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 July 2014, FDA issued a draft product-specific guidance for industry on generic ethinyl estradiol; norethindrone acetate. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

**Active Ingredients:** Ethinyl estradiol; Norethindrone acetate

**Dosage Form; Route:** Tablet; 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:** 0.02 mg; 1 mg  
   **Subjects:** Non-pregnant, non-lactating females, general population  
   **Additional comment:** The tablet should be swallowed whole with 240 mL of water.
2. Type of study: Fed
   Design: Single-dose, two-treatment, two-period crossover in vivo
   Strength: 0.02 mg; 1 mg
   Subjects: Non-pregnant, non-lactating females, general population
   Additional comment: See comment above.

Analytes to measure: Ethinyl estradiol and norethindrone in plasma

Bioequivalence based on (90% CI): Ethinyl estradiol and norethindrone

Waiver request of in vivo testing: Not applicable

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 the test and reference products. Specifications will be determined upon evaluation of the ANDA.