news along the pike

DECEMBER 2003

CENTER FOR DRUG EVALUATION AND RESEARCH

VOLUME 9, ISSUE 6

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PIKE'S CORNERS . . .

Center conducts Fall Honor Awards ceremony

62 individuals, 39 groups recognized during November event

BY JACKIE BARBER-WASHINGTON

At the Center's Fall Honor Awards ceremony held Nov. 21 in Gaithersburg, 62 individuals and 39 teams were recognized. Acting Center Director **Steven K. Galson, M.D.,** and CDER's senior managers presented the awards. Award recipients and their guests were entertained by a musical prelude performed by the PHS Wind Ensemble (page 3). Kevin Barber sang the national anthem; and **John L. Emelio,** the director of the Division of Management Services in the Office of Management, was master of ceremonies.

In opening remarks, Dr. Galson praised the awardees for their hard work and contributions to the public health and the Center's mission.

The awards were:

FDA Outstanding Service Award

Herbert Gerstenzang

Roger C. Gregorio

Peter H. Hinderling

Rajeshwari Sridhara, Ph.D.

Toni Piazza-Hepp, Pharm.D.

Iris D. Khalaf

Judith A. Racoosin, M.D., MPH

CDER Best Pharmaceuticals for Children Virtual Team: **Rosemary Addy, Robert D.**

(Continued on page 6)

OCPB holds retreat; detailed to Center director's office

BY ROBERT SHORE, PHARM.D.

Nearly 80 reviewers and staff from the Office of Clinical Pharmacology and Biopharmaceutics, representing all three divisions of pharmaceutical evaluation and the immediate office, attended a one-and-a-half day, off-site retreat on Sept. 25 and 26.

During her keynote address at the retreat, Center Director **Janet Woodcock, M.D.,** announced that our office would be detailed to her office to link our scientific expertise to clinical evaluation earlier in the drug development process.

In her address, "Vision for CDER and OCPB's Role," Dr. Woodcock indicated that scientific discovery has generally increased in such areas as nanotechnology, pharmacogenetics and structural biology. The drug development process, however, has not kept pace with this progress. She said that the structure of—and processes within—CDER will have to be modified to accommodate this revolution in science.

OCPB, she said, is a "significant scientific force throughout the Center" and has expertise in dealing with scientific advances. Currently, Dr. Woodcock said, the clinical drug development process is mostly empirical: dose and observe.

(Continued on page 10)

Center proposes End-of-Phase 2A meeting to ID optimal doses

BY LARRY LESKO, PH.D.

Making better use of data collected early in drug development could help sponsors avoid some pitfalls that lead to either an extra cycle of review or Phase 4 commitments. CDER is undertaking a pilot program to discuss this early data with drug sponsors voluntarily at an End-of-Phase 2A meeting. We anticipate holding about two such meetings a month during a two-year evaluation period.

The hypothesis for this proposal is that meetings with sponsors early in the drug development process will focus greater attention on the analysis, in particular, of exposure-response data. We think this will improve dose selection and study design for subsequent clinical trials.

The End-of-phase 2A meeting occurs when we have sufficiently complete data from preclinical pharmacology studies, exposure-response studies in healthy volunteers and drug-dose tolerance studies. At that time, we also have some initial efficacy or proof-of-

(Continued on page 10)

JOE'S NOTEBOOK

IOM calls data standards crucial to safety

To significantly reduce the tens of thousands of deaths and injuries caused by medical errors every year, a new report from the Institute of Medicine says that health care organizations must adopt information technology systems that are capable of collecting and sharing essential health information on patients and their care. These systems should operate seamlessly as part of a national network of health information that is accessible by all health care organizations, including:

- Electronic records of patients' care.
- Secure platforms for the exchange of information among providers and patients.
- Data standards that will make health information uniform and understandable to all.

"It is time to shift the emphasis of patient safety programs from a strategy of reporting—focused on injuries after they have occurred—to one of prevention aimed at providing safe and effective care in the first place," said committee chair Paul Tang, chief medical information officer of the Palo Alto Medical Foundation in California.

Routine use of electronic health records would give health care providers and patients immediate access to complete patient information as well as tools to guide decision-making and help prevent errors. However, without standards for how and what data is collected, the different systems used in various organizations may not be compatible. The IOM report called for HHS to take the lead in establishing a public-private partnership to develop and promote national health data standards.

The study was sponsored by the Agency for Healthcare Research and Quality. The report, *Patient Safety: Achieving a New Standard for Care,* is available at http://www.nap.edu.

FDA plans regulation prohibiting sale of ephedra

FDA on Dec. 30 alerted the public to its forthcoming determination that dietary supplements containing ephedra present an unreasonable risk of illness or injury, and should not be consumed. The Agency has notified firms manufacturing and marketing these products that it intends to issue a final rule prohibiting their sale, which will become effective 60 days after its publication. FDA took this step after conducting an exhaustive and highly resource-intensive process required under the Dietary Supplement Health and Education Act of 1994 for banning a dietary supplement that presents a significant and unreasonable risk to human health.

To meet this challenging standard, FDA gathered and thoroughly reviewed a prodigious amount of evidence about ephedra's pharmacology; clinical studies of ephedra's safety and effectiveness; newly available adverse events reports; the published literature; and a seminal report by the RAND Corporation, an independent scientific institute. FDA also reviewed tens of thousands of public comments on the Agency's request in February, 2003 for information about ephedra-associated health risks.

The totality of the available data showed little evidence of ephedra's effectiveness except for short-term weight loss, while confirming that the substance raises blood pressure and otherwise stresses the circulatory system. These reactions have been conclusively linked to significant adverse health outcomes, including heart ailments and strokes.

By informing more than 60 dietary supplement firms about the upcoming final rule, FDA is sending a strong and unambiguous signal that dietary supplements containing ephedrine alkaloids present an unreasonable risk. Consumers are urged to stop buying and using these products immediately.

news along the pike

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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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NEWS ALONG THE PIKE
CDER Office of Training
and Communications (HFD-210)
Parklawn Building, Room 12B-31

Editor: Norman "Joe" Oliver (OLIVERN)
Associate Editors: Patrick Clarke,
Christine Parker
Phone: (301) 827-1695
Fax: (301) 827-3055

COMMISSIONED CORPS NOTES

Scientists, medical professionals volunteer musical talents

BY PATRICK E. CLARKE

The talented musicians who played at CDER's Fall Honor Awards Ceremony (page 1) are part of the Public Health Service's Commissioned Corps Ensemble. The 10-member Wind Ensemble was doing the honors that day. There's also a String Ensemble and a Choral Group.

