These summary minutes for the October 4, 2006, joint meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Advisory Committee for Pharmaceutical Sciences were approved on October 17, 2006 .

I certify that I attended the October 4, 2006, joint meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and the Advisory Committee for Pharmaceutical Sciences of the Food and Drug Administration and that these minutes accurately reflect what transpired.

//S//	//S//
Victoria Ferretti-Aceto, Pharm.D.	Nelson Watts, M.D.
Acting Designated Federal Officer	Chair

Joint Meeting between the Endocrinologic and Metabolic Drugs Advisory Committee and the Advisory Committee for Pharmaceutical Sciences

October 4, 2006

The following is an internal report, which has not been reviewed. A verbatim transcript will be available in approximately two weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/ohrms/dockets/ac/cder06.html# Slides shown at the meeting will be available at least 3 business days after the meeting at the same website.

All external requests for the meeting transcripts should be submitted to the CDER Freedom of Information office.

The joint meeting between the Endocrinologic and Metabolic Drugs Advisory Committee and the Advisory Committee for Pharmaceutical Sciences of the Food and Drug Administration, Center for Drug Evaluation and Research, met on October 4, 2006, at the Gaithersburg Hilton, 620 Perry Parkway, Gaithersburg, Maryland. Nelson Watts, M.D. chaired the meeting. There were approximately 150 in attendance.

Endocrinologic and Metabolic Drugs Advisory Committee Members (voting):
Nelson B. Watts, M.D. (Chair), Kenneth D. Burman, M.D., Thomas O. Carpenter, M.D., Jessica W. Henderson, Ph.D. [C.R.], Katherine M. Flegal, Ph.D., Michael Proschan, Ph.D., Clifford J. Rosen, M.D., Morris Schambelan, M.D., Margaret E. Wierman, M.D.

Advisory Committee for Pharmaceutical Sciences (voting):
Charles L. Cooney, Ph.D. (Chair), Carol Gloff, Ph.D., Meryl H. Karol, Ph.D., Melvin V. Koch, Ph.D., Kenneth R. Morris, Ph.D., Cynthia R. D. Selassie, Ph.D., Nozer Singpurwalla, Ph.D., Marc Swadener, Ed.D.[C.R.], Jürgen Venitz, M.D., Ph.D.

Endocrinologic and Metabolic Drugs Advisory Committee Members (absent):
Sonia Caprio, M.D., Jorge Plutzky, M.D.

Advisory Committee for Pharmaceutical Sciences (absent):
Gerald P. Migliaccio (Industry Representative)

Endocrinologic and Metabolic Drugs Advisory Committee Members (non-voting):
Steven W. Ryder, M.D. (Industry Representative)

Advisory Committee for Pharmaceutical Sciences (non-voting):
Paul H. Fackler, Ph.D. (Industry Representative)

Consultants/Special Government Employees (voting):
Adrian S. Dobs, M.D., Arthur H. Kibbe, Ph.D., Lynne Levitsky, M.D., Michael R. McClung, M.D., Marvin C. Meyer, Ph.D., William V. Tamborlane, M.D., Paul D. Woolf, M.D

Consultants/Regular Government Employee (voting)
Monica Skarulis, M.D.

Consultants/Special Government Employee (non-voting)
Robert M. Tuttle, M.D.

FDA Participants:
Jane Axelrad, J.D., Eric Duffy, Ph.D., John Jenkins, M.D., Robert Meyer, M.D., Mary Parks, M.D.

FDA Speakers:
Jane Axelrad, J.D., Mary Parks, M.D., Eric Duffy, Ph.D.

Open Public Hearing Speakers:

- Leonard Wartofsky, M.D. The Endocrine Society
- Jeffrey R. Garber, M.D., American Association of Clinical Endocrinologists
- James V. Hennessey, M.D., American Thyroid Association

On October 4, 2006, the joint committee discussed FDA's efforts to assess the product quality of currently marketed levothyroxine sodium drug products. Earlier this year, FDA requested that manufacturers of currently marketed levothyroxine sodium products provide to it certain product release and stability information. The joint committee considered FDA's analyses of the information and any clinical significance.

Nelson Watts, M.D. (the Endocrinologic and Metabolic Drugs Advisory Committee Chair), called the meeting to order at 8:00 a.m. The Committee members, consultants, and FDA participants introduced themselves. The conflict of interest statement was read into the record by Victoria Ferretti-Aceto, Pharm.D. The agenda proceeded as follows:

Call to Order and Introductions	Nelson Watts, M.D., Chair Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC)
Conflict of Interest Statement	Victoria Ferretti-Aceto, Pharm.D. Acting Designated Federal Officer, EMDAC
FDA Presentation	
Introduction to Meeting	Mary H. Parks, M.D., Director, Division of Metabolism and Endocrinology Products
Regulatory History of Levothyroxine Products	Jane A. Axelrad, J.D., Associate Director for Regulatory Policy
Clinical Perspectives on Levothyroxine Products	Mary H. Parks, M.D.
Stability of Levothyroxine Sodium Products	Eric P. Duffy, Ph.D., Director, Division of Post Marketing Evaluation
Industry Presentation	
Levothyroxine Sodium	John Leonard, M.D., Vice President, Global Pharmaceutical Research and Development, Abbott Laboratories
Global Experience: Levothyroxine Quality and Safety	Bonnie Southorn, Ph.D., Director, Core Technical Documentation and Submissions, Genpharm Inc.
Levothyroxine Sodium Tablets: A Manufacturer's Perspective	Ronald Steinlauf, Vice President, Jerome Stevens Pharmaceuticals

Industry Presentation (continued)

Mylan's Unique Formulation and Process for the Consistent Production of a Potent, Uniform and Stable Levothyroxine Sodium Product	David Wargo, R.Ph., Ph.D.
Open Public Hearing Statement	
FDA Summary of Issues	Mary H. Parks, M.D.

Question to the Committee:

1. Does a 10% loss in potency over shelf life raise clinically significant concerns?

Yes – 23 ***No – 2*** ***Abstain - 1***

Discussion

● *One major concern is that variation (as high as 10%) over the shelf life of the product could be problematic for vulnerable patient populations such as infants, elderly, pregnant, and thyroid cancer patients.*

●*Some members commented that this one isolated piece of the picture (that of 10% potency loss over the shelf life of the product) may not necessarily translate to clinical significance.*

Please see transcript for detailed discussion.

2. Question 2. was modified to the following:

   If there are clinically significant concerns, should the potency specifications for levothyroxine sodium products be narrowed from 90% to 110% potency specifications to 95% to 105%?

Yes – 24 ***No – 1*** ***Abstain – 1***

Discussion

The committee largely agreed that the impact of tightening specifications would decrease the problems associated with variability. However, there was concern that there are no specific data to confirm that narrowing potency specifications to the plus or minus 5% range (or any other specific range) would correlate to quantifiable clinical improvements (markers indicating improved delivery of therapeutic value). Other concerns included analytical limitations of assay or methods of testing and how that figures into the variance.

Please see transcript for detailed discussion.

The meeting adjourned at approximately 3:00 p.m.