

Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Cephalexin

February 2026

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Active Ingredient: Cephalexin

Dosage Form: Tablet

Route: Oral

Strengths: EQ 250 mg Base, EQ 500 mg Base, EQ 1 gm Base

Recommended Study: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 1 gm Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Applicants may consider conducting the study by using one cephalexin tablet (1 × EQ 1 gm Base) of the test product and two cephalexin tablets (2 × EQ 500 mg Base) of the designated reference standard (RS) listed in the Orange Book.

Analyte to measure: Cephalexin in plasma

Bioequivalence based on (90% CI): Cephalexin

Waiver request of in vivo testing of additional strengths: EQ 250 mg Base and EQ 500 mg Base strengths based on (i) an acceptable bioequivalence study on the EQ 1 gm Base strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

The bioequivalence study for the EQ 1 gm Base strength may be waived if the applicant holds an approved abbreviated new drug application for the EQ 500 mg Base strength and provides adequate justification that both strengths (EQ 500 mg Base and EQ 1 gm Base) utilize the same manufacturing process, maintain formulation proportionality, and exhibit comparable in vitro dissolution profiles across both strengths.

Dissolution: Dissolution test(s) should be included for quality control and to support waiver request of in vivo testing of additional strengths.

Dissolution test method and sampling times: Provide a dissolution method development report for the test product containing information and data that demonstrate appropriateness of the selected dissolution method¹ and sampling times, such as the discriminating ability to detect changes in critical quality attributes that could potentially impact drug product performance.

For drug products containing high solubility drug substances that meet the rapidly dissolving criteria, demonstration of discriminating ability may not be needed. For additional information, refer to the most recent version of the guidance for industry *Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances*.^a

If any strength of the tablet product has a functional score, additional dissolution profile testing should be conducted for each segment of the split tablet after manual and mechanical splitting as per the most recent version of the guidance for industry *Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation*.^a

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Unique Agency Identifier: PSG_050440

^a For the most recent version of a guidance, refer to the FDA guidance website at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>

¹ Applicant-developed, United States Pharmacopeia drug product monograph or Dissolution Methods database, <https://www.accessdata.fda.gov/scripts/cder/dissolution/index.cfm>