

**- DRAFT \*-**

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

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## 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

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\*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 societies<sup>1</sup>

11:30 AM Patient Advocacy and Education Groups<sup>2</sup>

12:00 Noon Lunch

1:00 PM Pharmaceutical Industry<sup>3</sup>

2:00 PM FDA

3:00 PM Coffee Break

3:30 PM Open Comment Period

4:30 PM Concluding Remarks and Adjournment

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<sup>1</sup> 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.

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

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