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January 9, 2004

BY HAND DELIVERY

Dockets Management Branch (HFA-305)
Food and Drug Administration
Department of Health and Human Services
Room 1061
5630 Fishers Lane
Rockville, MD 20852

2800 '04 JAN -9 P1:11

Re: **Docket No. 03P-0126**
Supplement to Citizen Petition

Dear Sir or Madam:

On behalf of Abbott Laboratories, we submit the attached letter and draft agenda to the above-referenced Docket No. 2003P-0126.

Sincerely,

David Fox (KM)

David M. Fox
Katlin E. McKelvie
Hogan & Hartson L.L.P.

cc: Neil B. Parker
Abbott Laboratories

03P-0126

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The American Thyroid Association

Scientists and Physicians Dedicated to Better Understanding and Treatment of Thyroid Diseases

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HOME

PROFESSIONALS

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ABOUT THE ATA

FDA Bioequivalence Workshop Plans continue with ATA, Endocrine Society and AACE leaders

December 30, 2003



**AMERICAN
THYROID
ASSOCIATION**
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2003-2004

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

Dear Dr. Galson:

I am writing on behalf of the American Thyroid Association, the Endocrine Society, and the American Association of Clinical Endocrinologists to follow-up on your November 5 invitation to draft an agenda and propose a list of participants for a workshop addressing issues regarding dose precision and bioequivalence standards for levothyroxine sodium formulations.

Our societies were very encouraged by the commitment that Dr. Woodcock made at our September 15 meeting, and by your subsequent invitation to propose an agenda for a workshop of sufficient depth and duration to address all of the relevant issues. These include bioequivalence testing baseline correction, optimal test subjects, and acceptable confidence limits, and TSH as a pharmacodynamic measure. We propose covering all of these matters, as well as considerations in design of a crossover chronic thyroxine therapy trial with serum TSH as an outcome, in the enclosed draft agenda.

We welcome FDA's review of this proposal and your comments regarding the format, schedule, content, and potential presenters for this meeting. Please note that none of the individuals tentatively designated in this draft have yet been contacted. We look forward to collaborating with you to define the final form and content of the workshop program.

Anne Henig in your office informed Dr. Brent that your staff would be meeting to discuss this matter in early January. I look forward to hearing from you or her soon thereafter.

Sincerely,

Paul W. Ladenson, M.D.
President-Elect, American Thyroid Association

Steven I. Sherman, M.D.
Houston, Texas

PWL:sr
Enclosure

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[Draft Levothyroxine Workshop Agenda \(PDF File,108KB\)](#)

[FDA invites ATA, TES & AACE to Plan Workshop on Thyroxine Bioequivalence](#)

[ATA Continues Dialog With FDA on Levothyroxine Dose Precision and Bioequivalence Standards](#)

[ATA asks the FDA to ensure safe and effective levothyroxine preparations](#)

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U.S. FOOD AND DRUG ADMINISTRATION

AMERICAN THYROID ASSOCIATION

THE ENDOCRINE SOCIETY

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS

**JOINT WORKSHOP ON THERAPEUTIC INTERCHANGEABILITY CRITERIA
FOR LEVOTHYROXINE SODIUM DRUG PRODUCTS**

AGENDA & SCHEDULE

Day 1

7:45 AM Welcoming Remarks and Workshop Objectives

Session 1: Levothyroxine Sodium: A Widely Employed Narrow Therapeutic Range Drug

8:00 AM Epidemiology of Thyroid Disease and Levothyroxine Usage

8:25 AM Adequacy and Consistency of Levothyroxine Therapy

8:45 AM Consequences of Minimal Thyroid Hormone Excess: Lessons from Endogenous Disease States and Pharmacotherapy

9:15 AM Consequences of Minimal Thyroid Hormone Deficiency: Lessons from Endogenous Disease States and Pharmacotherapy

9:45 AM Coffee Break

Susceptible Populations

10:15 AM Pregnancy and Fetal Effects

10:35 AM Childhood Hypothyroidism

10:55 AM Thyroid Cancer

11:15 PM Associated Cardiovascular Disease

11:35 PM Panel Discussion and Comments

12:00 PM Lunch

Draft Levothyroxine Workshop Agenda

Session 2: Defining Bioequivalence of Levothyroxine Sodium Formulations

- 1:00 PM Rationale for Current Guidance for Bioequivalence Methodology*
- 1:30 PM Limitations and Potential Clinical Consequences of Current Methodology
- 2:00 PM Panel Discussion and Comments
- 2:30 PM Coffee Break

Session 3: Potential Enhancements of Method for Defining Levothyroxine Bioequivalence

- 3:00 PM Biostatistical Considerations in Determining Thyroxine Bioequivalence: Baseline Correction and Confidence Intervals
- 4:00 PM Optimal Human Subjects for Determining Thyroxine Bioequivalence
- 4:20 PM Panel Discussion and Comments
- 5:00 PM Adjournment

Day 2

- 8:00 AM Recap Day 1

Session 4: Serum Thyrotropin (TSH) Concentration as a Pharmacodynamic Measure of Thyroxine Bioequivalence

- 8:10 AM Rationale for TSH as a Marker of Tissue Effects of Thyroid Hormones
- 8:35 AM Potential Limitations of TSH as a Marker of Tissue Effects of Thyroid Hormones: Molecular and Physiological Considerations
- 9:00 AM Potential Limitations of TSH as a Marker of Tissue Effects of Thyroid Hormones: Methodological and Regulatory Considerations
- 9:25 AM TSH as a Bioequivalence Measure: Study Design Considerations

*Presentation covering FDA's general approach to bioequivalence assurance for both conventional and narrow therapeutic index drugs, and guidance to industry regarding levothyroxine sodium products.

Draft Levothyroxine Workshop Agenda

9:45 AM Panel Discussion and Comments

10:15 AM Coffee Break

Session 5: Discussion and Comment Session

10:40 AM Professional societies¹

11:30 AM Patient Advocacy and Education Groups²

12:00 Noon Lunch

1:00 PM Pharmaceutical Industry³

2:00 PM FDA

3:00 PM Coffee Break

3:30 PM Open Comment Period

4:30 PM Concluding Remarks and Adjournment

¹ Invitees to include American Thyroid Association, Endocrine Society, American Association of Clinical Endocrinologists, American Society of Reproductive Medicine, American Society for Bone and Mineral Research, American Medical Association, American College of Physicians, AAFP, American Medical Women's Association, and other interested societies.

² Thyroid Foundation of America, ThyCa: Thyroid Cancer Survivors' Association, National Graves' Disease Foundation, Light of Life Foundation, and potentially others.

³ Abbott Laboratories, Forest Pharmaceuticals, Monarch-King Pharma, and other branded and generics thyroxine manufacturers.