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## Draft Guidance on Propafenone Hydrochloride

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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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<b>Active Ingredient:</b>	Propafenone hydrochloride
<b>Dosage Form:</b>	Tablet
<b>Route:</b>	Oral
<b>Strengths:</b>	150 mg, 225 mg, 300 mg
<b>Recommended Study:</b>	One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover in vivo  
Strength: 300mg  
Subjects: Healthy males and non-pregnant, non-lactating females  
Additional comments: Applicants may consider using a reference-scaled average bioequivalence approach for this drug product. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability  $\geq 30\%$ ) for the reference listed drug (RLD). For detailed information on this approach, refer to the most recent version of the FDA guidance for industry on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.<sup>a</sup>

**Analytes to measure:** Propafenone and its metabolite 5-OH propafenone in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C<sub>max</sub>.

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

**Waiver request of in vivo testing:** 150 mg and 225 mg strengths based on (i) acceptable bioequivalence study on the 300 mg strength, (ii) acceptable dissolution testing across all strengths, and (iii) proportional similarity in 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 each of all strengths of the test product and reference listed drug.<sup>1</sup> Specifications will be determined upon review of the abbreviated new drug application.

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**Document History:** Recommended May 2009; Finalized October 2011; Revised July 2017, October 2024

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<sup>a</sup> For the most recent version of a guidance, check the FDA guidance website at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

<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*.