### Guidance on Simvastatin

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.

<table>
<thead>
<tr>
<th>Active ingredient:</th>
<th>Simvastatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Form/Route:</td>
<td>Tablets/Oral</td>
</tr>
<tr>
<td>Recommended studies:</td>
<td>2 studies</td>
</tr>
</tbody>
</table>

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:**

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:**

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**Analytes to measure:** Simvastatin and its beta-hydroxyacid metabolite in plasma.  
Please submit the metabolite data as supportive evidence of comparable therapeutic outcome.  
For the beta-hydroxy metabolite of simvastatin, 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 Cmax

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

**Waiver request of in-vivo testing:** 5 mg, 10 mg, 20 mg, 40 mg based on (i) acceptable bioequivalence studies on the 80 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 conduct comparative dissolution testing on 12 dosage units of all strengths of the test and reference products using the method specified in the USP method.

*Finalized May 2008*