

## Draft Guidance on Glyburide; Metformin Hydrochloride

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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 ingredients:** Glyburide; Metformin Hydrochloride

**Form/Route:** Tablets/Oral

**Recommended studies:** 2 studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in-vivo  
Strength: 2.5 mg/500 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments: To avoid hypoglycemic episodes in healthy volunteers, the drug products should be administered with 240 mL of a 20% glucose solution in water, followed by 60 mL of the glucose solution administered every 15 min for up to 4 hours after dosing.

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2. Type of study: Fed  
Design: Single-dose, two-way crossover in-vivo  
Strength: 2.5 mg/500 mg  
Subjects: Healthy males and nonpregnant females, general population  
Additional Comments: Please see comment above.

**Analytes to measure (in appropriate biological fluid):** Glyburide and metformin in plasma

**Bioequivalence based on (90% CI):** Glyburide and metformin

**Waiver request of *in-vivo* testing:** 1.25 mg/250 mg and 5 mg/500 mg based on (i) acceptable bioequivalence studies on the 2.5 mg/500 mg strength, (ii) acceptable in vitro dissolution testing across all strengths, and (iii) proportional similarity in the formulations across 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.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.