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Draft Guidance on Clindamycin Phosphate

May 2026

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Active Ingredient:	Clindamycin phosphate
Dosage Form:	Suppository
Route:	Vaginal
Strength:	100 mg
Reference Listed Drug:	NDA 050767
Recommended Studies:	Two options: (I) one in vitro bioequivalence study and other characterization tests or (II) one comparative clinical endpoint bioequivalence study

Option I: In vitro bioequivalence study and other characterization tests

Eligibility: To demonstrate bioequivalence for clindamycin phosphate vaginal suppository, 100 mg using in vitro studies, the test product should contain no difference in inactive ingredients or in other aspects of the formulation relative to the reference standard (RS) that may significantly affect the local or systemic availability of the active ingredient. For example, if the test product and RS are qualitatively (Q1) and quantitatively (Q2) the same, as defined in the guidance for industry *ANDA Submissions – Refuse-to-Receive Standards*[a], and the criteria below are also satisfied, the bioequivalence of the test product may be established using a characterization-based bioequivalence approach.

Class of study: Comparative characterization
Type of study: Characterization studies for the following physicochemical and structural (Q3) attributes:

a. Visual appearance (dimensions) with high resolution photographs
b. Structural organization of matter
    - Microscopic examination with representative high-resolution microscopic images at multiple magnifications
    - Analysis of particle size distribution, crystal habit, and polymorphic form of clindamycin phosphate in the drug product, as applicable
c. Viscosity at 37°C
d. Oleaginous components
e. Melting point
f. Specific gravity

Study design recommendations:

- The test product and RS should have the same Q3 attributes, based upon acceptable comparative Q3 characterization tests with a minimum of three batches of the test product and three batches (as available) of the RS.
- The test product and RS batches should ideally represent the product at different ages throughout its shelf life.
- Refer to the guidance for industry *Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in ANDAs*[a] for additional information regarding comparative Q3 characterization tests. The comparison of the test product and RS should include characterizations of the following Q3 attributes:

1. Class of study: Bioequivalence
Type of study: In Vitro Release Test (IVRT)
Design: Single-dose, two-treatment, parallel, multiple-replicate per treatment group study design using an occluded pseudo-infinite dose, in vitro
Strength:100 mg
Test system: A synthetic membrane in a diffusion cell system
Analyte to measure: Clindamycin phosphate in receptor solution
Bioequivalence based on: Clindamycin phosphate (IVRT endpoint: drug release rate)
Study design recommendations :
    - The test product and RS should have an equivalent rate of clindamycin phosphate release based upon an acceptable IVRT bioequivalence study comparing a minimum of one batch each of the test product and RS using an appropriately validated IVRT method.
    - The IVRT study should be conducted at 37°C based on the route of administration of this drug product.
    - The method used to load the suppository into the donor chamber should be justified based on appropriate development and validation studies and should be consistent between the test product and RS.

- Refer to the guidance for industry *In Vitro Release Test (IVRT) Studies for Topical Drug Products Submitted in ANDAs*[a] for additional information regarding the development, validation, conduct and analysis of acceptable IVRT methods/studies.
- The batches of test product and RS evaluated in the IVRT bioequivalence study should be included among those for which the Q3 attributes are characterized.

Option II: One in vivo comparative clinical endpoint bioequivalence study

1. Class of study: Bioequivalence
   Type of study: Comparative clinical endpoint bioequivalence study
   Design: Randomized, double-blind, three-arm, parallel, placebo-controlled in vivo
   Strength: 100 mg
   Subjects: Non-pregnant, non-lactating females with bacterial vaginosis (BV)

Additional study design recommendations for the comparative clinical endpoint bioequivalence study:

1. FDA recommends conducting a comparative clinical endpoint bioequivalence study in the treatment of BV. Subjects are to be randomized to receive the test product versus the RS or vehicle (placebo) as one suppository administered intravaginally once daily at bedtime for 3 consecutive days.