In addition to playing the trumpet, **LCDR Elise Young** from the Health Resources and Services Administration is the lead coordinator of the Wind Ensemble. She said the groups got their start in 2000 as a result of the efforts of **CAPT (Ret.) John Bartko** and the late **CAPT Derek Dunn** and the support of the Scientist Professional Advisory Committee.

"They felt there was a need," Young said. "The other six services had ceremonial bands, and we didn't." More than 75 officers from across the country responded to the call for a Commissioned Corps Ensemble, including vocalists.

CDER members of the Wind Ensemble are **CAPT Paul Hepp,** euphonium, **CDR Charlie Hoppes,** French horn, **LCDR Daryl Allis,** tenor sax, and **LCDR Charlie Lee**, tenor sax.

Members from the Center for Biologics Evaluation and Review are **CAPT Steven Rosenthal,** clarinet, **LCDR Angela Shen,** violin, and **LCDR Barbara Sanchez,** flute. Rounding out the group are **CDR Joseph Despins,** violin, from FDA's Office of Regulatory Affairs, and **CAPT John Bartholomew,** trumpet, from the National Institutes of Health.

"Many of us were musicians in high school and college and also play in community orchestras," Young said. "Some of the officers in the field have bachelor's degrees in music, then went on to scientific fields such as pharmacy."

The Wind Ensemble rehearses in the Parklawn building every other week for about an hour. "We have patriotic and holiday tunes and other pieces that we work on continually," Young said.

She estimates the ensemble has about 20 pieces ready for performance level at any given time. "It can be a challenge because of the mixture of instruments. We frequently have to transpose music to suit our needs," she said.

They've played at FDA and HRSA promotion and award ceremonies, at Commissioned Officer Association meetings and in the lobby of the Parklawn Building.

"To me, our most memorable performance, but most solemn, was when all the ensembles played at CAPT Dunn's memorial service earlier this year," Young said.

For CDR Hoppes, a safety evaluator and pharmacist in the Division of Medication, Errors and Technical Support in the Office of Drug Safety, his most memorable performance was the first, in September 2000. That's because his son was the conductor.

"Back in the early days of the ensemble we found it helpful to have my son Charlie conduct the group," Hoppes said. Father and son, now 16, are still in the same group these days as they both play for the Frederick Orchestra.

Hoppes also points out: "The PHS has its own March, written by George King III of the U.S. Coast Guard."

LCDR Lee, a medical reviewer for the Division of Pulmonary and Allergy Drug Products, said his most memorable performance was playing at the welcome reception for Surgeon General **Richard H. Carmona, M.D., MPH,** and his wife in January 2002.

Lee has been playing the tenor saxophone since he was in the 7th grade.

"I've been playing with the ensemble since March 2002," he said. "I was interested in playing with a group, and the ensemble gives me that chance, plus I'm supporting the Commissioned Corps. And we have a lot of fun."

It can also be hard work, particularly coordinating with instrumentalists out in the field who can join the ensemble when the ensemble is playing as part of a trip, such as a Commissioned Corp conference.

"Fortunately, one of our officers can make music CDs called Music Minus 1," Young said. "You can hear the selection played both with and without your instrument. So, when instrumentalists join us, it's not as if they come in completely cold. Actually, they're like an extended musical family."

Young is hoping the ensemble will be able to play at the Spring Commissioned Officers' Association meeting in Anchorage, Alaska.

And, she'd like to see the group expand. Young and others in the group share a dream of being able to play more. "We always welcome officers who play an instrument or want to sing with the ensembles," Young said.

Meanwhile they perform whenever opportunity and schedules come together, such as their most recent performance playing Christmas music in the fifth floor lobby of the Parklawn Building. Amid the hustle and bustle of people meeting and greeting each other, security guards making announcements and the X-ray machine going off periodically, the group never lost their focus or concentration.

Group members were laughing and joking with each other, particularly over a music stand that refused to stand, and they were quite obviously having fun. But, the songs, such as "Silent Night," "Away in a Manger" and "Joy to the World" kept on coming. And every now and then, someone would stop rushing into the building, listen for a bit and smile.

FDA approves new drug for advanced prostate cancer

FDA on Nov. 25 approved abarelix (Plenaxis) for advanced prostate cancer in patients who have no alternative therapy. The drug is indicated for the treatment of the symptoms of men with advanced prostate cancer who cannot take other hormone therapies and who have refused surgical castration. Because of an increased risk of serious and potentially life-threatening, allergic reactions associated with its use, the drug will be marketed under a voluntary risk management program agreed to and administered by the sponsor that will restrict the use of abarelix to patients with advanced prostate cancer, who have no alternative therapy. About 5 percent to 10 percent of men with prostate cancer have the type of advanced, symptomatic disease that would make them candidates for abarelix.

OCPB SCIENCE DAY

Clinical pharmacologists discuss the impact of 'systems biology'

BY RAY BAWEJA, PH.D., VENKAT JARUGULA, PH.D., SOPHIA ABRAHAM, PH.D., SANDRA SAUREZ, PH.D., ABIMBOLA ADEBOWALE, PH.D., CHARLES BONAPACE, PHARM.D., PATRICK NWAKAMA, PHARM.D, AND LARRY LESKO, PH.D.

The 12th Science Day sponsored by the Office of Clinical Pharmacology and Biopharmaceutics was enthusiastically celebrated with the theme of "Systems Biology" at the University of Maryland, Shady Grove campus on Oct. 3.

Opening remarks

In Science Day opening remarks, Center Director **Janet Woodcock, M.D.,** emphasized the importance of clinical pharmacology and biopharmaceutics and stressed its role in the overall review process. Dr. Woodcock is a strong supporter of efficient drug development but acknowledged that even today this process is quite empirical. She said that this should change considerably with the coming of age of the new science of pharmacogenomics.

A draft guidance document for pharmacogenomic data submissions was issued in November and, when final, should provide great benefit from a scientific and regulatory viewpoint in bringing efficiency to overall drug development procedures.

Keynote address

Stephen Naylor, Ph.D., the keynote speaker and chief scientific officer at PsyCheMonics Corp. in Concord, Mass., gave his presentation on "Systems Biology: Impact on Drug Discovery and Development." He divided his talk into several parts. By defining the study of DNA and RNA as "genomics," the understanding of proteins as "proteonomics" and the metabolic fate of chemical entities as "metabolomics," he set the stage for integrating these emerging sciences.

