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Draft Guidance on Bupivacaine

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This guidance, which interprets the Agency’s regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

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This is a new draft product-specific guidance for industry on generic bupivacaine.

Active Ingredient:	Bupivacaine
Dosage Form; Route:	Solution, extended release; infiltration
Strength:	660 mg/5 mL (132 mg/mL)
Recommended Studies:	Two options: (1) In vitro comparative drug release testing with one supportive characterization study or (2) one in vivo bioequivalence study with pharmacokinetic endpoints

I. Option 1: In vitro comparative drug release testing with one supportive characterization study

To be eligible for the in vitro bioequivalence study recommended in this guidance, the test product should meet the following criteria:

- Qualitatively (Q1) and quantitatively (Q2) the same as the Reference Listed Drug (RLD)
- Comparable viscosity compared to the Reference Standard (RS)

1. Type of study: Comparative in vitro drug release testing
Additional Comments: The method should show discriminatory power for detecting potential formulation differences. The applicant is encouraged to explore a method that is able to capture the initial burst release phase and the sustained release phase.

II. Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Bioequivalence study with pharmacokinetic endpoints
Design: Single-dose, two-way crossover in-vivo
Subjects: Healthy males and non-pregnant, non-lactating females
Additional Comments: Delivered via trailing subcutaneous injection of bupivacaine solution into abdominal subcutaneous space. The trailing injection should be accomplished by advancing a needle into the subcutaneous space and injecting continuously as the needle withdrawn.

Analyte to measure: Bupivacaine in plasma

Bioequivalence based on (90% CI): Bupivacaine

Waiver request of in vivo testing: Not applicable

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 and reference products. Specifications will be determined upon review of the abbreviated new drug application.

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