlook calendar. The current standard is the Russell Calendar Manager.

Starting Jan. 1, however, the Center standard calendar system will be Outlook. You should plan on scheduling all your meetings taking place after Jan. 1 in Outlook.

In order to become familiar with the calendar feature, we encourage you to take a look and try out some of the features. Please wait to schedule official meetings in Outlook until the migration has started, as meetings will appear in some calendars but not in others. Training and demonstrations for Outlook calendar will be offered beginning mid-September.

Please check the OIT intranet (http://oitweb) for more information.

FormFlow 99

FormFlow 99 is a Web-based advancement from DVision Forms, CDER's current DOS-based forms package. FormFlow offers increased accessibility and ease of use when filling out government forms.

The initial deployment of FormFlow is intended to replace and mimic what is currently found in DVision Forms. Forms are currently being converted to this new format, and OIT plans on having all current forms, with the exception of certain insurance forms, available by roll-out in October. The Center has purchased a limited number of licenses for the initial implementation and will deploy FormFlow in phases.

Drug Firm Annual Registration

OIT released its third Web-based searchable database on the Internet in July.

The Drug Firm Annual Registration Status query is a database that will be used primarily by industry to check current site registration status and can be found at http://www.fda.gov/cder/dfars/default.htm.

The Food, Drug and Cosmetic Act requires manufacturers, repackers and relabelers to register their establishments with the FDA and submit listing information for all drugs and biological products in commercial distribution.

Annually, firms must re-register, updating and validating current site information.

FDA is currently developing software to make possible the electronic submission of the required registration and listing information for drug and biological products.

Contact **Mary Ann Holovac, R.Ph.** (HOLOVACM) for more information.

Help Desk FAQ

Q: Are there any special e-mail addressing precautions I should take when I switch to Outlook from TeamLinks?

A: Yes. There are distinct differences in designating e-mail addresses and distribution lists in Outlook from what you are used to in TeamLinks.

While addressing e-mails in Outlook will not be a difficult transition, please make sure to observe these practices while you are getting used to the new Outlook system:

- Avoid sending e-mails to live recipients in training. Training accounts are live!
- Double check the e-mail address in the "To:" field. Outlook's e-mail database includes FDA staff outside of CDER. Make sure the name of the person you are sending to is correct.
- Be careful when clicking to move ahead with your message. Unlike TeamLinks, Outlook will not ask you to confirm each address.
- Attend the training.

These precautions will help you avoid any e-mail addressing problems during the transition. Please contact the Help Desk for more information.

September IT Training

Monday	Tuesday	Wednesday	Thursday
3	4	5	6
10 Word Intro (C) 1:00 – 4:00	11 Word Formatting (C) 9:00 – 12:00 MS Outlook (Reserved) (P) 9:00 – 12:00 JMP Session I (C) 1:00 – 4:00 MS Outlook (Reserved) (P) 1:00 – 4:00	12 DFS (C) 9:00 – 12:00 MS Outlook (Reserved) (P) 9:00 – 12:00 MS Outlook (Reserved) (P) 1:00 – 4:00	13 Word Tables (C) 9:00 – 12:00 MS Outlook (Reserved) (P) 9:00 – 12:00 MS Outlook (Reserved) (P) 1:00 – 4:00
17	18 MS Outlook (Reserved) (P) 9:00 – 12:00 JMP Session II (C) 1:00 – 4:00 MS Outlook (Reserved) (P) 1:00 – 4:00	19 MS Outlook (Reserved) (P) 9:00 – 12:00 MS Outlook (Reserved) (P) 1:00 – 4:00	20 MS Outlook (Reserved) (P) 9:00 – 12:00 MS Outlook (Reserved) (P) 1:00 – 4:00
24	25 MS Outlook (Reserved) (P) 9:00 – 12:00 MS Outlook (Reserved) (P) 1:00 – 4:00	26 MS Outlook (Reserved) (P) 9:00 – 12:00 MS Outlook (Reserved) (P) 1:00 – 4:00	27 MS Outlook (Reserved) (P) 9:00 – 12:00 MS Outlook (Reserved) (P) 1:00 – 4:00

Key: Corporate Boulevard (C), Park Building (P)

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

High School/High Tech Has Fourth Success

(Continued from page 4)

and supervisors to give up $1000 to participate in the program. This summer, it took me only a few days to place all the students.

