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VA ResearchCurrents

Update from the Cooperative Studies Program

VA taking extra measures to protect human subjects in trials

By Steve Berkowitz, PhD, assistant director, and Joe Gough, MA, program manager

Like most national agencies, VA follows the federal government's "Common Rule" for the protection of human research subjects. This means, primarily, that each of our research sites must establish an Institutional Review Board (IRB). All studies must gain IRB approval before any participant is allowed to enter a research protocol. Any issues of patient safety must be resolved before the study is approved. These responsibilities extend through the life of each project.

But VA has gone beyond this basic requirement and implemented several programs to further protect research participants. Below is an overview of these programs. The first two apply to all VA research, while the remaining ones are specific to VA's Cooperative Studies Program (CSP).

• ***IRB Accreditation***—VA has established the federal government's first external accreditation program to ensure that local IRBs are functioning properly and effectively. In 2000, a five-year, $5.8 million contract was awarded to the National Committee on Quality Assurance (NCQA), a private, nonprofit healthcare quality organization, to develop IRB accreditation standards and conduct on-site accreditation visits throughout the VA system. The NCQA standards ensure that our medical centers meet the highest standards of human subjects protection.

• ***ReDACT (The R&D Accreditation Consultation Team)***—ReDACT offers consultation, coaching, and counseling for local IRBs and research personnel. The team is staffed by experts in human subjects protection and NCQA standards, and is a key part of VA's effort to ensure strict compliance with current regulations and ethical standards.

• ***Informed Consent Focus Groups***—In an effort to engage our veteran stakeholders in the research development process, CSP has collaborated with veterans service organizations to convene focus groups on informed consent. These groups review informed-consent documents and procedures, with the goal of making the process more meaningful and understandable to veteran participants.

• ***Human Rights Committee (HRC)***—Each CSP trial is reviewed and monitored, from beginning to end, by an HRC, located at one of CSP's five coordinating centers. The HRC ensures that human subjects issues are addressed in protocol development and refinement, and makes random site visits throughout the trial to ensure that appropriate protections are in place.

• ***Data Safety and Monitoring Board (DSMB)***—Each CSP trial has a DSMB that works with the HRC to monitor the ongoing trial, assess study progress, and assess safety and efficacy from a statistical perspective. If adverse events become statistically and clinically significant, indicating that participant safety is at risk, the DSMB has the authority and responsibility to stop the trial. If it becomes apparent through data review that one treatment is significantly superior to another, the DSMB can recommend stopping the trial and providing that treatment to all participants.

• ***Investigator Training***—Prior to receiving funding, CSP trial investigators and coordinators must receive formal training in human research protection. Additionally, each investigator and coordinator must attend standard "Good Clinical Practices" (GCP) training. GCP is the internationally accepted gold standard for conducting clinical trials. This training is provided by the CSP Site Monitoring and Review Team (see below) and updated periodically.

• ***Site Monitoring and Review Team (SMART)***—The CSP SMART group, housed within the FDA-approved CSP Clinical Research Pharmacy Coordinating Center in Albuquerque, provides 'in-house" capability to perform site monitoring and GCP reviews in an effort to continuously improve the conduct of VA CSP

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Outgoing R&D chief honored with surprise dedication

Research imaging center at West Roxbury VAMC named for Feussner

Most dedications happen only after months of planning, with fancy invitations and formal programs. This one took shape only at the "eleventh hour," according to Raj Goyal, MD, associate chief of staff for research at the West Roxbury (Mass.) VA Medical Center, as a spontaneous show of appreciation.

The "John R. Feussner Research Center of Excellence in Imaging" was dedicated July 19 at the West Roxbury site, part of the VA Boston Healthcare System, in honor of VA's retiring chief research and development officer. Feussner is leaving VA this month after a prolific 28-year career to chair the department of medicine at the Medical University of South Carolina. He inaugurated West Roxbury's research-imaging center in 1999, and Goyal gives him much of the credit for enabling the lab to expand into a state-of-the-art core facility serving the VAMC and its affiliate, Harvard Medical School.

Today, the center has more than $1 million in advanced imaging equipment, including a multiphoton microscope, calcium imaging system and laser capture microscope. It has resulted in a number of patents that VA and Harvard are developing jointly *(see sidebar)*. Some of the funding came from outside VA—a shining example of the type of leveraging pushed strongly during Feussner's six-year tenure as chief R&D officer.