Genes provide insight into disease mechanisms but, in and of themselves, are not active agents. Proteins and metabolites are causative factors. His presentation was a systematic approach to understanding the role of genomics, proteomics, metabolomics and microchip mass spectrometry. He also discussed the very important role and use of biomarkers and their impact on developing new approaches to drug discovery and development.

He defined "systems biology" as the integrated analysis of genetic, protein, metabolite, cellular and pathway events that are in flux and are interdependent on each other. Thus, systems biology is the amalgamation of all "-omics" where genomic analysis is currently the bright spot. His central theme was integrating all the emerging sciences that are playing a very important role in the overall drug development process.

For each of these "-omics," he showed slides to demonstrate their compositional, structural and temporal complexity. His talk highlighted how expression arrays and mass spectrometry have increased in prominence in biomedical sciences. This, in turn, has made them invaluable technologies for the detection and identification of biopolymers and metabolites derived from complex body tissues and fluids. Thus, in the "-omics" revolution, mass spectrometry has emerged as the premier platform for metabolomic and proteomic analyses.

To be able to understand systems biology, a "perturbation" study is undertaken during drug discovery and development to look for differences between healthy and diseased states. These studies compare genetic makeup, protein differences and metabolites. Thus, systems biology attempts to obtain molecular signatures that will be able to compare healthy or control environments to diseased environments.

Dr. Naylor illustrated this with examples of atherosclerotic drugs. The opportunities for the application of systems biology are endless, he explained, as first there will be a greater understanding of diseases, which in turn will help find novel new drugs. However, he admitted that the practicality of systems biology is that it is "not there yet" as some parts are fertile and advanced, while other seem to be lagging behind. Dr. Naylor concluded by stating that it will take a while for systems biology to mature, just as it will take time for all of the sciences that constitute systems biology to grow and integrate.

Scientific presentations

This year the podium presentations set the theme and included research from individuals who presented on the following topics:

- Early phase exposure-response study aids optimal dosing regimen selection in pivotal trials: A retrospective case study.
- Human microdosing: An innovative approach in the selection of new chemical entities—Concepts and regulatory perspective.
- Rapidly disintegrating/dissolving dosage forms: Regulatory expectations from a clinical pharmacology and biopharmaceutics perspective.
- Scientific and clinical challenges on optimization of dosage regimen of radiotherapeutic drug H.
- Comparison of estimated and measured creatinine clearance: Impact of ideal vs. actual body weight.
- An exposure-risk analysis for Drug X: Possible implications in drug development and lessons learned.
- Quantitative risk-benefit analysis during the regulatory review: A case study.

In addition to podium presentations, individual poster presentations covered a wide variety of issues, including:

- Comparison of confidence intervals derived using four different methods.
- Population pharmacokinetic modeling and simulation-derived dosing of intravenous anticancer drug in pediatric patients.
- Population pharmacokinetic model for a bisphosphonate drug for patients with bone metastases.
- Elimination half life as a tool for predicting the QT prolongation effect of a drug.
- Influencing factors on bioequivalence between IR and MR formulation via simulation.
- Pharmacokinetic and QT interval pharmacodynamics of single intravenous doses of a neuroleptic agent.
- Summary basis for approval of an antiepileptic agent as monotherapy in pediatric patients with partial seizures

(Continued on page 5)

COUNTERTERRORISM CORNER

In 2003, Center approves 3 drug countermeasures to threat agents

BY DIANNE MURPHY, M.D.

In 2003, the Center continued efforts to facilitate the development of new drugs and new uses for already approved drugs that could be used as medical countermeasures to terrorism attacks. Highlights included:

- Approving three drugs.
- Publishing findings of safety and efficacy for Prussian blue and intravenous chelators for exposure to radioisotopes to encourage submissions of NDAs.
- Publishing information on how to dissolve and mix doxycycline tablets for administration to children if pediatric formulations are not available.

In February, the Center announced the approval of pyridostigmine bromide as a pretreatment to increase survival after exposure to Soman "nerve gas" poisoning. The product is approved for combat use by U.S. armed forces. This is the first drug approved under an FDA rule issued in 2002 and frequently referred to as the "animal efficacy rule." The rule allows use of animal data for evidence of a drug's effectiveness when the drug cannot be ethically or feasibly tested in humans.

In June, the Center approved the atropine autoinjector (AtroPen) for use in children and adolescents exposed to certain nerve agents and insecticides. The atropine autoinjector was approved for adult use in 1973.

In September, the Center announced a determination that pentetate calcium trisodium (Ca-DTPA) and pentetate zinc trisodium (Zn-DTPA) are safe and effective, when produced under conditions specified in approved marketing applications, for treatment of contamination with radioactive isotopes of the elements plutonium, americium and curium. The Center is encouraging manufacturers to use these findings to submit NDAs.

In October, the Center approved Prussian blue (Radiogardase) to treat people exposed to radiation contamination from harmful levels of cesium-137 or thallium. The NDA for this drug was sent in response to an announcement in January 2003 that Prussian blue would be safe and effective for this indication when produced under conditions specified in approved marketing applications.

Because stockpiled tablets of doxycycline may be provided to parents to treat children exposed to inhalational anthrax, the Center published instructions on the World Wide Web on how to dissolve the tablets and mix them with food or drinks to make them palatable to small children.

The Center has continued its collaboration with the National Institute of Allergy and Infectious Diseases and the U.S. Army Medical Research Institute of Infectious Diseases to investigate the use of gentamicin and other therapies for the treatment of pneumonic plague.

Natural history, pharmacokinetic and toxicology studies were performed to support planned efficacy studies utilizing a non-human primate model of pneumonic plague.

More information on last year's activities is available on our Web site at http://www.fda.gov/cder/drugprepare/default.htm.

Dianne Murphy is director of CDER's Office of Counter Terrorism and Pediatric Drug Development.

'Systems biology' seen as integrating emerging sciences

(Continued from page 4)

without the need for controlled clinical trials.

