

Draft Guidance on Carbamazepine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

Form/Route: Extended Release Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover *in-vivo*
Strength: 400 mg
Subjects: Normal healthy males and females, general population.
Additional Comments: Females must have a negative baseline pregnancy test within 24 hours prior to receiving the drug. Females should not be pregnant or lactating, and if applicable, should practice abstinence or contraception during the study.

2. Type of study: Fed
Design: Single-dose, two-treatment, two-period crossover *in-vivo*
Strength: 400 mg
Subjects: Normal healthy males and females, general population.
Additional Comments: Please see comments above.

Analytes to measure (in appropriate biological fluid): Carbamazepine in plasma.

Bioequivalence based on (90% CI): Carbamazepine

Waiver request of in-vivo testing: 100 mg and 200 mg, based on acceptable (i) bioequivalence studies on the 400 mg tablet, and (ii) proportional similarity of the formulations 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.

In addition to the method above, for modified release products, dissolution profiles on 12 dosage units each of test and reference products generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5 and 6.8 buffer) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. Please include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released, to provide assurance against premature release of drug (dose dumping) from the formulation. Specifications will be determined upon review of the data submitted in the application.