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*Draft – Not for Implementation*

## **Draft Guidance on Varenicline Tartrate**

**November 2022**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

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<b>Active Ingredient:</b>	Varenicline tartrate
<b>Dosage Form; Route:</b>	Spray; nasal
<b>Strength:</b>	EQ 0.03 mg base/spray
<b>Recommended Studies:</b>	Six in vitro bioequivalence studies

FDA recommends the following in vitro studies to establish bioequivalence of the test (T) and reference (R) nasal sprays containing varenicline tartrate.

### **Six in vitro bioequivalence studies:**

FDA recommends that prospective applicants conduct the following in vitro bioequivalence studies on samples from each of three or more batches of the T product and three or more batches of the R product, 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 the T product should be manufactured from, at minimum, three different batches of the drug substance, three different batches of critical excipients, and three different batches of the device components (e.g., pump and actuator) proposed for the final device configuration of the commercial product. The T product should consist of the final device constituent part and the final drug constituent formulation intended to be marketed. The following in vitro bioequivalence studies are recommended:

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

Additional comments: Refer to the most recent version of the FDA guidance for industry on *Fluticasone Propionate Nasal Spray Metered* (NDA 020121)<sup>a</sup> 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.

**Additional information:**

Formulation:

FDA recommends that the T formulation be qualitatively (Q1)<sup>1</sup> and quantitatively (Q2)<sup>2</sup> the same as the R formulation.

Device:

The Reference Listed Drug (RLD) product is presented in a nasal pump dispenser that is a device constituent.

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 of the RLD:

- Metered, multi-dose format of RLD device
- Same number of doses

User interface assessment:

An Abbreviated New Drug Application (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*.<sup>b</sup>

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<sup>1</sup> Q1 (qualitative sameness) means that the T product uses the same inactive ingredient(s) as the R product.

<sup>2</sup> Q2 (quantitative sameness) means that concentrations of the inactive ingredient(s) used in the T product are within  $\pm 5\%$  of those used in the R product.

<sup>a</sup> For the most recent version of the product-specific guidance, check the FDA product-specific guidance web page at: <https://www.accessdata.fda.gov/scripts/cder/psg/index.cfm>.

<sup>b</sup> 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>.