2. Inclusion criteria (the sponsor may add additional criteria):
   a. Non-pregnant, non-lactating female aged ≥ 18 years.
   b. Diagnosis of BV, defined as the presence of all of the following:
      - Off-white or gray, thin, homogenous vaginal discharge associated with minimal or absent pruritus or inflammation of the vulva and vagina
      - Saline wet mount of vaginal discharge demonstrating the proportion of clue cells to be ≥ 20% of the total epithelial cells
      - Vaginal pH > 4.5, using pH paper that measures from 4.0-6.0
      - Positive "whiff test" (a fishy odor of the vaginal discharge) after addition of a drop of 10% potassium hydroxide (KOH) to vaginal discharge
      - Gram stain Nugent score ≥ 7 on first day of dosing (study Day 1)
   c. Any subject with childbearing potential has a negative urine pregnancy test on the first day of dosing (study Day 1) using a pregnancy test with a sensitivity of at least 25 mIU/mL hCG
   d. Willing to refrain from using any intra-vaginal product or device other than the study treatment (e.g., other vaginal drugs, spermicide, tampon, douche, diaphragm, condom, or other products) on study Days 1-6, for 48 hours prior to the first dose of study product, and for 48 hours prior to Test of Cure visit.
   e. Agrees to abstain from sexual intercourse on study Days 1-3 and for 48 hours prior to Test of Cure visit.

3. Exclusion criteria (the sponsor may add additional criteria):

a. Menstruating at the baseline visit (when evaluation for BV is performed) or anticipate onset of menses during study drug administration
b. History of regional enteritis, ulcerative colitis, or a history of "antibiotic-associated" colitis.
c. Evidence of any vulvovaginitis other than BV (e.g., candidiasis, *Trichomonas vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Herpes simplex,* or human papilloma virus)
d. Subject with another vaginal or vulvar condition, which would confound the interpretation of clinical response
e. Subject will be under treatment during the study period for cervical intraepithelial neoplasia or cervical carcinoma
f. History of hypersensitivity to clindamycin, lincomycin, or any of the components of the formulation
g. Use within 2 weeks prior to baseline of (1) topical or systemic antibiotics (2) topical or systemic antifungal, or (3) systemic steroids (oral or injectable).

4. At the baseline visit, documentation of the participant's medical history should include menopausal status. For postmenopausal women, document the month and year of the last menses. For premenopausal women, documented information should include: the first day of the last menstrual period, regularity of menses, use of contraception, past episodes of BV, and sexual history (e.g., sex of intimate partners and history of sexually transmitted infections).

5. The protocol should include a list of the prescription and over-the-counter drug products, procedures, and activities that are prohibited during the study, such as:
    a. Systemic corticosteroid or immunosuppressive drugs
    b. Systemic or topical antibiotics, other than study product
    c. Neuromuscular blocking agents

6. The primary endpoint of the study is the therapeutic cure rate, defined as both a clinical cure (resolution of clinical signs and symptoms, e.g., normal physiological vaginal discharge, whiff test is negative for any amine "fishy" odor, saline wet mount is negative for clue cells, and vaginal pH is < 4.7, using pH paper that measures pH from 4.0-6.0) and a bacteriological cure (Nugent score <4), evaluated at the Test of Cure visit (study Day 22-30). Subjects who used any BV therapy, other than study product, during the study or had a Nugent score >3 at the Test of Cure visit should be considered therapeutic failures.

