

June 30, 2005

Steven Galson, M.D.  
Director, Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane, HFD-240  
Rockville, MD 20857

Dear Dr. Galson:

We are writing on behalf of our societies--the American Thyroid Association, The Endocrine Society, and American Association of Clinical Endocrinologists--to follow-up on the May 23, 2005 Thyroxine Equivalence Workshop that FDA co-sponsored with us.

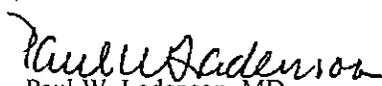
First, we would like to thank you for following through on Dr. Woodcock's commitment to hold this meeting. Despite the long delay in convening the meeting, we appreciated the opportunity to voice our serious concerns about FDA standards for determining the equivalence of thyroxine formulations and present data in support of those concerns.

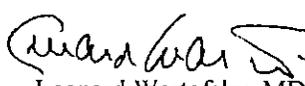
Although you did not participate in the meeting after your welcome message, we assume that Dr. Orloff and his colleagues briefed you on the serious and unanimous concerns that were expressed by our three societies, representing approximately 8,000 clinical experts in thyroidology in the United States, and by organizations representing the 13 million Americans who take levothyroxine products for thyroid disorders. Those concerns are:

1. Current FDA bioequivalence standards are too lax and overlook modest, but clinically important dosage differences in this narrow therapeutic index drug.
2. Current FDA standards for thyroxine therapeutic equivalence do not employ the pharmacodynamic measure that is used by clinicians around the world every day to determine if patients are optimally treated: TSH measurement.
3. Patients, pharmacists and physicians are unaware and confused by the complex set of relationships among approved thyroxine products, which are frequently being substituted for one another with little regard for which formulations have, in fact, been defined as equivalent by even today's lax standard.
4. A properly designed and executed clinical trial, including TSH measurement and appropriate control observations, needs to be performed to settle this issue.

We heard from FDA a willingness to talk further with us about points 3 and 4 above. Our societies are currently considering our next steps and will be in touch with you again later this summer to discuss what steps you are willing to take to improve the safety and efficacy of thyroxine products.

Respectively yours,

  
Paul W. Ladenson, MD  
President  
American Thyroid Association

  
Leonard Wartofsky, MD  
President-Elect  
The Endocrine Society

  
Carlos R. Hamilton, Jr., MD, FACE  
Immediate Past President, American Assn.  
of Clinical Endocrinologists