

## Draft Guidance on Naltrexone

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

**Active Ingredient:** Naltrexone

**Dosage Form; Route:** Extended-release suspension; intramuscular

**Recommended Studies:** One study

1. Type of study: In vivo single-dose fasting  
Design: Parallel  
Strength: 380 mg/vial (dose: 380 mg)  
Subjects: Healthy males and nonpregnant females, general population  
Additional comments: The 90% confidence intervals of the geometric mean test/reference (T/R) ratios for the metrics ( $C_{max}$ ,  $AUC_{1-10}$ ,  $AUC_{10-28}$ , and  $AUC_{0-\infty}$ ) should fall within the limits of 80-125%

---

As per 21 CFR § 314.94(a)(9)(iii), the proposed parenteral drug product should be qualitatively (Q1) and quantitatively (Q2) the same as the reference product.

---

**Analytes to measure (in appropriate biological fluid):** Naltrexone in plasma

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

The additional comments above provide more guidance regarding bioequivalence.

**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).

In addition to the method specified on the Dissolution Methods Web site, conduct comparative dissolution testing on 12 dosage units of the test and reference products at a strength of 380 mg/vial (dose: 380 mg) with the following method:

Strength: 380 mg/vial (dose: 380 mg)

Medium: Phosphate buffered saline with 0.02% Tween 20 and 0.02% sodium azide, pH  $7.4 \pm 0.05$  (final osmolality should be  $270 \pm 20$  mOsm)

Volume: Add 200 mL of release medium to a 250 mL HDPE plastic bottle containing  $600 \pm 10$  mg of microspheres (203 mg naltrexone) at room temperature

Temperature:  $37 \pm 0.3$  °C

Samples should be taken at frequent time intervals and should also include samples on Day 1, Day 7, Day 14, and Day 28.