7. Provide the Subject-Level Analysis Dataset (ADSL), once record per subject, using the following headings, if applicable:
    a. Study identifier
    b. Subject identifier
    c. Study site identifier
    d. Age
    e. Age units (years)
    f. Sex

g. Race
h. Name of planned treatment: test product, RS, placebo
i. Name of actual treatment: test product, RS, placebo
j. Date of enrollment
k. Date of randomization
l. Date/time of exposure to treatment
m. End of study date
n. Completed the study (yes/no)
o. Reason for premature discontinuation of subject
p. Per-protocol (PP) population inclusion (yes/no)
q. Reason for exclusion from PP population
r. Modified Intent to Treat (mITT) population inclusion (yes/no)
s. Reason for exclusion from mITT population
t. Safety population inclusion (yes/no)
u. Reason for exclusion from safety population
v. Subject required additional treatment due to unsatisfactory treatment response (yes/no).
w. Baseline vaginal discharge consistent with clinical diagnosis BV (yes/no)
x. Baseline clue cells on wet mount (≥20%, <20%, or none)
y. Baseline vaginal pH
z. Baseline KOH "whiff test" (positive/negative)
aa. Baseline Nugent score
bb. Baseline Nugent score ≥ 7 (yes/no)
cc. Chlamydia trachomatis (positive/negative)
dd. Neisseria gonorrhoeae test (positive/negative)
ee. Urine pregnancy test (positive/negative)
ff. Normal physiological vaginal discharge (Day 22-30) (yes/no)
gg. KOH "whiff test" (Day 22-30) (positive/negative)
hh. Clue cells on wet mount (Day 22-30) (≥20%, <20%, or none)
ii. Clinical cure (Day 22-30) (yes/no)
jj. Nugent score (Day 22-30) (0, 1, 2, 3…10)
kk. Bacteriological cure (Day 22-30) (yes/no)
ll. Therapeutic cure (Day 22-30) (responder; treatment success) (yes/no)
mm. Adverse event reported (yes/no)
nn. Concomitant medication (yes/no)

8. Provide the basic data structure (BDS) dataset with records per subject, per visit, per analysis timepoint, using the following headers, if applicable:
    a. Study identifier
    b. Subject identifier
    c. Study site identifier
    d. Name of planned treatment
    e. Name of actual treatment (exposure): test product, RS, placebo
    f. Visit number
    g. Visit date
    h. Number of days since baseline visit

i. Study visit within the designated window (yes/no)
j. Evaluator: identity of evaluator
k. Abnormal vaginal discharge (yes/no)
l. Normal physiological vaginal discharge (yes/no)
m. KOH "whiff test" (positive/negative)
n. Clue cells on wet mount (≥20%, <20%, or none)
o. Clinical cure (yes/no)
p. Nugent score (0, 1, 2, 3…10)
q. Bacteriological cure (yes/no)
r. Therapeutic cure (responder) (yes/no)
s. Additional treatment required during the visit (yes/no)
t. Adverse event reported during the visit (yes/no)
u. Use of any vaginal products other than study product (yes/no)
v. Concomitant medication during the visit (yes/no)

9. Refer to the product-specific guidance *Adapalene; Benzoyl Peroxide Topical Gel* (NDA 207917)[b] for a recommended approach to statistical analysis and study design for the comparative clinical endpoint bioequivalence study.

10. Refer to the Study Data Standards Resources website https://www.fda.gov/industry/fda-resources-data-standards/study-data-standards-resources.

Additional information for both options:

Device: The reference listed drug (RLD) is presented as vaginal suppositories co-packaged with a reusable vaginal applicator. The device constituent part is the applicator. FDA recommends that prospective applicants examine the size and shape, the external critical design attributes, and the external operating principles of the RLD device when designing the test device including:

- Applicator can be disassembled and washed with soap and water

User interface assessment: An abbreviated new drug application for this product should include complete comparative analyses so FDA can determine whether any differences in design for the user interface of the proposed generic product, as compared to the RLD, are acceptable and whether the product can be expected to have the same clinical effect and safety profile as the RLD when administered to patients under the conditions specified in the labeling. For additional information, refer to the guidance for industry *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[a]

Document History: Recommended March 2012; Revised May 2026

[a] We update guidances periodically. For the most recent version of a product-specific guidance, refer to the FDA guidance webpage at https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm.
[b] We update guidances periodically. For the most recent version of a guidance, refer to the FDA guidance webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.