The HS/HT program provides a great experience for CDER employees to work with persons with disabilities. Our employees become comfortable dealing with co-workers with disabilities and grow accustomed to the idea that disabilities are not a hindrance to one's ability to contribute to a diverse and productive workforce.

Gloria Sundaresan is a member of the Center's EEO Staff and coordinates the HS/HT program for CDER.

DTD Honors 165 Volunteers for Teaching 29 Courses in 2000-2001

By Chris Nguyen

The Division of Training and Development's annual awards ceremony honored 165 volunteers. They donated their time and effort to develop and teach the 29 courses for CDER staff that DTD offered last academic year.

The event, held in June in Gaithersburg, was DTD's way of thanking the course instructors, organizers and speakers for all their hard work. Opening remarks at the ceremony were provided by **Janice Newcomb,** DTD's director and **Nancy Smith, Ph.D.,** director of the Office of Training and Communications.

The courses and instructors were:

New Employee Orientation: **Thomas Abrams, R.Ph., MBA, Laura Bradbard, Magdalene D. Carolan, M.S., MSLS, Roy Castle, Heather Chafin, Nichelle Cherry, Lois Chester, MLS, Jean-Ah Choi, Pharm.D., Mike Jones, Deborah L. Kallgren, Karen Kapust, MLS, Lana Kostecka, Kathryn W. Kruse, MLS, Buck Ledford, Andrea Masciale, Wayne H. Mitchell, Brian Pendleton, Crystal Rice, Terri F. Rumble, Ellen Shapiro, Ted Sherwood, John Simmons, Ph.D., Sally Winthrop** and **Robert Young.**

New Reviewers Workshop: **Funmilayo O. Ajayi, Ph.D., FCP, Fred K. Alavi, Ph.D., Hamid R. Amouzadeh, Ph.D., Debra E, Boxwell, Pharm.D., Magdalene D. Carolan, M.S., MSLS, Igor Cerny, Pharm.D., Nichelle Cherry, Kim Colangelo, Susan M. Cruzan, Gregory Davis, Bonnie B. Dunn, Ph.D., Antoine El-Hage, Ph.D., Amy L. Ellis, Ph.D., Joe Hanig, Ph.D., Mark S. Hirsch, M.D., Dena Hixon, M.D., Everett H. Jefferson Sr., Linda M. Katz, M.D., MPH, Margie Kober, R.Ph., Kathleen Kolar, Kofi A. Kumi, Ph.D., Randy Levin, M.D., Sheldon Markofsky, Ph.D., Frederic J. Marsik, Ph.D., ABMM, Kathrin L. McConnell, M.S., Kate Meaker, M.S., Jim Morrison, Nancy L. Muir, MLS, Hasmukh B. Patel, Ph.D., Lana L. Pauls, MPH, Lisa Rarick, M.D., Nancy Smith, Ph.D., Lisa L. Stockbridge, Ph.D., Anne Trontell, M.D., MPH, Michael J. Verdi** and **Janet Woodcock, M.D.**

Leadership Development Skills: **Bonnie B. Dunn, Ph.D., Roswitha Kelly, M.S.,** and **Lana L. Pauls, MPH.**

Presenting at Advisory Committee Meetings: **Heather Chafin, Mark S. Hirsch, M.D., Susan Honig, M.D., Lana Kostecka, Gemma Kuijpers, Ph.D., Marianne Mann, M.D., Andrea Masciale, Joy Mele, M.S., Michael Ortwerth, Ph.D., Lisa Rarick, M.D., Kathleen R. Reedy, R.D.H., M.S.,** and **Kimberly Littleton Topper, M.S.**

