This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

This guidance, which interprets the Agency’s regulations on bioequivalence at 21 CFR part 320, provides product-specific recommendations on, among other things, the design of bioequivalence studies to support abbreviated new drug applications (ANDAs) for the referenced drug product. FDA is publishing this guidance to further facilitate generic drug product availability and to assist the generic pharmaceutical industry with identifying the most appropriate methodology for developing drugs and generating evidence needed to support ANDA approval for generic versions of this product.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in FDA guidances means that something is suggested or recommended, but not required.

This is a new draft product-specific guidance for industry on generic cobicistat; darunavir; emtricitabine; tenofovir alafenamide fumarate.

<table>
<thead>
<tr>
<th>Active Ingredients:</th>
<th>Cobicistat; Darunavir; Emtricitabine; Tenofovir alafenamide fumarate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage Form; Route:</td>
<td>Tablet; oral</td>
</tr>
<tr>
<td>Recommended Studies:</td>
<td>Two in vivo bioequivalence studies with pharmacokinetic endpoints</td>
</tr>
</tbody>
</table>

1. **Type of study:** Fasting  
   **Design:** Single-dose, two-treatment, two-period crossover in vivo  
   **Strength:** 150 mg; 800 mg; 200 mg; EQ 10 mg Base  
   **Subjects:** Healthy males and non-pregnant, non-lactating females  
   **Additional comments:** Exclude subjects with any combination of abnormal liver function tests, a history of drug-induced skin reactions or allergic reactions to sulfa drugs. Applicants may consider using a reference-scaled average bioequivalence approach for darunavir. If using this approach, provide evidence of high variability in the pharmacokinetic parameters (i.e., within-subject variability ≥30%) for the reference
product. For detailed information on this approach, refer to the most recent version of the FDA guidance for industry on *Bioequivalence Studies with Pharmacokinetic Endpoints for Drugs Submitted Under an ANDA*.\(^a\)

2. **Type of study:** Fed  
   **Design:** Single-dose, two-treatment, two-period crossover in vivo  
   **Strength:** 150 mg; 800 mg; 200 mg; EQ 10 mg Base  
   **Subjects:** Healthy males and non-pregnant, non-lactating females  
   **Additional comments:** See comments above.

**Analytes to measure:** Cobicistat, darunavir, emtricitabine, and tenofovir alafenamide in plasma

**Bioequivalence based on (90% CI):** Cobicistat, darunavir, emtricitabine, and tenofovir alafenamide

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

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found in the FDA’s Dissolution Methods database, [http://www.accessdata.fda.gov/scripts/cder/dissolution/](http://www.accessdata.fda.gov/scripts/cder/dissolution/). Conduct comparative dissolution testing on 12 dosage units for each of the test and reference products. Specifications will be determined upon review of the ANDA.

**Unique Agency Identifier:** PSG_210455

\(^a\) For the most recent version of a guidance, check the FDA guidance web page at [https://www.fda.gov/regulatory-information/search-fda-guidance-documents](https://www.fda.gov/regulatory-information/search-fda-guidance-documents).