This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency’s regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

In December 2009, FDA issued a draft product-specific guidance for industry on generic methylphenidate hydrochloride. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

**Active Ingredient:** Methylphenidate hydrochloride

**Dosage Form; Route:** Tablet, chewable; oral

**Recommended Studies:** Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. **Type of study:** Fasting  
   **Design:** Single-dose, two-treatment, two-period crossover in vivo  
   **Strength:** 10 mg  
   **Subjects:** Healthy males and non-pregnant, non-lactating females  
   **Additional comment:** The tablet should be chewed, then swallowed with 240 mL of water.
2. Type of study: Fed  
   Design: Single-dose, two-treatment, two-period crossover in vivo  
   Strength: 10 mg  
   Subjects: Healthy males and non-pregnant, non-lactating females  
   Additional comment: See comment above.

**Analyte to measure:** Methylphenidate in plasma

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

**Waiver request of in vivo testing:** 2.5 mg and 5 mg strengths based on (i) acceptable bioequivalence studies on the 10 mg strength, (ii) acceptable in vitro dissolution testing of all the strengths, and (iii) proportional similarity of the formulations of all strengths

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found in the FDA’s Dissolution Methods database, [http://www.accessdata.fda.gov/scripts/cder/dissolution/](http://www.accessdata.fda.gov/scripts/cder/dissolution/). Conduct comparative dissolution testing on 12 dosage units for each of all strengths of the test and reference products. Specifications will be determined upon evaluation of the ANDA.

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**Revision History:** Recommended December 2009; Revised August 2022

**Unique Agency Identifier:** PSG_021475