

## Draft Guidance on Levorphanol Tartrate

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

<b>Active Ingredient:</b>	Levorphanol tartrate
<b>Dosage Form; Route:</b>	Tablet; oral
<b>Recommended Studies:</b>	Two options: Biopharmaceutics Classification System (BCS) or in vivo studies

### I. BCS waiver option:

It may be possible to request a waiver of in vivo testing for this product provided that the appropriate documentation regarding high solubility, high permeability and rapid dissolution as detailed in the guidance for industry *Waiver of In Vivo Bioavailability and Bioequivalence for Immediate – Release Solid Oral Dosage Forms Based on the Biopharmaceutics Classification System* is submitted in the application. You may use information contained in the approved labeling of the reference product. Peer-reviewed articles may not contain the necessary details of the testing for the Agency to make a judgment regarding the quality of the studies. A decision regarding the acceptability of the waiver request can only be made upon review of the data submitted in the application.

### II. In vivo option: Two studies

1. Type of study: Fasting

Design: Single-dose, two-way crossover in-vivo

Strength: 2 mg

Subjects: Males and non-pregnant, non-lactating females, general population.

Additional Comments: Please use a narcotic antagonist such as naltrexone. Please consult a physician who is an expert in the administration of opioids for an appropriate dose of narcotic antagonist.

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2. Type of study: Fed

Design: Single-dose, two-way crossover in-vivo

Strength: 2 mg

Subjects: Males and non-pregnant, non-lactating females, general population.

Additional Comments: Please see comments above.

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**Analyte to measure (in appropriate biological fluid):** Levorphanol in plasma

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

**Waiver request of in-vivo testing:** Not applicable

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods web site, available to the public at the following location: <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 (ANDA).