This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 February 2010, FDA issued a draft product-specific guidance for industry on generic carbidopa; levodopa. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

**Active Ingredients:** Carbidopa; Levodopa

**Dosage Form; Route:** Tablet, orally disintegrating; oral

**Recommended Studies:** Two studies

1. Type of study: Fasting
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 25 mg; 250 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: The orally disintegrating tablet should be placed on the tongue, allowed to disintegrate, and swallowed without water.
2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 25 mg; 250 mg
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments: See comments above

Analytes to measure: Carbidopa and levodopa in plasma

Bioequivalence based on (90% CI): Carbidopa and levodopa

Waiver request of in vivo testing: 10 mg; 100 mg and 25 mg; 100 mg based on (i) acceptable
bioequivalence studies on the 25 mg; 250 mg strength, (ii) acceptable dissolution among all
strengths, and (iii) proportional similarity of formulations across 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/. Conduct comparative dissolution testing
on 12 dosage units for each of all strengths of the test and reference products. Specifications will
be determined upon review of the abbreviated new drug application.

Revision History: Recommended February 2010; Revised November 2021

Unique Agency Identifier: PSG_076699