This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This is a new draft product-specific guidance for industry on generic esomeprazole magnesium.

**Active Ingredient:** Esomeprazole magnesium

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

**Recommended Studies:** Two studies

1. **Type of study:** Fasting  
   **Design:** Single-dose, two-treatment, two-period crossover in vivo  
   **Strength:** EQ 20 mg Base  
   **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:** EQ 20 mg Base  
   **Subjects:** Males and non-pregnant, non-lactating females, general population

*Recommended Aug 2021*
Additional comments: See comments above.

**Analyte to measure:** Esomeprazole in plasma using an achiral assay

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

**Additional strengths:** Not applicable

**Dissolution test method and sampling times:**
For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA’s database, [http://www.accessdata.fda.gov/scripts/cder/dissolution/](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, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units for each of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

**Alcohol dose dumping studies:**
Due to concerns of dose dumping of drug from this product when taken with alcohol, conduct additional dissolution testing using various concentrations of ethanol in the dissolution medium as follows:

Testing Conditions: 300 mL, 0.1N HCl, USP Apparatus 2 (paddle) at 100 rpm, with or without alcohol;

- Test 1: 12 units tested according to the proposed method (with 0.1 N HCl) with data collected every 15 minutes for a total of 2 hours
- Test 2: 12 units analyzed by substituting 5% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours
- Test 3: 12 units analyzed by substituting 20% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours
- Test 4: 12 units analyzed by substituting 40% (v/v) of test medium with Alcohol USP and data collection every 15 minutes for a total of 2 hours

Conduct testing on both test and reference products accordingly, and provide data on individual unit, means, range and %CV.

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