

## Draft Guidance on Levetiracetam

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**Active ingredient:** Levetiracetam

**Form/Route:** Tablet/Oral

**Recommended studies:** **2 Options: BCS or In-Vivo Studies**

### I. BCS Waiver option:

It may be possible to request a waiver of in-vivo testing for all the strengths of 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 BE studies option

1. Type of study: Fasting  
Design: Single-dose, two-treatment, two-period crossover *in-vivo*  
Strength: 1000 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional Comments:  

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2. Type of study: Fed  
Design: Single-dose, two-treatment, two-period crossover *in-vivo*  
Strength: 1000 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional comments:  

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**Analytes to measure:** Levetiracetam using an achiral assay.

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

**Waiver request of in-vivo testing:** 250 mg, 500 mg and 750 mg based on (i) acceptable bioequivalence studies on the 1000 mg strength, (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

### 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.fda.gov/cder/ogd/index.htm>. 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.