



October 6, 2006

Society President Testifies before FDA on Levothyroxine Bioequivalence

President Leonard Wartofsky testified at a Joint Advisory Committee meeting on levothyroxine (L-T4) products, on October 4, held by the Center for Drug Evaluation and Research (CDER), which is part of the U.S. Food and Drug Administration (FDA). The joint committee comprised members of the Endocrinologic and Metabolic Drugs Advisory Committee and the Advisory Committee for Pharmaceutical Science, which advises CDER on regulations concerning the control and monitoring of pharmaceutical products.

The purpose of the meeting was to discuss FDA's findings on the stability of L-T4 products over time and to determine whether additional regulatory actions are necessary to prevent patients from suffering potentially harmful results of unstable products. FDA decided to embark on the study after The Endocrine Society, the American Association of Clinical Endocrinologists (AACE), and the American Thyroid Association (ATA) raised a related, but separate, issue last year regarding the clinical implications of pharmacists substituting L-T4 products for one another. At that time, the societies requested that FDA alter its methods for determining bioequivalence of L-T4 products to a more sensitive and precise method, as L-T4 has a very narrow therapeutic index, and even slight variations of dose can result in clinical implications for patients. Rather than taking action to eliminate substitution by pharmacists, the FDA undertook the stability study of individual products.

In his presentation to the joint committee, Dr. Wartofsky again addressed the implications to patients and physicians and the financial burden on the healthcare system that result from patients being switched from one brand of L-T4 to another without the knowledge of the patient or the doctor. Even slight changes in dose can result in dramatic differences in levels of thyroid stimulating hormone (TSH), the most sensitive and reliable measure of L-T4 activity, and a clinically relevant parameter. Although FDA did not intend for the joint committee to consider the issue of inter-brand switching, Dr. Wartofsky and the representatives from AACE and ATA impacted the course of the discussion such that several members of the Joint Committee raised the issue and strongly recommended that FDA address it.

Dr. Wartofsky stated the Society's support of all reasonable regulatory measures that would improve the clinical outcomes of patients treated with L-T4, including stricter regulations on the stability of individual L-T4 products and more precise determination of bioequivalence among L-T4 products. It is unclear at this time whether FDA will take immediate steps to address the bioequivalence issue. The Endocrine Society will continue to advocate for the

necessary changes in regulation that would improve patient outcome and ease physician burden with regard to treatment with L-T4.

Lawmakers Head Home without Addressing Physician Payment Cuts

Centers for Medicare & Medicaid (CMS) released a second Proposed Rule in the August 22, 2006 *Federal Register* that calls for an across-the-board cut of 5.1 percent in physician payment fees in 2007. This decrease is greater than the 4.6 percent originally projected and 2007 is the first of nine years of payment cuts that will total nearly 40 percent. This cut, coupled with the proposed reduction in payments for office-based imaging services, could have a drastic effect on endocrinologists. In late July, the Society sent a letter to the American Medical Association (AMA) expressing concerns on the issue of office-based imaging cuts for inclusion in the AMA's comments to CMS. The Society will also submit its own comments to the agency.

Despite the efforts of legislators and specialty groups, a solution to the proposed cuts has yet to be reached. A draft bill written by Rep. Joe Barton (R-Texas) has been viewed favorably by a number of specialty groups. Barton's solution would increase payment rates for 2007-2009 by 0.5 percent each year with an additional 0.25 percent increase in 2008 and 2009 if relevant quality measures are met. The bill could also provide payments for physicians who spend extra time communicating with patients by phone or e-mail.

During a September 28 hearing of the House Energy and Commerce Committee in which solutions to the proposed cuts were discussed, Barton expressed his intention to identify an alternative to the Sustainable Growth Rate (SGR) formula. Lawmakers and medical professionals agree that the formula for calculating physician payment must be redesigned, but do not agree on how. Many medical groups believe that the SGR formula will only be eliminated if future payment updates are tied to quality reporting.

Because lawmakers tend to focus on passing only those bills that are deemed necessary during lame-duck sessions, specialty groups are pinning their hopes on an amendment attached to an appropriations bill that has a favorable chance of receiving the attention of lawmakers when they return after the November 7 election.

The Endocrine Society will continue to advocate for a favorable solution to the across-the-board cuts, the proposed adjustments for payments for imaging services, and a change to the flawed SGR formula.

NIH Announces CTSA Recipients and Describes Consortium

Clinical and Translational Science Awards (CTSAs) are expected to be instrumental in realizing the vision of the NIH Roadmap for Biomedical Research. A major initiative of the roadmap is to streamline the process by which basic discoveries are translated into patient care. CTSAs are awarded to institutions that provide academic homes to all players in the bench to bedside venture, including basic researchers, clinical and translational scientists, and academic and community practitioners. These institutes and centers, in addition to providing a collaborative research environment, are expected to have the resources with which to reach out to the community, thereby speeding the second step of translational research—the incorporation of the newest treatments into the daily routine of patients.

The agency received 35 applications for CTSA during the first cycle. This was a greater number than expected and resulted in the granting of CTSA to 12 institutions. Additionally, NIH has awarded 52 planning grants to institutions that require more time to prepare full applications.

During a telebriefing on October 3, 2006, Dr. Zerhouni described the CTSA and the national consortium of translational research centers expected to be established by 2010. The telebriefing was open to the press and was attended by several reporters, one of whom asked why it is necessary to overhaul the nation's clinical and translational research enterprise.

