

Draft Guidance on Simvastatin

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Orally Disintegrating Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 80 mg
Subjects: Normal healthy males and females, general population
Additional Comments: Females should not be pregnant or lactating, and if applicable, should practice abstinence or contraception during the study.
The whole tablet should be placed on the tongue and allowed to disintegrate for 30 seconds. After 30 seconds, all subjects should consume 240 mL of water.

2. Type of study: Fed
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 80 mg
Subjects: Normal healthy males and females, general population
Additional comments: Please see comments above.

Analytes to measure (in appropriate biological fluid): Simvastatin and its metabolite, beta-hydroxyacid in plasma.

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C_{max}.

Bioequivalence based on (90% CI): Simvastatin

Waiver request of in-vivo testing: 10 mg, 20 mg, and 40 mg based on (i) acceptable bioequivalence studies on the 80 mg strength, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in 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.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.