- Establishing key clinical pharmacology and biopharmaceutics principles for orally disintegrating tablets: Formation of an OCPB working group.
- Echinacea alters cytochrome P450 activity *in vivo.*
- Effect of St. John's Wort on oral contraceptive efficacy.
- Changes in urinary tract drug exposure as a function of renal impairment: Dosage adjustment for patients with renal impairment.
- Physical and dissolution stability evaluation of suspensions of sustained-release spheres prepared using fluid bed coater.
- Experience with evaluating QT prolongation data.
- Disease progress models for simulation that employ the American College of Rheumatology 20 percent Improvement Criterion, ACR20, in patients with rheumatoid arthritis using logistic regression analysis.
- Critical evaluation of handheld electronic prescribing guides for physicians.
- Palmitoylation regulates regulator of G-protein signaling 16 function.
- Mechanism of differential induction of CYP3A4 by paclitaxel and docetaxel.
- Modulation of drug metabolism and drug efflux pathways: A review of effects of inhibition and induction of CYP3A4 and PgP on substrate drug disposition.
- *In-vitro* release test methods and specifications for depot injectables: An NDA survey.
- Cellular uptake and efflux of the tea flavanoid epicatechin gallate in the human intestinal cell line CaCO-2.

Puzzle key: 1c; 2i; 3h; 4f; 5a; 6b; 7j; 8e

Larry Lesko, Ph.D., the OCPB director, in his introductory remarks stated that the main goal of Science Day all along has been to share and exchange the latest scientific information and ideas among clinical pharmacologists. Science Day, which began in 1996, features both podium and poster presentations, a lecture from a distinguished scientific guest speaker, and participation by all in the "Science Funstation" game.

Over the years, the event has seen participation of clinical pharmacologists from Uniformed Services University, Office of Generic Drugs, CBER, Center for Drug Development Science at Georgetown and the National Institutes of Health. To date, there have been about 200 scientific presentations, including seven podiums and 20 posters this year.

The finale of the day was the participation by all in Science Funstation, a team-based game that challenged everyone's knowledge of clinical pharmacology. Teams were formed of about 25 individuals each. It was a very close race to the finish and fun was had by all.

The authors are all members of OCPB.

CDER's Fall Honor Awards ceremony held in Gaithersburg

(Continued from page 1)

Barnie, Debra L. Birenbaum, M.D., ShaAvhree Buckman, M.D., Grace N. Carmouze, Nancy S. Chang, M.D., Susan K. Cummins, M.D., Vickie Kao, Abraham M. Karkowsky, M.D., Russell G. Katz, M.D., Zelda R. McDonald, Cecelia M. Parise, Rosemary Roberts, M.D., William J. Rodriquez, M.D., Hari C. Sachs, M.D., and **Douglas C. Throckmorton, M.D.** PHS Outstanding Unit Citation: **CDR Terrie L. Crescenzi, CAPT Philip H. Sheridan** and **CDR Jacqueline H. Ware.**

Prussian Blue Federal Register and Outreach Team: **Jane A. Axelrad, J.D., Laura Bradbard, Yuan-Yuan Chiu, Ph.D., Young Moon Choi, Ph.D., Bronwyn E. Collier, David J. Cummings, Eric P. Duffy, Ph.D., Maureen A. Hess, MPH, Joanne M. Holmes, Florence Houn, M.D., Kyong A. Kang, R.Ph., Adebayo A. Laniyonu, Ph.D., John K. Leighton, Ph.D., Brad G. Leissa, M.D., Eldon E. Leutzinger, Ph.D., Sally A. Loewke, M.D., Patricia Love, M.D., Theresa M. Martin, Wayne H. Mitchell, M. Diane Murphy, M.D., David A. Place, Ph.D., Rosemary Roberts, M.D., Alfredo R. Sancho, Ph.D., Orhan H. Suleiman, Ph.D., Michael E. Welch, Ph.D.,** and **Robert J. Yaes, M.D.** PHS officers nominated for PHS companion award: **LCDR Mary E. Kremzner, CAPT Sandra L. Kweder, CDR Mitchell V. Mathis Jr.,** and **CAPT Mary E. Purucker.**

FDA Group Recognition Award

Division of Library and Information Services Acquisitions Group: **Colleen A. Pritchard** and **Elizabeth C. Smith.**

Division of Library and Information Services, Drugs@FDA Web Project Team: **Carol S. Cavanaugh, Paul K. Stauffer, Monica A. Unger, Sally Winthrop** and **William B. Woodard Jr., Ph.D.**

Part 11 Team: **Patricia M. Beers-Block, Alieen Ciampa, Nancy E. Derr, Joseph D. Doleski, Joseph C. Famulare, Erik N. Henrikson, Scott J. MacIntire, Terry M. Martin, Nicole K. Mueller, John F. Murray, George R. Smith, Vernon D. Toelle, Sonal Vaid, Randy L. Woods, Sion Wyn** and **JoAnn Ziyad.**

Prilosec Review Group: **Mark I. Avigan, M.D., Julie G. Beitz, M.D., Wen Jen Chen, Ph.D., Jasti B. Choudary, Browyn E. Collier, Helen Cothran, Walter J. Ellenberg, Ph.D., Melissa H. Furness, Charles J. Ganley, M.D., Hugo E. Gallo-Torres, M.D., Ph.D., Dave Hilfiker, Florence Houn, M.D., Robert L. Justice, M.D., Linda M. Katz, M.D., Daniel Keravich, R.Ph., Joyce A. Korvick, M.D., MPH, Karen J. Lechter, Ph.D., Andrea Leonard-Segal, M.D., Thomas J. Permutt, Ph.D., Mary S. Robinson, Timothy W. Robison, Arthur B. Shaw, Ph.D., Daiva Shetty, M.D., Maria R. Walsh, Maria E. Ysern, Ph.D.,** and **Liang Zhou, Ph.D.** PHS officer nominated for PHS companion award: **CDR Laura E. Shay.**

FDA Leveraging/Collaboration Award

Anthony A. Charity

Post-Anthrax Event Treatment Outcome Team: **Debra E. Boxwell, Joanne M. Holmes, Brad G. Leissa, M.D., Stella G. Machado, Lewis K. Schrager, M.D., Douglas N. Shaffer, M.D., Sara J. Singer, Mary E. Willy** and **Juan Zhang.**

Center Director's Special Citation

Mark J. Goldberger, M.D., MPH

Shirley J. Murphy, M.D.

Lilia Talarico, M.D.

CDER Special Recognition Award

John J. Alexander, M.D., MPH

Maria A. Dorantes, Ph.D.

Joseph P. Hanig, Ph.D.

