

*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

## **Draft Guidance on Triamcinolone Acetonide**

**November 2021**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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 2018, FDA issued a draft product-specific guidance for industry on generic triamcinolone acetonide. We are now issuing revised draft guidance for industry that replaces the previously issued guidance.

---

<b>Active Ingredient:</b>	Triamcinolone acetonide
<b>Dosage Form; Route:</b>	Injectable; injection
<b>Recommended Studies:</b>	Two options: in vitro or in vivo studies

### **I. In vitro option:**

To qualify for the in vitro option for this drug product, all the following criteria should be met:

1. The test and reference listed drug (RLD) formulations are qualitatively (Q1)<sup>1</sup> and quantitatively (Q2)<sup>2</sup> the same (Q1/Q2).

---

<sup>1</sup> Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference product.

<sup>2</sup> Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within  $\pm 5\%$  of those used in the reference product.

2. Acceptable comparative physicochemical characterizations of the test and the reference standard (RS) products. The comparative study should be performed on a minimum of three exhibit batches of the test product<sup>3</sup> and three batches of the RS product (as available) for all three strengths (10 mg/mL, 40 mg/mL, and 80 mg/mL) and should include:
  - a. Polymorphic form of triamcinolone acetonide.
  - b. Crystalline shape and morphology of triamcinolone acetonide.
  - c. Appearance, pH, osmolality, viscosity over a range of shear rates, specific gravity.
  - d. Drug particle size and size distribution. The particle size distribution should be compared using population bioequivalence (PBE) (95% upper confidence bound) based on D50 and SPAN [i.e. (D90-D10)/D50]. The applicant should provide no fewer than ten data sets from three different batches of both the test and RS products for PBE analysis. Full profiles of the particle distribution should also be submitted for all samples tested. Refer to the draft product-specific guidance on *Budesonide, Inhalation; Suspension* for additional information regarding PBE.
3. Acceptable comparative in vitro drug release of triamcinolone acetonide from the test and RS products for all three strengths (10 mg/mL, 40 mg/mL, and 80 mg/mL). The methodology used for in vitro drug release testing should be able to discriminate the effect of process variability in the production of the test formulation.

## II. In vivo option:

1. Type of study: BE study with pharmacokinetic endpoint  
Design: Single-dose, two-way, parallel in-vivo (intramuscular administration)  
Strength: Single-dose of 10 mg (0.25 mL x 40 mg/mL)  
Subjects: Healthy males and non-pregnant, non-lactating females, general population  
Additional Comments: None

**Analyte to measure:** Triamcinolone acetonide in plasma

**Bioequivalence based on (90% CI):** Triamcinolone acetonide

**Waiver request of in-vivo testing:** 10 mg/mL and 80 mg/mL based on (i) acceptable bioequivalence study on the 40 mg/mL strength, (ii) acceptable dissolution testing across all strengths, (iii) proportional similarity in the formulations across all strengths, and (iv) qualitatively (Q1) and quantitatively (Q2) the same as the respectively RLD strength.

**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

---

<sup>3</sup> The manufacturing process for the exhibit batches should be reflective of the manufacturing process to be utilized for commercial batches.

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.

---

**Revision History:** Recommended August 2009; Revised February 2010, February 2011, July 2018, November 2021

**Unique Agency Identifier:** PSG\_012041