Basic Concepts for the Non-Reviewer: **Mike Jones, Mary Kremzner, Pharm. D., Brian Pendleton, Rebecca Redman, Pharm.D., Evelyn M. Rodriguez, M.D., MPH, John Simmons, Ph.D.,** and **Margaret Tart.**

An Introduction to the Center for Drug Evaluation and Research—CDER 101: **Nicholas Buhay, Jean-Ah Choi, Pharm. D., John Dietrick, Eric P. Duffy, Ph.D., Antoine El-Hage, Ph.D., John Friel, J. D., David J. Graham, M.D., MPH, Nancy Haggard, MPH, Debbie Henderson, R.N., MSN, Carol Holquist, R.Ph., Deborah L. Kallgren, David Lepay, M. D., Ph.D., Norman Marks, M.D., M.H. A., Justina A. Molzon, M.S., Pharm., J. D., Andrea Neal, D.M.D., MPH, Toni Piazza-Hepp, Pharm.D., Barry W. Poole, R.Ph., Terri F. Rumble, Ellen Shapiro, Ted Sherwood, Nancy Smith, Ph.D., Kimberly Littleton Topper, M.S., Marcia Trenter, Sally Winthrop, Janet Woodcock, M.D., Stan W. Woollen** and **Deborah Yaplee.**

FDA/DIA Overview of the Pharmaceutical Industry: An FDA-Industry Dialog on the Drug Development Process: **Susan Allen, M.D., MPH, LCDR James Lindsay Cobbs, Lisa Rarick, M.D.,** and **Nancy Smith, Ph.D.**

FDA/AAPS Workshop on Biopharmaceutics Classification System—Guidance and Implementation: **Mei-Ling Chen, Ph.D., Dale P. Conner, Pharm.D., Ajaz S. Hussain, Ph.D., Lawrence Lesko, Ph.D., Hank Malinowski, Ph.D., Mehul Mehta, Ph.D., Vinod P. Shah, Ph.D.,** and **Helen Winkle.**

Foreign Regulator Series: **Joseph J. DeGeorge, Ph.D., Justina A. Molzon, M.S. Pharm., J.D.,** and **Janet Woodcock, M.D.**

Postmarketing Commitments Policy Training: **LCDR James Lindsay Cobbs, Lisa Rarick, M.D.,** and **Leah Ripper.**

Statistical Approaches to Establishing Bioequivalence: **Mei-Ling Chen, Ph.D., Lawrence Lesko, Ph.D., Donald J. Schuirmann** and **Helen Winkle.**

Bioavailability and Bioequivalence Studies for Orally Administered Drug Products—General Considerations: **Funmilayo O. Ajayi, Ph.D., F.C.P., E. Dennis Bashaw, Pharm.D., Mei-Ling Chen, Ph.D., Barbara Myers Davit, Ph.D., Andre J. Jackson, Ph.D., John A. Lazor, Pharm.D., Lawrence Lesko, Ph.D., Chandra Sahajwalla, Ph.D., Vinod P. Shah, Ph.D.,** and **Helen Winkle.**

Successful Meetings/Minutes: **Julieann DuBeau, R.N., MSN, Patrick Guinn, Alice Kacuba, R.N., MSN, RAC, Deborah L. Kallgren, Crystal King, P.D., MGA, Judit Milstein, Maureen A. Pelosi, R.Ph.,** and **Jean A. Yager.**

IND course: **Tawni M. Brice, Bronwyn Collier., Deborah L. Kallgren, Andrea Masciale, Melodi McNeil, R.Ph., Robbin Nighswander, R.Ph., M.S., Cathie Schumaker,** and **Matthew Tarosky, Pharm.D.**

NDA course: **Laurie Burke, R.Ph., MPH, Bronwyn Collier, Julieann DuBeau, R.N., MSN, Michael M. Folkendt, Ellen C. Frank, R.Ph., Lisa M. Hubbard, R.Ph., Deborah L. Kallgren, Melodi McNeil, R.Ph., Robbin Nighswander, R.Ph., M.S., Rebecca Redman, Pharm.D., Dave Roeder** and **Cathie Schumaker.**

