Draft Guidance on Clobetasol Propionate

I. Waiver option:

a. To qualify for a waiver of the in vivo bioequivalence (BE) study requirements under 21 CFR 320.22(b)(3), a generic Clobetasol Propionate Aerosol, Foam/Topical, 0.05% must be a solution for aerosolization, have the same active ingredient in the same concentration and dosage form as the reference listed drug product (RLD) and must not have an inactive ingredient or other change in formulation from the RLD that may significantly affect systemic or local availability.

b. For a topical drug product with inactive ingredients that differ from the RLD or are present in significantly different amounts [as permitted by the chemistry, manufacturing and controls regulations for abbreviated new drug applications (ANDAs), 21 CFR 314.94(a)(9)(v)], the regulation specifies that the applicant must identify and characterize the differences and provide information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product. If the generic Clobetasol Propionate Aerosol, Foam/Topical, 0.05% has different inactive ingredients compared to the RLD or differences in the amounts of the same inactive ingredients that are proportionally more than +/- 5% compared to the RLD, then the Office of Generic Drugs (OGD) may request a bioequivalence study with clinical endpoints to determine bioequivalence between the products.

c. For products applied to the scalp, differences in surfactants or potential penetration enhancers may change the distribution of the product over the scalp or penetration of the drug into the diseased tissues. Therefore, clinical endpoint bioequivalence studies are requested for generic shampoo products with differences in these ingredients that are proportionally more than +/- 5% compared to the RLD.

d. To support the waiver request, data from the following comparative in vitro assays of test vs. reference are requested:
   • Microscopic Birefringence Analysis on the dispensed foam after complete collapse to determine whether any crystals of undissolved clobetasol propionate form during dispensing.
   • Time to Break Analysis, conducted at 30°C, 33°C, 35°C, and 40°C. Time to break is the time from dispensing to complete foam collapse (break). The testing should be done on at least 3 different lots of the RLD and at least 3 lots of the test product (with each lot manufactured separately).
   • Weight per volume of uncollapsed foam.

Active ingredient: Clobetasol Propionate

Form/Route: Aerosol, Foam/Topical

Recommended Feb 2011
II. In Vivo option:

**Recommended studies:** 1 study

- **Type of study:** Clinical Endpoint Bioequivalence (BE) Study
- **Design:** Randomized, double blind, parallel, placebo-controlled in vivo
- **Strength:** 5%
- **Subjects:** Healthy males and females with moderate to severe corticosteroid-responsive scalp psoriasis
- **Additional comments:** FDA recommends submitting a protocol for review and comment prior to conducting the study.

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**Analytes to measure (in appropriate biological fluid):** Not Applicable

**Bioequivalence based on (90% CI):** Clinical endpoint (in vivo option)

**Dissolution test method and sampling times:** Not Applicable