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Draft Guidance on Desmopressin Acetate

December 2025

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Active Ingredient:	Desmopressin acetate
Dosage Form:	Spray, metered
Routes:	Nasal
Strength:	0.01 mg/spray
Recommended Studies:	Two options: (1) Six in vitro bioequivalence studies or (2) One in vivo bioequivalence study with pharmacokinetic endpoints

I. Option 1: Six in vitro bioequivalence studies

To demonstrate bioequivalence by this option, 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, the test product can be qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the RS to satisfy no difference in inactive ingredients.

FDA recommends that prospective applicants conduct the following in vitro bioequivalence studies for the test product and RS. Use at least three batches each of the test product and RS, with no fewer than 10 units from each batch. FDA recommends that three primary stability batches be also used to demonstrate in vitro bioequivalence. The three batches of test product should be manufactured from, at a minimum, three different batches of drug substances, excipients, and device constituent part components. The test product should consist of the final device constituent part (e.g., pump and actuator) and final drug constituent formulation intended

[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RS.
[2] Q2 (Quantitative sameness) means that concentrations of the inactive ingredient(s) used in the test product are within ± 5% of those used in the RS.

to be marketed. The following in vitro bioequivalence tests are recommended:

1. Single actuation content (SAC)
2. Droplet size distribution by laser diffraction
3. Drug in small particles/droplets
4. Spray pattern
5. Plume geometry
6. Priming and re-priming

Additional comments: Refer to the most recent version of the product-specific guidance for *Fluticasone Propionate Nasal Metered Spray* (020121)[a] for recommendations on design and equivalence criteria for the aforementioned in vitro bioequivalence studies, and general recommendations on the conduct of the in vitro bioequivalence studies and data submission.

II. Option 2: One in vivo bioequivalence study with pharmacokinetic endpoints

1. Type of study: Fasting
   Design: Single-dose, two-way crossover
   Strength: 0.01 mg/spray
   Dose: 0.01 mg, administered as one spray in one nostril
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional comments: Subjects should adhere to the reference listed drug (RLD) product labeling for administration.

   Analyte to measure: Desmopressin in plasma

   Bioequivalence based on (90% CI): Desmopressin

Additional information:

Device:
The RLD is presented in a bottle with a nasal pump and actuator. The pump with actuator is the device constituent part.

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

- Metered, multi-dose format
- Number of doses

User interface assessment:
An ANDA 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 most recent version of the FDA

guidance for industry on *Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA*.[b]

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[a] For the most recent version of a product-specific guidance, check the FDA product-specific guidance website at https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm.
[b] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.