Videoconferencing Skills Course: **Pam Winbourne.**

Videoconferencing Focal Points: **Jay Black, Joan Broadwater, Mandy Eisemann, Devota D. Herbert, Ayse Hisim, Patricia A. Johnson, Merla Matheny, Jamie Metz, Paul Neff, Delores Pinkney, Laura Riddle, Doris Robinette, Christine Shipe, Richard G. Sponaugle, Ruth Warzala, Pam Winbourne** and **Donnie Wisner.**

Dialog Select Training: **Karen Kapust, MLS.**

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FDA Recognizes Dr. Kelsey's Induction into Women's Hall of Fame

Frances O. Kelsey, Ph.D., M.D., was praised for her courage and influence at a special FDA reception to commemorate her induction last October into the National Women's Hall of Fame (November *Pike).* About 40 currentt and former FDA officials, friends, colleagues and family members attended the ceremony during which she was presented a special citation from Acting Commissioner **Bernard Schwetz, DVM, Ph.D.**

Center Director **Janet Woodcock, M.D.,** noted that Dr. Kelsey, a pharmacologist and physician, has long been honored for her role in blocking approval of the drug thalidomide in the l960s. Dr. Kelsey's refusal to approve thalidomide for use in the United States earned her national recognition, and her work led to strengthened regulation of the pharmaceutical industry.

Dr. Woodcock said that Dr. Kelsey has been an inspiration to many scientists in the Center who "stuck to their guns under great pressure." She said that it was a fitting tribute that so many of Dr. Kelsey's friends were at the ceremony to help her celebrate.

"Role models are harder to come by than a generation ago," Dr. Schwetz said. He recalled that when he was a graduate student in the 1960s, the thalidomide incident had a strong influence on his and others' career choices. "Thalidomide resulted in a lot of us becoming teratologists and helping keep other thalidomides off the market," he said.

Dr. Kelsey said of her induction into the National Women's Hall of Fame in Seneca Falls, N.Y., that she "was awed by what so many women went through." Considering the struggles that many of them faced, Dr. Kelsey said she had both good luck and "good assistants" through her long career.

Also attending the reception were former Commissioner Jane Henney, M.D., former Center Director Carl Peck, M.D., Deputy Center Director **Steven Galson, M.D., MPH,** and **Robert Young,** president of Chapter 282 of the National Treasury Employees Union. The reception was coordinated by **Tanya Abbott.**

Pictures from the reception are at http://www.fda.gov/cder/pike/julyaug-2001.htm#photos.

More information about the National Women's Hall of Fame is at http://www.greatwomen.org.

DTD Honors 165 Volunteers for Teaching 29 Courses in 2000-2001

(Continued from page 6)

Regulatory Science: **E. Dennis Bashaw, Pharm.D., Debra E. Boxwell, Pharm. D., Bronwyn Collier, Antoine El-Hage, Ph.D., Charles P. Hoiberg, Ph.D., Thomas Laughren, M.D., Robert E. Osterberg, Ph.D., Nancy M. Ostrove, Ph.D., Grant Williams, M.D., Steve Wilson, Dr.P.H. (Biostatistics).**

Design, Conduct and Review of Clinical Trials: **Aloka G. Chakravarty, Ph.D., Victor Raczkowski, M.D., M.Sc., Kathy M. Robie-Suh, M.D., Ph.D., Robert J. Temple, M.D., Grant Williams, M.D.,** and **Steve Wilson, Dr.P.H. (Biostatistics).**

Special Topics in Pharmacoepidemiology: Drug Induced Disease: **Syed Rizwanuddin Ahmad, M.D., MPH, Allen Brinker, M.D., M.S., David J. Graham, M.D., MPH, Lois LaGranade, Judy A. Staffa, Ph.D., R.Ph.,** and **Paul Stolley, M.D.**

Overview of Toxicology Pathology: **Elizabeth Hausner, DVM, DABT.**

Basic Statistical Methods: **Ruthanna Davi, M.S., Karen Higgins, Sc.D., Kate Meaker, M.S.,** and **George Rochester, Ph.D.**

