

## Draft Guidance on Lidocaine Hydrochloride

May 2026

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**Active Ingredient:** Lidocaine hydrochloride

**Dosage Form:** Jelly

**Route:** Topical

**Strength:** 2%

**Reference Listed Drug:** NDA 008816

**Recommended Studies:** In vitro bioequivalence study and other characterization tests

**Eligibility:** To demonstrate bioequivalence for lidocaine hydrochloride topical jelly, 2% 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*<sup>a</sup>, and the criteria below are also satisfied, the bioequivalence of the test product may be established using a characterization-based bioequivalence approach.

1. Class of study: Comparative Characterization  
Type of study: Characterization studies for the following physicochemical and structural (Q3) attributes:
  - a. Visual appearance and texture
  - b. Structural organization of matter
    - Microscopic examination with representative high-resolution microscopic images at multiple magnifications

- c. Rheological behavior which may be characterized using a rheometer that is appropriate for monitoring the non-Newtonian flow behavior of semi-solid dosage forms. Rheological behavior should be assessed at both 25°C and 37°C. The following evaluations are recommended:
  - A characterization of shear stress vs. shear rate and viscosity vs. shear rate. At minimum, this should consist of numerical viscosity data at three shear rates (low, medium, and high).
  - A complete flow curve across the range of attainable shear rates, until low or high shear plateaus are identified.
  - Yield stress values should be reported if the material tested exhibits plastic flow behavior.
- d. pH
- e. Specific gravity

Study design recommendations:

- The test product and RS should have the same Q3 attributes, based upon acceptable comparative Q3 characterization of 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 most recent version of the guidance for industry *Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in ANDAs*<sup>a</sup> for additional information regarding comparative Q3 characterization tests
- When the test product has tube packaging configurations with and without a detachable cone tip, the characterization of rheological behavior should be conducted for product samples dispensed both with and without the detachable cone tip attached to the tube.
- Other Q3 characterization tests may be conducted with product samples consistently dispensed either with or without the detachable cone tip attached to the tube. When the test product has a pre-filled syringe packaging configuration, product samples should be dispensed from the pre-filled syringe for all Q3 characterization tests.

2. 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: 2%

Test system: A synthetic membrane in a diffusion cell system

Analyte to measure: Lidocaine in receptor solution

Bioequivalence based on: Lidocaine (IVRT endpoint: drug release rate)

Study design recommendations:

- The test product and RS should have an equivalent rate of lidocaine 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 bioequivalence study should be conducted at 37°C.
- Refer to the guidance for industry *In Vitro Release Test Studies for Topical Drug Products Submitted in ANDAs*<sup>a</sup> 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.
- Applicants may utilize the above recommendations to establish bioequivalence of a test product in a different packaging configuration compared to the RS (e.g., tube versus pre-filled syringe).

**Meeting recommendations:** Due to the potential safety concerns related to lidocaine hydrochloride topical jelly, 2%, if a prospective generic lidocaine hydrochloride topical jelly, 2% does not meet the formulation criteria outlined above, the applicant should clearly characterize the differences and provide sufficient scientific evidence that the difference will not change the local or systemic availability of the drug or otherwise change the safety or efficacy of the product. Applicants intending to propose an alternative approach by which to demonstrate bioequivalence should refer to the guidance for industry *Controlled Correspondence Related to Generic Drug Development and the guidance for industry Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*<sup>a</sup> for additional information describing the procedures on how to clarify regulatory expectations regarding their individual drug development program.

**Device:** The reference listed drug (RLD) has two presentations that are drug-device combination products:

- A 30 mL tube co-packaged with a detachable cone tip for urethral instillation; the cone tip is the device constituent part.
- 10 mL and 20 mL single-use prefilled syringes with an integrated tapered tip for urethral instillation; the syringe is the device constituent part.

FDA recommends that prospective applicants examine the size and shape, external critical design attributes, and external operating principles of the RLD device when designing the test device including the following characteristics:

- Cone tip forms secure attachment and seal with opening of 30 mL tube
- Single-use syringe

**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*.<sup>a</sup>

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**Document History:** Recommended August 2023; Revised May 2026

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<sup>a</sup> 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>.