

Draft Guidance on Calcitriol

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Capsules/Oral

Recommended studies: 1 study

Type of study: Fasting

Design: Single-dose, two-way crossover *in-vivo*

Strength: 0.5 mcg

Subjects: Normal healthy males and females, general population.

Additional Comments: A baseline calcitriol should be determined by taking blood samples at 0, -6, -12, and -18 hours prior to dosing. Subjects should be housed at the clinic, and served standardized meals with similar Vitamin D content to that of the meals served on the pharmacokinetic sampling day. For each subject, an average baseline calcitriol concentration should be determined and subtracted from the plasma concentrations determined on the pharmacokinetic sampling day. Baseline concentrations should be determined for each dosing period, and baseline corrections should be period specific. If a negative plasma concentration value results after baseline correction, this should be set to 0 prior to calculating the baseline-corrected AUC.

Analytes to measure (in appropriate biological fluid): Calcitriol in plasma

Bioequivalence based on (90% CI): Baseline-corrected Calcitriol

Waiver request of in-vivo testing: 0.25 mcg based on (i) acceptable bioequivalence studies on the 0.5 mcg strength, (ii) proportionally similar 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.