

**Draft Guidance on Disulfiram**

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

**Active ingredient:** Disulfiram

**Form/Route:** Tablets/Oral

**Recommended studies:** 2 studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in-vivo  
Strength: 500 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments:

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2. Type of study: Fed  
Design: Single-dose, two-way crossover in-vivo  
Strength: 500 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments: Please refer to the Amantadine Hydrochloride Tablet Draft Guidance for additional information regarding fed studies.

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**Analytes to measure (in appropriate biological fluid):** Disulfiram and its active metabolites N,N-diethyldithiocarbamate (DDC) and S-methyl N,N-diethyldithiocarbamate (Me-DDC), in human plasma.

Please submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolite, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for AUC and C<sub>max</sub>.

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

If disulfiram can be reliably measured, please analyze the data for the parent compound using the confidence interval approach. The data for the active metabolites can be used as supportive evidence. However, if you can demonstrate that it is not possible to measure disulfiram in plasma accurately and reliably, please analyze the primary metabolite DDC using the confidence interval approach. If you demonstrate that DDC in plasma cannot be reliably and accurately measured, please analyze the secondary metabolite MeDDC using the confidence interval approach.

**Waiver request of in-vivo testing:** Disulfuram Tablet, 250 mg based on (i) acceptable bioequivalence studies on the 500 mg strength, (ii) acceptable in-vitro dissolution testing of all strengths, and (iii) proportional similarity of the formulations across all strengths. Please refer to the Mirtazapine Tablet Draft Guidance for additional information regarding waivers of in-vivo testing.

**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.accessdata.fda.gov/scripts/cder/dissolution/>. 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.