Florida THYROID & ENDOCRINE Clinic

To the FDA Advisory Committee for Pharmaceutical Science

Dear Sirs:

As a Past President of the American Association of Clinical Endocrinologists and as a practicing endocrinologist for the past 29 years, I would like to make two comments concerning the method of determining bioequivalence of l-thyroxine preparations.

1. Whenever possible, I urge that hormone bioequivalence studies be performed in subjects who are deficient in that hormone. Specifically, l-thyroxine studies should be done in patients who are totally hypothyroid. When normal subjects are used, the endogenous hormone interferes significantly with the measurements, and the administered hormone alters the dynamics of hormone secretion. These effects decrease sensitivity and compromise any credible testing of bioequivalence.

2. Over the last decade most clinicians have come to rely upon a normal thyrotropin (TSH) rather than a normal l-thyroxine (T4) as the most sensitive and specific endpoint for treating hypothyroid patients. While patients frequently have a "normal" T4 on three or more different doses of l-thyroxine, they generally feel best and have a normal TSH on only one dose of l-thyroxine. Therefore it would be more appropriate to use TSH rather than T4 in establishing therapeutic equivalence

Sincerely,

H. Jack Baskin

H. Jack Baskin, MD, MACE

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