

Draft Guidance on Triamcinolone Acetonide

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Active Ingredient: Triamcinolone acetonide

Dosage Form; Route: Suspension; injectable

Recommended Studies: Two options: in vitro and in vivo

I. In vitro option:

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

- i. The test and Reference Listed Drug (RLD) formulations are qualitatively (Q1)¹ and quantitatively (Q2)² the same (Q1/Q2).
 - ii. Acceptable comparative physicochemical characterizations of the test and Reference Standard (RS) products. The comparative study should be performed on at least three exhibit batches of both the test and RS products and should include:³
 - Polymorphic form of triamcinolone acetonide.
 - Crystalline shape and morphology of triamcinolone acetonide.
 - Appearance, pH, osmolality, viscosity over a range of shear rates, specific gravity.
 - Drug particle size and size distribution. The particle size distribution should be compared using population bioequivalence (PBE) (95% upper confidence bound) based on D_{50} and SPAN [i.e. $(D_{90}-D_{10})/D_{50}$]. 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. Please refer to the Guidance on Budesonide inhalation suspension for additional information regarding PBE.
 - iii. Acceptable comparative in vitro drug release tests of triamcinolone acetonide from the test and RS products. 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.
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¹ Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the reference product.

² 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.

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

II. In vivo option:

Type of study: Fasting

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, general population.

Additional Comments: As per 21 CFR § 314.94, the proposed parenteral drug product should be qualitatively (Q1) and quantitatively (Q2) the same as the RLD.

Analytes to measure (in appropriate biological fluid): Triamcinolone Acetonide in plasma.

Bioequivalence based on (90% CI): Triamcinolone Acetonide

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

Dissolution test method and sampling times: The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: <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 (ANDA).