"Since 1999 the imaging center has grown a lot and it embodies the principles put forth by Dr. Feussner," said Goyal. "Its development involved obtaining original seed money from Dr. Paul Hoffman, director of the Medical Research Service, in the form of a large-equipment grant, and then leveraging those investments to obtain support from the National Institutes of Health, Harvard Medical School, our nonprofit VA research corporation, and private industry."

According to Goyal, whose research in neurotransmission has benefited from the imaging center, "Such centers are critical if VA is to stay competitive in the development of medical technology and research."

When Goyal learned—just a week in advance—that Feussner and VA Secretary Anthony Principi were to be at West Roxbury July 19 for the

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New patent—enabled by imaging center—may ease coronary bypass complications

In coronary artery bypass surgery, surgeons take a piece of vein from the patient's leg and reattach it between the aorta and the coronary artery. This enables blood flow to bypass clogged arteries and reach the heart. One of the procedure's risks, though, is that the lining of the grafted vein may lose some of its natural clot-fighting ability, and may be susceptible to other problems, such as plaque formation and narrowing.

Using the sophisticated multiphoton microscope at the West Roxbury imaging center, a research team led by cardiac surgeon Shukri Khuri, MD, examined veins removed from bypass patients prior to grafting. They found that much of the vessel lining, or endothelium, had actually died. They believe this may explain the failure over time of many bypass operations.

The advantage of multiphoton microscopy is that it allows researchers to examine a whole piece of thick tissue, such as a leg vein, without sectioning it. It also allows researchers to analyze intact, living tissue with fluorescent probes to observe physiological changes.

The West Roxbury researchers went on to improve the chemical solution that heart surgeons use to preserve cardiovascular tissue. The new solution keeps alive the endothelium of the vein, and therefore may prevent many of the complications associated with bypass surgery.

"We believe the technology we

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Recent publications and presentations

"Anticonvulsant Activity of a Nonpeptide Galanin Receptor." Claude Wasterlain, MD. **West Los Angeles.** *Proceedings of the National Academy of Sciences,* May 14, 2002.

"Are Women Worrying About Heart Disease?" Mimi S. Biswas, MD; Patrick S. Calhoun, PhD; Hayden B. Bosworth, PhD; Lori A. Bastian, MD, MPH. **Durham.** *Women's Health Issues,* July-Aug. 2002.

"Common Methodological Terms in Health Services Research and Their Symptoms." Matthew L. Maciejewski, PhD. **Puget Sound.** *Medical Care,* June 2002.

"Decision-Making for PEG Tube Placement in Dementia Patients." Ursula K. Braun, MD; Rebecca J. Beyth, MD, MS. **Houston.** International Alzheimer's Conference, July 2002.

"Depressive Symptomatology and Early Attrition from Intensive Outpatient Substance Use Treatment." Geoffrey M. Curran, PhD; JoAnn E. Kirchner, MD; Mark Worley, MD; Craig Rookey, PhD; Brenda M. Booth, PhD. **Little Rock.** *Journal of Behavioral Health Services and Research,* May 2002.

"Diabetes Increases the Risk of Acute Hepatic Failure." Hashem B. El-Serag, MD, MPH. **Houston.** *Gastroenterology,* June 2002.

"Further Evidence for the Role of Fibrosis in the Pathobiology of Rhinophyma." Wyatt G. Payne, MD; Francis Ko; Terry E. Wright, MD; Martin C. Robson, MD. **Bay Pines.** *Annals of Plastic Surgery,* June 2002.

"Health Status Predicts Long-Term Outcome in Outpatients with Coronary Disease." John A. Spertus, MD; Mary McDonell, MS; Stephan D. Fihn, MD, MPH. **Puget Sound.** *Circulation,* July 2002.

"Helicobacter Pylori in North and South America Before Columbus." Yoshio Yamaoka, MD; Francisco C. Ramirez, MD; David Y. Graham, MD. **Houston** (YY, DYG) and **Phoenix** (FCR). *Federation of Eur. Biochemical Societies Letters,* April 24, 2002.

"Myelperoxidase, a Leukocyte-Derived Vascular NO Oxidase." William M. Nauseef, MD. **Iowa City.** *Science,* June 28, 2002.

