*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

**Draft Guidance on Haloperidol**

**October 2024**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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**Active Ingredient:** Haloperidol

**Dosage Form:** Tablet

**Route:** Oral

**Strengths:** 0.5 mg, 1 mg, 2 mg, 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: 2 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: To prevent severe dystonia, subjects should be pre-medicated with benztropine tablets, 1 mg every 10 to 12 hours beginning 4 to 6 hours before dosing with haloperidol and continuing for a total of 4 doses to provide coverage during periods of substantial haloperidol levels. In the event of breakthrough acute dystonia, diphenhydramine hydrochloride 50 mg could be administered intramuscular or intravenous.

**Analyte to measure:** Haloperidol in plasma

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

**Waiver request of in vivo testing:** 0.5 mg, 1 mg, 5 mg, 10 mg and 20 mg strengths based on (i) acceptable bioequivalence study on the 2 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).[1] Specifications will be determined upon review of the abbreviated new drug application.

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**Document History:** Recommended December 2008; Revised February 2019, October 2024

**Unique Agency Identifier:** PSG_015921

[1] 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*.