Basic Topics in Applied Statistics—Survival Data Analysis: **Kate Meaker, M.S.**

Topics in Applied Statistics—Issues in Design and Analysis of Diagnostic Clinical Trials: **Victor Raczkowski, M.D., M.Sc.,** and **Michael Welch, Ph.D.**

Topics in Clinical Trials: **Susan S. Ellenberg, Ph.D., Thomas Laughren, M.D.,** and **Robert J. Temple, M.D.**

QT Prolongation and Drug Development: **Peter Honig, M.D., MPH, Robert J. Temple, M.D.,** and **Douglas C. Throckmorton, M.D.**

Understanding the Disciplines Involved in Reviewing Drug and Biologic Products for Cancer: **Grant Williams, M.D.**

Health Related Quality of Life Measures Workshop: **Judith A. Racoosin, M.D., MPH,** and **Mary Purucker, M.D., Ph.D.**

Chris Nguyen is a training specialist in DTD.

Pike's Puzzler: Guess the Dates

BY TONY CHITE

1. The stethoscope was invented by the Frenchman, Renee Laennec, in:
a. 1779 b. 1819 c. 1879 d. 1902

2. Alexander Graham Bell invented the telephone in:
a. 1876 b. 1861 c. 1898 d. 1839

3. The Durham-Humphrey amendment requires prescription only labeling for drugs deemed unsafe for self-medication and that should be used only under a doctor's supervision. It was passed in:
a. 1939 b. 1941 c. 1948 d. 1951

4. The last year in which the Baltimore Orioles won the World Series was:
a. 1979 b. 1983 c. 1987 d. 1949

5. Seattle Slew and then Affirmed won horseracing's Triple Crown in the consecutive years of:
a. 1981 and 1982 b. 1967 and 1968 c. 1989 and 1990 d. 1977 and 1978

6. Microbiologist Selman Waksman discovered antibiotic streptomycin in:
a. 1939 b. 1941 c. 1943 d. 1947

7. The first U.S. dental school, Harvard School of Dental Medicine, was established in:
a. 1901 b. 1898 c. 1859 d. 1867

Key: 1b, 2a, 3d, 4b, 5d, 6c, 7d.

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

Cerivastatin withdrawn, Ribavirin Unbundled, Thyroid Hormone Transition

FDA today announced Aug. 8 that Bayer Pharmaceutical Division withdrew cerivastatin (Baycol) from the U.S. market because of reports of sometimes fatal rhabdomyolysis, a severe muscle adverse reaction from this cholesterol-lowering product. FDA agreed with and supported this decision.

FDA initially approved cerivastatin, in 1997. Fatal rhabdomyolysis reports with cerivastatin have been reported most frequently when used at higher doses, when used in elderly patients and particularly, when used in combination with gemfibrozil, another lipid lowering drug.

FDA has received reports of 31 U.S. deaths due to severe rhabdomyolysis associated with use of Baycol, 12 of which involved concomitant gemfibrozil use.

More information is on CDER's Website at http://www.fda.gov/cder/drug/infopage/baycol/default.htm.

On July 26, FDA approved a stand-alone package of ribavirin (Rebetol Capsules), an anti-viral drug for use with interferon alfa-2b (Intron A), for the treatment of patients with chronic hepatitis C infection.

In 1998, FDA approved Rebetron Combination Therapy, a combination package containing ribavirin and interferon alfa-2b for injection for treatment of patients with chronic hepatitis C infection who have not had previous interferon therapy or who have relapsed following successful interferon therapy.

This approval was based on Schering's application to provide both Rebetol and Intron A in a single package. Schering Corp. markets both products. The new stand-alone package of Rebetol Capsules provides patients and health care providers with flexibility in adopting individualized ribavirin and interferon-based therapies.

FDA published a guidance for industry July 12 explaining how the Agency plans to handle oral levothyroxine sodium products that are being marketed without an approved application after Aug. 14 of this year. The guidance is available at http://www.fda.gov/cder/guidance/4647fnl.htm.