Charlotte M. Henning

Parinda Jani

Myong-Jin Kim, Pharm.D.

Thomas A. Marciniak, M.D.

Lisa K. Naeger, Ph.D.

Nrapendra Nath, Ph.D.

Sandra Suarez-Sharp, Ph.D.

Sally U. Yasuda, Pharm.D.

Jenny H. Zheng, Ph.D.

Estratest Working Group: **Susan S. Allen, M.D., MPH, Albinus M. D Sa, Ph.D., Joseph C. Famulare, Brenda S. Gierhart, M.D., Ada Irizarry, Donna A. Katz, William McConagha, Lana L. Ogram, David T. Read** and **Christine F. Rogers.**

Midazolam Quality Team: **Arup K. Basak, Ph.D., Vilayat A. Sayeed, Ph.D.,** and **Glen J. Smith.**

Office of New Drugs Administrative Team: **Julie L. Basore, Christina L. Benton, Teresa L. Bushway, Kimberly A. Campbell, Eldridge F. Coles Jr., Thomas A. Cunningham, Shannon M. Freund, Jacquelyn S. Gianios, Mary E. Grieco, Tammy Grimm, Pamela M. Hampton, Rita Hecker, Joean E. James, Dwayne D. Keels, Leah M. Mader, Antoinette P. Mason, Merla R. Matheny, Zulema A. Miguele, William W. Oswald, LuDrean N. Peterson, Linda A. Ricketts, Bernice Rohdenburg, Tammy S. Russell, Anna M. Rubino, Barbara E. Shekitka, Laura M. West, Anne E. Wilcox, Jessica V. Wilcox, Krista C. Yazdani** and **Matthew A. Zell.**

OTC Drug Review Ingredient List Team: **William E. Gilbertson, Pharm.D.,** and **John P. O'Malley.**

VIREAD Exportation Team: **Deborah M. Autor, Chi-wan Chen, Ph.D., Marsha S. Holloman, J.D., Rao V. Kambhampati, Ph.D., Katherine A. Laessig, M.D., Jocelyn V. Lewis, Linda L. Lewis, M.D., Stephen Miller, Ph.D., Kellie S. Reynolds, Pharm.D., David L. Roeder, S. Mitchell Weitzman, J.D.,** and **Yuanchao Zhang, Ph.D.**

CDER Administrative/Program Management Excellence Award

Candee D. Chadwick

Christina L. Benton

Pamela M. Hampton

Paul G. Neff

Charis M. Miller

Christine Moser

Linda A. Ricketts

Office of Drug Safety Administrative Team: **Sandra Van Buskirk, Mary Anne Carter, Bibi F. Jakrali** and **Maureen D. Majors.**

CDER Excellence in Communication Award

Mary C. Gross

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62 individuals, 39 groups recognized during fall honor event

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Venkateswar R. Jarugula, Ph.D.

John K. Leighton, Ph.D.

Diana M. Willard

Pamela G. Winbourne

CDER's Trade Press Team: **Crystal L. Rice, Patrick E. Clarke** and **Christine S. Parker.**

Division of Drug Information: **Barbara Daciek, Harold Davis, Edward M. DePaola, Donald Dobbs, Gelind H. Grable, Brenda J. Kiliany, Michael G. Ledley** and **Joan K. Powers.** PHS officers nominated for PHS companion award**, LCDR Mary E. Kremzner, LCDR Fred L. Lockwood, LCDR Brenda L. Stodart, LCDR Catherine C. Yu, LCDR Larry P. Lim** and **LT Renu Chhabra.**

Division of Library and Information Services Hot Topic InfoWebs Group: **Magdalene D. Carolan, M. Nichelle Cherry, Lois G. Chester, Carol K. Lytle** and **Kathrin L. McConnell.**

OCTAP Pediatric Team: **Lisa L. Mathis, M.D., Kristin R. Phucas, Rosemary Roberts, M.D.** PHS officer nominated for PHS companion award: **CDR Terrie L. Crescenzi.**

OTC Internet Site Team: **Matthew R. Holman, Ph.D., John Lipnicki, Paul K. Stauffer** and **Sally Winthrop.**

CDER Information Technology Excellence Award

Oladiran Okusanya

William K. Roy

CDER Leadership Excellence Award

Marc Cavaille-Coll, M.D., Ph.D.

Nicholas Buhay

Dhruba J. Chatterjee, Ph.D.

Ann T. Farrell, M.D.

Dena R. Hixon, M.D.

Eileen Navarro-Almario, M.D.

Thomas F. Oliver, Ph.D.

Ameeta Parekh, Ph.D.

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Albert T. Sheldon Jr., Ph.D.

Elizabeth W. Shores, Ph.D.

Nancy D. Smith, Ph.D.

Kasturi Srinivasachar, Ph.D.

Neal J. Sweeney, Ph.D.

CDER Project Management Excellence Award

Amy C. Baird

Grace N. Carmouze

Cheryl J. Marshall

Judit R. Milstein

Lise Stevens

CDER Support Staff Excellence Award

Sandra R. Chung

Tara B. Garwood

Lisa J. Gilmer

Ellen L. White

Jo Ellen Dawson

Karen Konkolewski

DAAODP Support Staff: **Lori S. Benner** and **Betty L. Clark.**

DMPQ Support Team: **Sheila M. Banks** and **Nancy A. Hansen.**

OCPB Program Management Team: **Susan M. Banks, Clarence E. Bott, Patricia Carr, Lenore K. Foley, Karen Y. Graves** and **Mira V. Millison.**

CDER Team Excellence Award

Antimicrobial Resistance Team: **Leo Chan, Edward M. Cox, M.D.,** and **John H. Powers, M.D.**

Case Management Team: **Frederick W. Blumenschein, Raymond Brown, Mary D. Davis-Lopez, John M. Dietrick, Marta E. Gonzalez-Pineiro, Paul Haynie, Stephen C. Mahoney, Grace McNally, Rosa J. Motta, Barry Rothman** and **Steven J. Thurber.** PHS officer nominated for PHS companion award: **CDR Karen G. Hirshfield.**

