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*Draft – Not for Implementation*

## **Draft Guidance on Hydrocortisone**

**October 2024**

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In general, FDA’s guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

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**Active Ingredient:** Hydrocortisone

**Dosage Form:** Tablet

**Route:** Oral

**Strengths:** 5 mg, 10 mg, 20 mg

**Recommended Study:** One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 20 mg  
Subjects: Healthy males and non-pregnant, non-lactating females  
Additional comments: A dose of 4 mg dexamethasone should be administered 10 hours prior to drug administration as a pre-treatment to lower endogenous hydrocortisone levels.

**Analyte to measure:** Hydrocortisone in plasma

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

**Waiver request of in vivo testing:** 5 mg and 10 mg strengths based on (i) acceptable bioequivalence study on the 20 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths

**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 all strengths of the test product and reference listed drug (RLD).<sup>1</sup> Specifications will be determined upon review of the abbreviated new drug application.

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**Document History:** Recommended April 2013; Finalized August 2017; Revised October 2024

**Unique Agency Identifier:** PSG\_008697

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<sup>1</sup> If the RLD is not available, refer to the most recent version of the FDA guidance for industry on *Referencing Approved Drug Products in ANDA Submissions*.