On Aug. 14, 1997, FDA announced in the *Federal Register* that orally administered levothyroxine sodium drug products are new drugs and that manufacturers who wish to continue marketing these products must submit a new drug application for approval. The Agency based its decision on a history of potency and stability problems with orally administered levothyroxine products. The notice stated that after Aug. 14, 2000, any unapproved levothyroxine sodium drug product on the market would be subject to regulatory action by FDA.

On April 26 last year, FDA extended the deadline to Aug. 14 of this year. As of July 2001, two levothyroxine sodium products have been approved by FDA to treat hypothyroidism.

Unithroid, manufactured by Jerome Stevens Pharmaceuticals, was approved on Aug. 21, 2000. Levoxyl, manufactured by Jones Pharma, was approved on May 25. Now that two products have been approved, FDA is issuing guidance regarding the transition from unapproved to approved products.

Because there is no public health emergency that requires an immediate switch to the approved drugs, FDA has established a gradual phase out of distribution of the unapproved products to allow manufacturers of approved products to scale up to meet demand and to allow adequate time for patients and health care providers to make an orderly transition from unapproved to approved products.

Under the phase out, manufacturers of unapproved oral levothyroxine sodium drug products with NDAs pending as of Aug. 14, 2001, should begin an incremental reduction of the distribution of these products. Manufacturers of unapproved oral levothyroxine sodium drug products who do not have an NDA pending with FDA by Aug. 14, should cease distribution of their products. By August 14, 2003, all distribution of unapproved oral levothyroxine sodium products must cease.

Medical Library Launches Hot Topic InfoWebs to Keep You Up to Date

The FDA Medical Library has created a new CDERnet site called Hot Topic InfoWebs. The site brings together basic background information, on one Web page, that FDA staff can use to stay current on Agency initiatives and subjects of high interest.

Currently, three InfoWebs have been completed on the drugs alosetron (Lotronex), mifepristone (Mifeprex) and oxycodone (OxyContin). The Hot Topic InfoWebs are updated frequently and designed to provide easy access to several full-text electronic resources. You can access this service via the Library's home page on CDER's intranet at http://medlib.cder.fda.gov.

The InfoWebs summarize the issues surrounding the topics and link to relevant FDA Internet and intranet pages, such as major drug information pages, which can be found at http://www.fda.gov/cder/drug/default.htm, and the FDA Daily Clips at http://intranet.fda.gov/clips/. When available, links to the new drug approval package, the *Orange Book*, advisory committee transcripts, press releases and talk papers can be found under the FDA information portion of the InfoWeb.

In addition to FDA sites, the resources on the Hot Topic InfoWebs range from commercial databases that provide full-text information on adverse events to relevant Internet sites, such as the National Library of Medicine's PubMed at http://pubmed.gov and ChemID at http://chem.sis.nlm.nih.gov/chemidplus. Drug InfoWebs typically cover adverse events, chemical information, news and worldwide marketing status of the drug.

Your feedback is critical to making this an effective information tool. Please let the library staff know if this is useful to you and what topics you would like to see addressed. If you have additional suggestions, e-mail **Kathrin McConnell,** the reference and research team leader, (MCCONNELLK).

Gender Differences Course Aims to Improve Review Consistency

(Continued from page 1)

Women's health issues and their implications are important topics for all reviewers. FDA addressed the inclusion of women in clinical drug trials with three documents, a guidance in 1993 and regulations in 1998 and 2000:

- The 1993 guidance recommends that clinical studies include enough men and women to detect clinically significant sex differences in drug efficacy and safety, and that analyses of sex differences should be reported in new drug applications.
- The 1998 rule requires that safety and efficacy data already collected be presented separately for men and women in new drug application summary documents. It also requires the tabulation of the number of study participants by sex in investigational new drug annual reports.
- The 2000 rule allows FDA to halt research programs for drugs for life-threatening conditions if otherwise eligible men or women are excluded from participation in studies based solely on their reproductive potential.

In addition to these documents, the new course addresses:

- Participation of women in clinical studies.
- Pharmacokinetic and pharmacodynamic differences among patients.
- FDA guidance on individualization of treatment.
- Pharmacokinetic issues related specifically to women.
- Clinical protocols.