CDER TOPOFF 2 Exercise Team: **Julie G. Beitz, M.D., David C. Bostwick, Yuan Yuan Chiu, Ph.D., Young Moon Choi, Ph.D., Philip M. Colangelo, Pharm.D., Ph.D., Bronwyn E. Collier, Eric P. Duffy, Ph.D., Joanne M. Holmes, Florence Houn, M.D., Kyong A. Kang, Pharm.D., Adebayo A. Laniyonu, Ph.D., Brad G. Leissa, M.D., Eldon E. Leutzinger, Ph.D., Ralph B. Lillie, Sally A. Loewke, M.D., Frederic J. Marsik, Ph.D., Mary D. Murphy, M.D., Terry S. Peters, DVM, David A. Place, Ph.D., David B. Ross, M.D., Lewis K. Schrager, M.D., Janice M. Soreth, M.D., Patricia A. Stewart, Susan D. Thompson, M.D., Dorothy J. Wawrose, M.D.,** and **Robert J. Yaes, M.D.** PHS officers nominated for PHS companion award: **LCDR Michael P. Bourg, CAPT Sandra L. Kweder, LT Tracy C. MacGill, CDR Mitchell V. Mathis Jr., LTJG Raquel A. Peat** and **CAPT Mary E. Purucker.**

DDDDP Pharm/Tox Team: **David G. Allen, Ph.D., Paul C. Brown, Ph.D., Barbara A. Hill, Ph.D.,** and **Norman A. See, Ph.D.**

Division of Biometrics III Clin./Stat. Coordination Group: **Mohamed A. Alosh, Ph.D., Kathleen S. Fritsch, Ph.D.,** and **Shiowjen Lee, Ph.D.**

DSPIDP 2003 Retreat Planning Team: **Renata Albrecht, M.D., Shukla Bala, Ph.D., Dorothy C. Ballman, Sary O. Beidas, M.D., Rita Hecker, Steven C. Kunder, Ph.D., Janice L. Newcomb, Rigoberto A. Roca, M.D.,** and **Diana M. Willard.** PHS officers nominated for PHS companion award: **CDR Robin E. Anderson, LT Kristen E. Miller** and **LCDR Ellen Frank Molinaro.**

Emend Working Group: **Sushanta K. Chakder, Ph.D., Wen-Jen Chen, Ph.D., Jasti B. Choudary, Ph.D., Gary Della'Zanna, D.O., M.Sc., Suresh Doddapaneni, Ph.D. Mushfiqur M. Rashid, Ph.D., Hugo E. Gallo-Torres, M.D., Ph.D., Venkateswa R. Jarugula, Ph.D, Robert L. Justice, M.D., Myong Jin Kim, Pharm.D., Joyce A. Korvick, M.D., M.P.H., Thomas J. Permutt, Ph.D., David A. Place, Ph.D., Brian K. Strongin, R.Ph.,** and **Liang Zhou, Ph.D.**

Fuzeon (T-20) Review Team: **Kassa Ayalew, M.D., Narayana Battula, Ph.D., Melisse S. Baylor, M.D., James G. Farrelly, Ph.D., Steven N. Gitterman, M.D., Thomas S. Hammerstrom, Ph.D., Andrea N. James, M.D., Rao V. Kambhampati, Ph.D., Robert O. Kumi, Ph.D., Stephen P. Miller, Ph.D., Jeff D. O'Neill, Julian J. O'Rear, Ph.D., Kellie S. Reynolds, Pharm.D., Guoxing Soon, Ph.D.,** and **Virginia L. Yoerg.**

(Continued on page 8)

INTERNATIONAL PROGRAM CORNER

ICH6 focuses on new technologies, challenges for harmonization

BY JUSTINA MOLZON, M.S.PHARM., J.D.

The Sixth International Conference on Harmonization took place in Osaka, Japan, from Nov. 12 to 15. More than 1,800 participants attended the conference, representing regulatory and other government agencies and industry from ICH and non-ICH regions.

The Conference followed the regular meetings of the ICH steering committee and its expert working groups earlier in the week where the continued development of new guidances progressed as did work on the implementation of existing guidances.

ICH6 focused on areas such as:

- New technologies in the discovery of innovative drugs.
- Opportunities and new challenges for regulatory harmonization.
- Pharmacovigilance and global cooperation with regulatory harmonization initiatives outside the ICH regions.
- Practical implementation of the Common Technical Document.

The results of a survey on the impact of ICH presented at the conference clearly showed a high degree of satisfaction by both regulatory authorities and industry with the completed ICH guidances.

A major part of the survey focused on the practical use and implementation of the CTD and the electronic CTD. The survey showed unanimous support from both sides for a continuation of the ICH activities at two levels:

- Development of new harmonized guidances where and when necessary.
- Maintenance of the existing guidances keeping them up-to-date with the most current science and best practice.

More information on the meeting is available at http://www.ich.org.

Justina Molzon heads the Center's International Program.

62 individuals, 39 groups recognized Fall Honor Awards ceremony

(Continued from page 7)

Information Resources and Infrastructure Management Team: **Jill A. Babson, Wendy W. Cheng, Wanda J. Clabaugh, Lynnette V. Gray, Doreen Henderson, Sandra J. Lee, Epe Pacantara, John W. Stephens** and **Elizabeth A. Wack.**

Iressa NDA Review Team: **Sophia S. Abraham, Ph.D., Amy C. Baird, Martin H. Cohen, M.D., Peter H. Cooney, Ph.D., Tony El Hage, Ph.D., Ann T. Farrell, M.D., Joseph A. Grillo, Pharm.D., Cheng Yi Liang, Ph.D., Richard T. Lostritto, Ph.D., William D. McGuinn, Ph.D., Catherine A. Miller, Pharm.D., David E. Morse, Ph.D., Richard Pazdur, M.D., Dorothy W. Pease, Nam Atiqur Rahman, Ph.D., Rajeshwari Sridhara, Ph.D., Paul S. Stinavage, Ph.D., Eugene J. Sullivan, M.D., Robert Temple, M.D., Khin M. U, M.D.,** and **Grant A. Williams, M.D.,**

Medical Imaging and Radiopharmaceutical Drug Application Work Tracking Team: **Bronwyn E. Collier, Brenda S. Gierhart, M.D., Alfonso H. Janowski, M.D., Kyong A. Kang, Ramesh Raman, M.D., Maria R. Walsh, Russell M. Williams, Robert Yaes, M.D.,** and **Joseph Zolman, M.D.**

