

Draft Guidance on Liothyronine Sodium

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Liothyronine Sodium

Form/Route: Tablet/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way crossover in-vivo
Strength: 100 mcg (2 x 50 mcg)
Subjects: Healthy males and nonpregnant females, general population
Additional Comments: Baseline levels of liothyronine should be measured at 3 pre-dose time points (-30 min, -15 min, and 0 min). The mean of the three pre-dose samples should be subtracted from each measured post-dose concentration.

2. Type of study: Fed
Design: Single-dose, two-way crossover in-vivo
Strength: 100 mcg (2 x 50 mcg)
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments: Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

Analytes to measure (in appropriate biological fluid): Total (free + bound) liothyronine in plasma

Bioequivalence based on (90% CI): Total (free + bound) liothyronine in plasma after baseline correction

Waiver request of in-vivo testing: 5 mcg and 25 mcg based on (i) acceptable bioequivalence studies on the 50 mcg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.