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Draft Guidance on Sufentanil Citrate

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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 sufentanil citrate.

Active Ingredient: Sufentanil citrate

Dosage Form; Route: Tablet; sublingual

Recommended Study: One study

1. Type of study: Fasting
Design: Single-dose, two-treatment, two-period crossover in vivo
Strength: EQ 0.03 mg Base
Subjects: Healthy males and non-pregnant, non-lactating females
Additional comments: Sufentanil citrate tablets are approved with a Risk Evaluation and Mitigation Strategy (REMS) with an Elements to Assure Safe Use (ETASU), which restricts its use. All pertinent elements of the REMS must be incorporated into the protocol and informed consent. Exclude subjects who are on CYP3A4 inducers or inhibitors. Include sufficient sampling time points, including at 1 hour, to adequately delineate the pharmacokinetic profile of sufentanil during the early phase of absorption. Naltrexone or other opioid antagonist should be incorporated to block the pharmacodynamic effects of the opioid. The opioid antagonist should be administered

well in advance of opioid dosing to achieve adequate blockade of opioid receptors. The most common approach is to administer 50 mg of naltrexone at the following times: 12 hours prior to dosing; at the time of study drug dosing; and 12 hours after the last dose of study drug. Consult with a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist. The reference listed drug (RLD) is a drug-device combination product. Refer to the FDA's Guidance for Industry: *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*, which provides the FDA's current thinking on the identification and assessment of any differences in the design of the user interface for a proposed generic drug-device combination product when compared to its RLD.

Analyte to measure: Sufentanil in plasma

Bioequivalence based on (90% CI): Sufentanil

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

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