"Physician-Assisted Death—A Last Resort?" (Editorial) Linda K. Ganzini, MD. **Portland.** *New England Journal of Medicine,* May 23, 2002.

"Trust in Communication Between Mexican-Americans and Their Physicians." Serena Chu, PhD; Kimberly O'Malley, PhD; Paul Haidet, MD, MPH; Clint Ladd; Tracie Collins, MD, MPH; Michael Johnson, PhD; Anh Tran, MPH. **Houston.** Annual Meeting of the Academy for Health Services Research and Health Policy, June 2002.

"An Update on the Health Economics of Asthma and Allergy." Todd A. Lee, PharmD, PhD; Kevin B. Weiss, MD. **Hines.** *Current Opinion in Allergy and Clinical Immunology,* June 2002.

Career milestones

Rory A. Cooper, PhD, director of the VA Center of Excellence for Wheelchair and Related Technology in Pittsburgh, will receive the agency's prestigious 2002 Olin E. Teague Award at a Washington ceremony on Sept. 18. Cooper's nomination cites his role as "probably the most visible advocate and scholar in the country in the area of rehabilitation of paralyzed individuals who use wheelchairs." In addition to his achievements as a scientist and advocate, Cooper was a bronze-medal winner in the 1988 Paralympic Games. The Teague Award, named for the late longtime chairman of the U.S. House Committee on Veterans Affairs, honors a VA employee who makes exemplary contributions toward improving the lives of war-injured veterans. Teague was awarded a Silver Star, Bronze Star and Purple Heart for his service in World War II.

Cooper was also recently elected to a two-year term as president-elect of the Rehabilitation Engineering and Assistive Technology Society of North America. Elected as honorary fellow in the group this year was **Mindy Aisen, MD,** director of VA Rehabilitation Research and Development.

Michael L. Boninger, MD, medical director of the VA Center of Excellence for Wheelchair and Related Technology, was named a 2002 Health Care Hero by the *Pittsburgh Business Times.*

Amy E. Bryant, PhD, and **Dennis L. Stevens, MD, PhD,** of the Boise VAMC received the Finegold Award at the recent biennial meeting of the Anaerobe Society of the Americas for their abstract "The Role of PLC-Induced Activation of Platelet Gpllbllla in Clostridial Myonecrosis." ■

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signing of a technology-transfer agreement between VA and Harvard, he hastily put together plans for the surprise dedication. His office even rush-ordered a plaque from a nearby shop.

"This dedication was so unorthodox, so spontaneous," said Goyal. "Everyone was indeed surprised—there wasn't enough time for anyone to know what was going on."

Perhaps no one was more surprised than Feussner himself. Goyal delivered remarks mentioning Feussner, and then asked Principi to unveil the plaque with his name—yet it still took the chief R&D officer a few moments to register what was going on.

"My colleagues know how infrequent it is that something can make me speechless. This dedication succeeded," said Feussner. "Oftentimes we labor hard in VA Central Office, and wonder whether anyone in the 'field' notices. This is evidence that those efforts were recognized and appreciated."

Added Feussner: "I have often said that success comes easy when one is surrounded with such brilliant and dedicated physician scientists. While this honor reflects favorably on me, it really emphasizes the outstanding work our researchers do every day. To their brilliance and hard work, I merely added a dollop of leadership and an optimistic, but tenacious, vision." ■

PATENT (cont. from pg. 2)

developed may become standard operational procedure in cardiac surgery," said Hermant Thatte, PhD, director of the imaging center.

The new solution is the basis of a patent—one of four to result so far from the Feussner imaging center—that is being developed and licensed for commercial use through VA's Technology Transfer Program.

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clinical trials. SMART conducts approximately 125 random or requested site visits per year, helping local research teams ensure that GCP and ethics standards are optimized at all sites.

Through a supportive matrix of local and national programs, VA is "leading by example" among federal agencies in the research assurances arena. The Office of Research and Development and the CSP are dedicated to ensuring the best possible clinical care for our study participants, and the utmost respect for their human rights.

Wanted: Photos of VA researchers in action

VA Research and Development Communications is seeking high-quality photos showing VA investigators at work for use in the VA Research annual report and other projects. For details call (410) 962-1800, ext. 252, or e-mail mitch@vard.org.

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