NDA 20-414 (Pyridostigmine Bromide Tablets) for Chemical Weapons Defense: **Shawnte L. Adams, Raman E. Baweja, Ph.D., Jeanine A. Best, Brian P. Booth, Ph.D., Heidi Forster, J.D., Jogarao V. Gobburu, Ph.D., Maryla E. Guzewska, Ph.D., Donna Katz, J.D., Ronald E. Kavanagh, Pharm.D., Ph.D., Karen J. Lechter, Ph.D., J.D., Ider P. Lee, Ph.D., Theresa R. Martin, Robbin M. Nighswander, R.Ph., Francis R. Pelsor, Pharm.D., Donna Porter, Barry N. Rosloff, Ph.D., Waclaw J. Rzeszotarski, Ph.D., Lisa L. Stockbridge, Ph.D., Jeb S. Taylor, Robert Temple, M.D.,** and **Ann Wion, J.D.** PHS officers nominated for PHS companion award: **CAPT John J. Feeney, CDR Mitchell V. Mathis Jr.,** and **CDR Kevin Prohaska.**

Pediatric Adverse Events Team: **Min Chiu Chem, Pharm.D.,** and **Solomon Iyasu, M.D.** PHS officer nominated for PHS companion award: **CDR Terrie L. Crescenzi.**

QT Risk Management Development Team: **George S. Benson, M.D., Debra E. Boxwell, Eufrecina P. DeGuia, Evelyn R. Farinas, Paula Gish, Donna J. Griebel, M.D., Mark S. Hirsch, M.D., Venkateswa R. Jarugula, Alexander W. Jordan, Leslie A. Kenna, Laurie L. Mcleod-Flynn, Ameeta Parekh, Moo-Jhong Rhee, Yangmee Shin, Sally Singer, R.Ph., Mahboob Sobhan, Norman L. Stockbridge, M.D., He Sun, Douglas C. Throckmorton, M.D., Suong T. Tran, Melissa M. Trugga, R.Ph., Sue Jane Wang, Ronald T. Wassel, Pharm.D., Michael E. Welch** and **Marcea B.Whitaker, M.D.** PHS officer nominated for PHS companion award: **CDR Jean R. King.**

Statistical Review Template Development Team: **Rafia N. Bhore, Ph.D., Stella C. Grosser, Ph.D., Kun He, Ph.D., Kooros Mahjoob, Ph.D., Joy D. Mele, Lillian Patrician, Rajeshwari Sridhara, Ph.D.,** and **Jyoti Zalkikar, Ph.D.**

Trileptal Team: **John Z. Duan, Ph.D., Jogarao V. Gobburu, Ph.D.,** and **Ramana S. Uppoor, Ph.D.**

USP Reference Standards Team: **James F. Allgire Sandra J. Logan, Arthur R. Bryant Terry W. Moore, Jo Ann Bulmahn Larry K. Revelle, Ph.D., Sylvia H. Colson Robert L. Scott, Jonathan Drews Tatyana Senderovich, Julie Ellis Anjanette P. Smith, Andrew Fussner Kimberly D. Story, Almetia L. Hoskins Duckhee Toler, Susan Jenney Anna M. Wokovich, Jared Jones Hongping Ye, Ph.D., Richard E. Kolinski Wei Ye** and **Terra G. Lipe.**

Valdecoxib Postmarketing Safety Review Team: **Renan A. Bonnel, Pharm.D., Allen D. Brinker, M.D., M.P.H., Lawrence Goldking, M.D., Lois A. La Grenade, M.D., M.P.H., Joyce P. Weaver, Pharm.D.,** and **James P. Witter, M.D.** PHS officer nominated for PHS companion award: **CDR Nancy M. Halonen.**

Zometa Team: **Brian P. Booth, Ph.D.,** and **Jogarao V. Gobburu, Ph.D.**

Jackie Barber-Washington is the Center's incentive awards officer.

Survey shows professional development highly valued by CDER

BY LESLIE D. WHEELOCK, M.S., R.N. AND NANCY SMITH, PH.D.

Because of the nature of the Center's work, professional development has been a major concern for our staff. Over the years, CDER has developed and implemented a number of opportunities for professional development. We conducted an employee survey to examine the current status of professional development.

There were 482 who completed the on-line survey with primary participation by medical officers, scientific reviewers and regulatory project managers. Other groups who participated were medical and regulatory policy staff, regulatory research scientists and review support staff. Of the participants, 107 were team leaders or supervisors.

The results provided evidence that professional development is very important to CDER staff with 75.4 percent of survey respondents participating in some form of professional development. Many CDER staff are participating in more than one activity. The top professional development activity at CDER is reading books and journals followed by:

- Attending seminars and rounds, conferences and meetings.
- Taking courses in one's discipline.

The major barriers for not participating in professional development are: not knowing what is available and individual workload. The results also report that team leaders and supervisors value professional development and that they themselves are not a major reason for non-participation in professional development.

Professional development ensures that individuals have the knowledge and skills to meet the changing needs of the work environment. The survey examples of professional development at CDER were:

- Participating in clinical work.
- Engaging in laboratory or regulatory research.
- Attending formal courses in one's discipline.
- Attending formal courses or programs outside one's discipline.
- Attending seminars and rounds.
- Attending events for continuing education.
- Attending or presenting at conferences and meetings.
- Writing and publishing manuscripts.
- Participating in details or cross-training opportunities.
- Teaching.
- Spending time in the library reading journals or books.
- Participating on committees that enhance the work of CDER such as guidance development.

The survey was conducted by **Laurie Lenkel, R.Ph., J.D., Maikel Kahiry, M.D., Karen Lechter, J.D., Ph.D., Amy Mason, Mathew Thomas, M.D., Brittany Price** and both of us.

The two of us presented the results of the survey to CDER's Senior Management Team this summer with the recommendation to develop a MAPP for professional development. The Office of Training and Communications will be coordinating this initiative. For more information about the survey send an e-mail to wheelockl@cder.fda.gov.

Leslie Wheelock, Associate Director for Communications, Division of Surveillance, Research, and Communication Support, Office of Drug Safety, was project manager for the survey while she was a member of OTCOM. Nancy Smith is the director of OTCOM.

FDA to require electronic filing of labeling

FDA is amending its regulations to require electronic submission of labeling for review with NDAs, certain BLAs, ANDAs, supplements and annual reports. Sponsors will now be required to submit electronically the content of the package insert or professional labeling, including all text, tables and figures. Labeling content must be submitted electronically in a form described in Agency guidance on electronic submissions.

This new rule will:

- Allow FDA to process, review, archive and distribute the information publicly.
- Improve the drug labeling review process.
- Speed up the approval and public dissemination of labeling changes.
- Help get important, up-to-date information on medications to doctors and patients more quickly.