Dr. Zerhouni responded by stating that the NIH has been successful in translating science into treatments, cures, and vaccines to combat the acute diseases that used to be prevalent in the U.S. Because of the agency's success on that front, Americans no longer worry about such acute diseases, but the country now faces the very different health problems of chronic and rare diseases. The new structure is designed to allow cross-disciplinary communication that would have been difficult or impossible under the old system and is absolutely required for scientists and doctors to make connections between discrete discoveries and potential treatments for specific diseases.

A recording of the telebriefing and a list of the CTSA and planning grant recipients can be found at: <http://www.ncrr.nih.gov/clinicaldiscipline.asp>.

Senate Passes Animal Enterprise Terrorism Act

The U.S. Senate passed the Animal Enterprise Terrorism Act (AETA) by unanimous consent on September 30, 2006. The AETA (S.3880) amends the Animal Enterprise Protection Act of 1992 by imposing stronger punishments to criminals, expanding the definition of crimes to include conspiracies and attempts, and extending protection to include the families of individuals engaged in animal enterprise.

The AETA will likely be considered by the House after lawmakers return from the mid-term elections. Both houses of Congress have been considering such legislation since last year, and the House and Senate versions contain many of the same provisions, all of which are designed to stiffen the punishment for acts of terrorism against those whose work involves the use of animals.

Punishment for the most egregious crimes—those causing substantial loss of property, serious bodily injury, or death—has not changed from that set forth in 1992, remaining at prison sentences of 20 years to life in addition to fines. What has changed is the punishment for lesser crimes, such as those causing loss of profit only, property or economic damage less than \$1M, and substantial bodily injury.

Previously, crimes involving economic damage carried a penalty of not more than 3 years imprisonment and a fine. The current bill provides for penalties of up to 10 years imprisonment and fines for such offenses. Additionally, the new legislation introduces a category of crimes that result in substantial (less than serious) bodily injury. Such acts carry

penalties of up to 10 years in addition to fines. All fines and penalties are assessed separately from and in addition to restitution for damages.

More information about S.3880 can be found by searching the bill number at The Library of Congress Thomas (<http://thomas.loc.gov/>).

Major Changes to Come in NIH's Peer Review Process

In the fall 2006 issue of *Peer Review Notes*, the Center for Scientific Review (CSR) at the National Institutes of Health (NIH) announces several potential or impending changes in the peer review process. Among the changes are shorter grant applications, the identification and funding of innovative research, and electronic submission of all NIH grants, including investigator initiated R01s.

Beginning in February 2007, all R01 applications must be submitted electronically. CSR has been slowly transitioning to electronic submission of all grant proposals. With electronic submission of R01s, about 2/3 of all grant proposals received by NIH will be electronic. In order to submit applications electronically, investigators must be registered with Grants.gov. Registration requirements and instructions can be found at: <http://era.nih.gov/ElectronicReceipt/preparing.htm>.

The NIH Peer Review Committee (PRAC), which was established to address concerns with the peer review system, has recommended that the agency consider two major initiatives. While no specific action is being taken at this time, PRAC has strongly encouraged CSR and NIH to consider ways in which to identify and fund significant, innovative, and high-impact research. The NIH Director's Pioneer Awards are one way in which the agency attempts to fund cutting-edge research, but PRAC recommended that the agency do more.

Another major change endorsed by PRAC is to shorten the grant application and process. The agency has established the Trans-NIH Committee to Shorten the Application to advance this initiative. In addition to easing the burden on applicants, a shorter application would help to streamline the review process (another objective of CSR) and make it easier for scientists to serve as reviewers.

Read about these changes and other news from CSR at: <http://www.csr.nih.gov/prnotes/prnotes.asp>.

Society Reorganizes and Expands Government and Public Affairs Department

In response to its growing advocacy and public affairs agenda, The Endocrine Society recently reorganized and continues to expand its Government and Public Affairs Department (formerly Government & Professional Affairs), which oversees the Society's advocacy program and now includes its media relations activities.

Spearheading this department is Janet B. Kreizman, who was named senior director of government and public affairs.

Within the new structure, Chuck Blue has been appointed to the position of director of communications. Blue was previously with the National Science Foundation where he

provided counsel on the NSF's Directorate for Engineering's outreaching activities. He also has many years of media relations experience in D.C. area associations.

Also recently appointed is Stephanie Kutler, who is the Society's new associate director of government and professional affairs. Kutler started her policy career on Capitol Hill in the office of Senator Russell Feingold (D-WI). Most recently, she served as senior research manager at The Advisory Board Company, managing the efforts of their Original Inquiry Research Service, which provides research information on medical topics for hospital executives.

A recently created position of manager of science policy was filled earlier this year by Loretta Doan, Ph.D. Prior to joining the Society, Doan was a postdoctoral fellow at the National Cancer Institute, where she studied the role of cytokine receptors in T cell development and biology.

Lisa Marlow, who has been with the Society for the last two and half years, is the Society's coordinator of government and public affairs. Prior to joining the Society, Marlow worked in the Government & Public Affairs Department at the American Medical Directors Association.

For questions regarding articles listed in *Endocrine Insider* or information on advocacy and policy activities within The Endocrine Society, contact the Government & Public Affairs department:

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