Draft Guidance on Acetaminophen; Propoxyphene Napsylate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Acetaminophen; Propoxyphene Napsylate

Form/Route: Tablets/Oral

Recommended studies: 2 studies

1. Type of study: Fasting
   Design: Single-dose, two-way crossover in-vivo
   Strength: 650 mg/100 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments:

2. Type of study: Fed
   Design: Single-dose, two-way crossover in-vivo
   Strength: 650 mg/100 mg
   Subjects: Healthy males and nonpregnant females, general population.
   Additional Comments:

Analytes to measure (in appropriate biological fluid): Acetaminophen and propoxyphene Napsylate in plasma.

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

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

Additional Comments: Since Acetaminophen and Propoxyphene Napsylate Tablets, 325 mg/50 mg and 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 (ANDAs) must 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 studies conducted on 650 mg/100 mg should be cross-referenced, along with the in-vivo waiver request. Refer to the Guidance for Industry, Variations in Drug Products that May Be Included in a Single ANDA located at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072892.pdf.

Dissolution test method and sampling times:

Please note that a Dissolution Methods Database is available to the public at the OGD website at http://www.accessdata.fda.gov/scripts/cder/dissolution/. Please find the dissolution information for this product at this website. Please 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 application.

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