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Draft Guidance on Acetaminophen; Propoxyphene Napsylate

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Tablet

Route: Oral

Strengths: 325 mg; 50 mg, 325 mg; 100 mg, 500 mg; 100 mg, 650 mg; 100 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: 650 mg; 100 mg
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: None

Analytes to measure: Acetaminophen and propoxyphene in plasma

Bioequivalence based on (90% CI): Acetaminophen and propoxyphene

Waiver request of in vivo testing: 325 mg; 50 mg, 325 mg; 100 mg, and 500 mg; 100 mg strengths based on (i) acceptable bioequivalence study on the 650 mg; 100 mg strength, (ii) acceptable in vitro dissolution testing of all strengths, and (iii) proportional similarity in the formulations across all strengths

Note: Since acetaminophen and propoxyphene napsylate tablets, 325 mg; 50 mg,650 mg; 100 mg. 325 mg; 100 mg, and 500 mg; 100 mg are the subject of three separate applications, three separate abbreviated new drug applications (ANDA) should be submitted. A waiver of in vivo bioequivalence testing of the 325 mg; 100 mg and the 500 mg; 100 mg strengths may be requested if the criteria are met. The in vivo bioequivalence study conducted on 650 mg; 100 mg should be cross-referenced, along with the in vivo waiver request. Refer to the most recent version of the FDA guidance for industry on *Variations in Drug Products that May Be Included in a Single ANDA.*[a]

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 ANDA.

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

[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.*