

**Draft Guidance on Sirolimus**

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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:** Sirolimus

**Form/Route:** Tablets/Oral

**Recommended studies:** 2 studies

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover *in-vivo*  
Strength: 2 mg  
Subjects: Normal healthy males and females, general population  
Additional Comments: Due to the long half-life, the blood sampling time can be truncated to 72-hours ( $AUC_{0-72h}$ ).

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

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**Analytes to measure (in appropriate biological fluid):** Sirolimus in the whole blood.

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

**Waiver request of in-vivo testing:** 1 mg based on (i) acceptable bioequivalence studies on the 2 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.