Draft Guidance on Simvastatin

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

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).