

Draft Guidance on Amoxicillin and Clavulanate Potassium

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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: Amoxicillin; Clavulanate potassium

Dosage Form; Route: Extended release tablet; oral

Recommended Studies: Two studies

1. Type of study: Fasting

Design: Single-dose, two-treatment, two-period crossover in vivo

Strength: 1 g; EQ 62.5 mg Base [Recommended dose: 2 x (1 g; EQ 62.5 mg Base) tablets]

Subjects: Males and non-pregnant, non-lactating females, general population

Additional comments: None

2. Type of study: Fed

Design: Single-dose, two-treatment, two-period crossover in vivo

Strength: 1 g; EQ 62.5 mg Base [Recommended dose: 2 x (1 g; EQ 62.5 mg Base) tablets]

Subjects: Males and non-pregnant, non-lactating females, general population

Additional comments: None

Analytes to measure: Amoxicillin and clavulanic acid in plasma

Bioequivalence based on (90% CI): Amoxicillin and clavulanic acid

Additional strengths: Not applicable

Dissolution test method and sampling times: For modified release drug products, FDA recommends that applicants develop specific discriminating dissolution methods. Applicants may also use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA's database (available at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>), provided that Applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed for the modified release drug product, FDA recommends that the submission includes the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Dissolution on split tablets should also be tested. Specifications will be determined upon review of the abbreviated new drug 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. 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.