Until now, FDA has focused on permitting but not requiring electronic submissions. This new regulation for the first time makes such e-submissions mandatory. This is an important step in FDA's larger initiatives involving electronic medical records and electronic health information systems such as the DailyMed project to promote patient safety through electronically accessible medication information. A copy of the rule is available at http://www.fda.gov/OHRMS/DOCKETS/98fr/cd0294.pdf.

Pike's Puzzler: Know your definitions

BY TONY CHITE, P.D.

Match the boldface word on the left with the correct definition on the right. All numbers match one letter, but some letters will have no matching number.

1. xerophthalmia	a. The cartilaginous projection anterior to the external opening of the ear
2. somnolence	b. The slender posts dividing a window into panes
3. micturition	c. Dryness of the eye
4. zoetrope	d. Insomnia
5. tragus	e. A monoamine oxidase inhibitor
6. mullions	f. Invented by an astrophysicist, this English toy displays a moving image seen through the slits of a small drum mounted on a spindle
7. triturate	g. One of two or more atoms whose nuclei have the same number of protons but a different number of neutrons
8. tranylcypromine sulfate	h. The passage of urine; or urination
	i. Sleepiness or drowsiness
	j. To rub, grind, crush or pound into fine particles

Answers: see page 5

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

OCPB holds triennial retreat; detailed to Office of Center Director

(Continued from page 1)

"How does the review process need to change?" she asked. One answer is that the early phases of drug development will have to become more important and more quantitative. This earlier focus will allow a more complete understanding of the drug and can lead to better, more efficient drug development.

The scientific expertise of OCPB, she said, will have to tie in more closely with clinical science. In general, Dr. Woodcock anticipates greater involvement of our reviewers in early drug development. To this end, she announced that, starting Oct. 1, our office would report to the Office of the Center Director on a detail basis.

The theme of the retreat, set by **Larry Lesko, Ph.D.,** our office director, was: "Our Future in Progress." The retreat began with some group warm-up activities, conducted by our facilitator Dan Feldman, to get all attendees thinking and interacting. Dr. Lesko started the formal presentations with opening remarks and background from the 2000 retreat as well as a review of what we had accomplished since then.

After Dr. Woodcock's address, Dr. Lesko elaborated on his thoughts for our office's strategic plan and vision. His ideas included:

- Greater integration of exposure-response data through the proposed end-of-Phase 2A meetings (page 1).
- Improved communications with our stakeholders.
- Better identification and management of drug-related risks.
- Integrating pharmacogenomics into review.
- Expanded professional development programs.

He indicated that OCPB can lead the way in improving drug development and taking responsibility for optimizing the risk and benefit for the individual patient.

Other presentations included:

- *End-of-Phase 2A meeting.* **Peter I. Lee, Ph.D.,** associate director of pharmacometrics, presented information on the implementation of the meetings, key issues to be discussed at the meetings and what process will be used for planning and conducting these meetings. These meetings will allow earlier involvement of OCPB and co-located disciplines in the drug development process.
- *Pharmacogenetics update.* **Lei Zhang, Ph.D.,** from DPE III, gave an update on proposed labeling changes made to a specific approved product based on pharmacogenetic analysis. Changes were made in these sections of the label: clinical pharmacology, warnings, precautions, adverse reactions and dosage and administration.
- *Knowledge management implementation.* I asked for input from the attendees on our office's knowledge management strategic plan.
- *Good Review Practices template.* **Shiew-Mei Huang, Ph.D.,** the deputy office director for science, updated us regarding efforts of an OCPB working group that has been busy trying to finalize this document to comply with the Center's Good Review Practices initiative.
- *IND process prioritization.* **Chandra Sahajwalla, Ph.D.,** the deputy director of DPE I, discussed the draft MAPP for prioritizing and processing INDs in OCPB.
- *Publication of the Summary Basis of Clinical Pharmacology Labeling: A Proposal.* **Joga Gobburu, Ph.D.,** pharmacometrics team leader in DPE I, spoke about publishing, in a peer-reviewed journal, a summary of the basis for clinical pharmacology labeling of new drugs. This is similar to what has already been done for oncology drugs.
- *Professional development.* **Jennifer DiGiacinto, Ph.D.,** from DPE III, summarized the professional development needs of our reviewers.

The retreat was organized by a steering committee that included **Abimbola O. Adebowale, Ph.D., Hae Young Ahn, Ph.D., Susan M. Banks, Brian P. Booth, Ph.D., Dhruba J. Chatterjee, Ph.D., Philip M. Colangelo, Ph.D., Patrick Marroum, Ph.D., Srikanth Nallani, Ph.D., Allen Rudman, Ph.D.,** and **Sally Yasuda, Ph.D.,** as well as Drs. DiGiacinto, Huang, Lesko, Lee and myself. Additional assistance was provided by **Clarence Bott,** an office automation assistant, **Patricia Carr,** a program specialist, and **Kathie Foley,** OCPB's management officer.

The retreat is an opportunity to build camaraderie and discuss office and scientific issues in a relaxing, off-site venue to build a strategic plan for our programs. We have traditionally held an off-site retreat every three years. This year's retreat took place in Berkeley Springs, West Virginia. Our last retreat was in September 2000.

Robert Shore is a pharmacologist in OCPB's Immediate Office.

Pilot end-of-Phase 2A meetings aim to integrate exposure-response data

(Continued from page 1)

concept data from the early Phase 2A studies in patients; and we have safety data in patients, albeit a relatively small database.

This is generally a point before a sponsor studies special populations such as children or the elderly or studies drug-drug and food-drug interactions. The information at this point represents a fairly rich database for an early meeting with sponsors and an opportunity to analyze exposure-response data in particular.

We think this would be an ideal place to discuss integrating data from emerging fields like pharmacogenomics. We envision that this meeting would involve significant modeling and simulation to analyze and integrate exposure-response data across studies and explore dose choices for both Phase 2B and Phase 3.

More information on our proposal is available in a concept paper we issued in October (http://www.fda.gov/ohrms/dockets/ac/03/briefing/3998B1_01_Topic%201-Part%20A.pdf) and from the transcript and presentations at a Nov. 17 advisory panel meeting (http://www.fda.gov/ohrms/dockets/ac/cder03.html#PharmaceuticalScience).

Larry Lesko is director of the Office of Clinical Pharmacology and Biopharmaceutics.