This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 July 2008, FDA issued a draft product-specific guidance for industry on generic leuprolide acetate. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

**Active Ingredient:** Leuprolide acetate

**Dosage Form; Route:** Implant; implantation

**Recommended Study:** One study

1. Type of study: In vivo
   Design: Randomized, single-dose, parallel
   Strength: EQ 65 mg Base
   Subjects: Prostatic carcinoma patients undergoing initial therapy or receiving a stable regimen of leuprolide acetate implant (EQ 65 mg Base)
   Additional Comments: The study should include either exclusively prostatic carcinoma patients undergoing initial therapy, or exclusively prostatic carcinoma patients receiving a stable regimen of leuprolide acetate implant (EQ 65 mg Base). If both types of patients are included in the study, proportions of the patients should be similar for the test and reference groups.
**Analyte to measure:** Leuprolide in plasma

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

The 90% confidence intervals of the following pharmacokinetic (PK) parameters should meet the acceptable limits of [80.00-125.00%]: Log-transformed AUC\(_{7-t}\), AUC\(_{0-t}\), and \(C_{\text{max}}\), where AUC\(_{7-t}\) is the area under the plasma-concentration vs. time curve from Day 7 to the last sampling time point with quantifiable concentration, AUC\(_{0-t}\) is the area under the curve from 0 to the last sampling time point with quantifiable concentration, and \(C_{\max}\) is the maximum plasma concentration.

In addition, for prostatic carcinoma patients undergoing initial therapy, after the PK study is completed, the treatment should not be discontinued or delayed for a second dose.

**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/](http://www.accessdata.fda.gov/scripts/cder/dissolution/). Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

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**Revision History:** Recommended July 2008; Revised November 2021

**Unique Agency Identifier:** PSG_021088