A two-page job aid is also available from DTD or online at the gender differences course site.

The GAO report and two studies by FDA's Office of Special Health Issues have generally found that women appear to participate in clinical trials at nearly the same rate as men. However, FDA oversight of the industry compliance with the regulations needed improvement.

Attention to gender-related issues by reviewers lacks consistency but should improve with the clinical review template. Both GAO and OSHI found that medical officer reviews had varying amounts of gender related information.

The GAO report is available at http://www.gao.gov/new.items/d01754.pdf.

The OSHI report is available at http://www.fda.gov/cder/reports/womens_health/women_clin_trials.htm.

To access the gender differences course, you'll need to obtain an enrollment access code from DTD's **Jack Morin** (morinj@cder.fda.gov). Then go to http://www.Blackboard.com on the Internet, type "GDCE-100" in the Find a Course box and press Go. Preview or enroll in the course.

Online education offers three benefits:

- You can complete the course at your own pace.
- You can start and stop the lessons as your schedule permits.
- You can access the online course material from your office or home.

If you have questions or would like a gender differences job aid, please contact Jack Morin by e-mail.

Free Online Training Offers Convenient Way to Improve Skills, Knowledge

By James Minter, Ed.D., and Noreen Gomez

CDER offers a free e-learning program that you can take advantage of to enhance your skills and knowledge. The pilot program started in April 2001 and continues indefinitely.

You can access these courses from home or work through your personal computer's Internet connection. The majority of the more than 1,000 courses offered can be completed in about eight hours.

Adults learn best when they can learn exactly what they need at precisely the time they need it. Online and on-demand training offers just that. This precision allows you to apply your newly gained knowledge right away. Immediate application will help you cement the knowledge you gained and improve retention.

Two contractors, Skillsoft and National Education Training Group, provide the 300 training slots CDER purchased for this program. So far, about 120 CDER employees have used this training.

Skillsoft offerings are primarily aimed at those seeking personal development in leadership, management and general office communications. NETg training is focused on information technology with some general skills subjects.

You can sign up for offerings from only one of the contractors.

Skillsoft

Skillsoft has a comprehensive library of more than 330 Web-delivered, self-paced and self-directed courses in topic areas such as communications, personal development and project management. Course listings range from "Succeeding as a First-Time Manager" to "Professional Telephone Skills." The courses can be completed in increments of time as small as 20 minutes.

A pre-assessment of your skills and knowledge in each course creates an individual learning path based on your training needs. End-of-course assessments can help you determine your overall understanding of the content. Each course has online job aids that can be used while taking a course. The aids can be used later as either a quick refresher or for on-the-job support.

Skillsoft's courses are organized into lessons and topics that allow you to get the piece of instruction or support you need, when you need it, for the job-at-hand. You don't have to complete a course to benefit from Skillsoft training.

NETg

NETg's course catalog contains emphasizes information technology subjects with more than 600 courses ranging from "Microsoft Excel 2000 Expert User" to "Novell NetWare User Fundamentals."

In addition, NETg provides courses in 18 general skills subjects such as diversity, leadership development and stress management.

You have one year from the date you sign up to take as many courses as you like. You can sign-up for classes by contacting either of us:

- James Minter (MINTERJ, 7-1448).
- Noreen Gomez (GOMEZN, 7-1261).

James Minter and Noreen Gomez are training specialists in DTD.

CDER Looks to Leveraging to Help Reduce Medical Gas Mix-Ups

(Continued from page 1)

seven deaths and 15 injuries associated with medical gas misconnections that occurred in acute care and nursing home settings. Patients who were supposed to receive medical grade oxygen received a different gas that had been mistakenly connected to the oxygen supply system.

