

*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

**Draft Guidance on Testosterone**

**May 2022**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 August 2011, FDA issued a draft product-specific guidance for industry on generic testosterone. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

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**Active Ingredient:** Testosterone

**Dosage Form; Route:** Pellet; implantation

**Recommended Study:** One study

1. Type of study: Bioequivalence study with pharmacokinetic endpoints  
Design: Single-dose, two-arm, parallel, in vivo  
Strength: 75 mg/pellet [Dose: 150 mg (two x 75 mg/pellet)]  
Subjects: Hypogonadal males (serum testosterone measurements below 300 ng/dL in the morning on at least two separate days) who are otherwise healthy  
Additional comments: Subjects should not currently be receiving any treatment for their hypogonadism. The parallel groups should be well-balanced with respect to the study population demographics.

**Analyte to measure:** Testosterone in plasma

Submit partial area under the curve (pAUC) data from Day 60 (2 months) to Day 90 (3 months) as supportive information to assess the similarity in exposure and sustained drug release during this time window.

An average baseline correction is obtained by averaging the three pre-dose sampling times (-1.0, -0.5 and 0 hours). The baseline corrected and uncorrected data and statistical analysis should be submitted to the FDA.

**Bioequivalence based on (90% CI):** Testosterone (baseline-corrected) in plasma

The confidence intervals of the geometric mean test to reference ratios for the metrics ( $C_{max}$ ,  $AUC_{0-t_{last}}$ , and  $AUC_{0-\infty}$ ) should fall within the limits of 80.00-125.00%, where  $C_{max}$  is the maximum plasma concentration,  $AUC_{0-t_{last}}$  is the area under the curve from zero to the last sampling time point,  $AUC_{0-\infty}$  is the area under the curve from zero to infinity.

**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 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 August 2011; Revised May 2022

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