

## Draft Guidance on Simvastatin

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

**Active Ingredient:** Simvastatin

**Dosage Form; Route:** Suspension; oral

**Recommended Studies:** One study

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in vivo  
Strength: 40 mg/5 mL  
Subjects: Healthy males, and non-pregnant and non-lactating females, general population.  
Additional comments: None

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**Analytes to measure (in appropriate biological fluid):** Simvastatin and its active metabolite, beta-hydroxyacid of simvastatin in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the beta-hydroxy metabolite, simvastatin acid, 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:** 20 mg/5 mL based on (i) acceptable bioequivalence study on the 40 mg/5 mL 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:** The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Note that a dosage unit for a suspension is the labeled strength (mL). Specifications will be determined upon review of the abbreviated new drug application (ANDA).