

*Contains Nonbinding Recommendations*  
**Guidance on Sibutramine Hydrochloride**

This guidance represents 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:** Sibutramine Hydrochloride

**Form/Route:** Capsule/Oral

**Recommended studies:** 2 studies

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover *in-vivo*  
Strength: 15 mg  
Subjects: Normal healthy males and females, general population  
Additional Comments: Due to safety concerns, studies should not be conducted using doses higher than 15 mg.

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2. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover *in-vivo*  
Strength: 15 mg  
Subjects: Normal healthy males and females, general population  
Additional comments: Please see comment above.

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**Analytes to measure:** Sibutramine, and the major first-generation active (desmethyl) metabolites M1 and M2, using an achiral assay.

**Bioequivalence based on (90% CI):** Sibutramine

If sibutramine can be reliably measured, a confidence interval approach for bioequivalence determination should be used for sibutramine. If sibutramine cannot be reliably measured, a confidence interval approach for bioequivalence determination should be used for major first-generation active (desmethyl) metabolites M1 and M2.

**Waiver request of in-vivo testing:** 5 mg and 10 mg based on (i) acceptable bioequivalence studies on the 15 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of 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.fda.gov/cder/ogd/index.htm>. 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.