The recent cases were:

- In December 2000, four people were killed and six injured in a nursing home in Bellbrook, Ohio, when a hospital worker connected nitrogen to the oxygen supply system.
- In April 1998, two patients in a hospital in Idaho died after a large vessel of industrial nitrogen was connected to the oxygen system supplying the operating rooms, labor and delivery rooms and emergency room.
- In October 1997, a patient undergoing minor surgery died at a hospital in Nebraska when a vessel containing argon was attached to the oxygen supply system.
- In December 1996, a children's' home in New York reported adverse reactions experienced by nine patients, including two critically injured, from carbon dioxide improperly connected to the oxygen system.

These cases revealed striking similarities. Employees connecting the vessel to the oxygen system were not properly trained and did not understand that the connectors for oxygen vessels are specially fitted so they are compatible only with oxygen delivery systems.

When the employees discovered, correctly, that they were unable to connect the wrong vessel to the oxygen system, they removed a fitting from an empty oxygen vessel and installed it on the incorrect vessel.

Prior to installing the wrong vessel to the oxygen supply system, employees making the connection did not examine the drug label applied to the cryogenic vessel to ensure that the product was medical oxygen.

For **David Horowitz,** acting director of the Office of Compliance, the incident in December was the last straw. In March, Horowitz established the Medical Gas Mix-Up Working Group, which includes representatives from CDER, CDRH and the Office of Regulatory Affairs.

The group has developed a plan that involves outreach to all of the relevant audiences, not just medical gas manufacturers. For example, using CDER's April guidance as the basis, the group asked more than two dozen health-care associations and organizations to post the advisory on their Web sites and include information about medical gas mix-ups in their newsletters.

The group worked with the Joint Commission for Accreditation on Healthcare Organizations, which issued a sentinel event alert on the problem at the end of July. Combined FDA-JCAHO mailings and e-mails total more than 100,000.

Members of the working group are working closely with Centers for Medicare and Medicaid Services (formerly HCFA), the Community Health Accreditation Program and the U.S. Pharmacopoeia to identify actions they can take in support of this effort.

All of these organizations have been enthusiastic about helping FDA tackle this issue. They know about the problem and are pleased that FDA is trying to do something about it. As of July, information on the risks of medical gas mix-ups could be found on 15 Web sites.

The Agency also is exploring ways to reduce, if not eliminate, medical gas mix-ups. Several practices that may contribute to continuing medical gas mix-ups are being addressed in a proposed rule:

- Many of the large vessels used to contain medical gases do not have permanently soldered or welded connections.
- Some medical gas vessels are not labeled using the 360-degree wrap-around tape that makes them easily distinguishable from vessels containing industrial grade gases.
- Separate storage areas often are not provided either in the delivering vehicle or at the receiving facility to sufficiently separate medical grade products from industrial grade products.

Because medical gases are prescription drugs, all medical gas manufacturers who receive reports of death or serious injury associated with their use are required to report them to the FDA.

Center contacts on the working group include **Pam Schweikert** (ORA), **Paula Simenauer** (CDRH) and **Duane Sylvia** (CDER).

Nancy Derr is a policy analyst on the Regulatory Policy Staff and spends a couple of days each week working on the medical gas mix-up project.

Medical Gas Working Group Uses Harvard Guru's Regulatory Approach

The Medical Gas Mix-Up Working Group is following recommendations for problem solving discussed by Malcolm K. Sparrow in his book, *The Regulatory Craft, Controlling Risks, Solving Problems and Managing Compliance*. The book was copublished last year by the Council for Excellence in Government and the Brookings Institution Press.

Sparrow is a professor of the practice of public management at Harvard's John F. Kennedy School of Government. His research interests include regulatory and enforcement strategy, fraud control and risk management and analysis

Sparrow recommends that agencies "pick important problems and fix them." He encourages regulators to move into unfamiliar areas and focus on the most important problems.

Sparrow believes we need regulations, but we also need to apply discretion and common sense. He advocates a very simple approach to problem solving:

- Nominate a problem.
- Define the problem precisely.
- Determine how to measure impact.
- Develop interventions.
- Implement the plan.
- Periodically monitor and adjust.
- Close the project.

Sparrow's concepts have been used successfully at other federal agencies, including the U.S. Customs Service, the Occupational Safety and Health Administration and the Environmental Protection Agency.

—Nancy Derr