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Draft Guidance on Liraglutide

December 2025

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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

Dosage Form: Solution

Route: Subcutaneous

Strength: 18 mg/3 mL (6 mg/mL)

Recommended Study: Request for waiver of in vivo bioequivalence study requirements

To qualify for a waiver from submitting an in vivo bioequivalence study on the basis that bioequivalence is self-evident under 21 CFR 320.22(b)(1), a generic liraglutide subcutaneous solution product should be qualitatively (Q1)[1] and quantitatively (Q2)[2] the same as the reference listed drug (RLD).

An applicant may seek approval of a drug product intended for parenteral use that differs from the RLD in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed drug product. [3]

[1] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RLD.
[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 RLD.
[3] 21 CFR 314.94(a)(9)(iii).

Refer to the most recent version of the FDA's guidance for industry on, *ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin*[a], for additional recommendations on conducting comparative studies between the proposed generic and RLD [4].

Non-clinical methods can be used to demonstrate comparable safety and efficacy profiles between a proposed generic peptide (recombinant or synthetically produced) and the reference standard (RS). Unlike synthetic peptides, recombinant peptides may also contain impurities, such as host cell proteins and residual DNA, from the host cell. Therefore, FDA recommends that applicants demonstrate and justify these host cell related impurities are well controlled if the proposed generic peptide product is manufactured using a recombinant process.[5]

Additional information:

Device:
The RLD is presented in a prefilled pen injector. The pen injector 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 device when designing the test device including:

- Multi-use disposable pen injector with variable-dose format
- Dose selector and dose button
- Needle connector compatibility

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*.[a]

[4] Demonstrating comparable innate immune activities can be accomplished through analyzing aggregates and non-peptide process-related impurities, which may alter the product's immunogenicity profile. Differences found in comparability studies assessing aggregates should be mitigated using manufacturing strategies. Levels of non-peptide process-related impurities including particulate matter, microbial contaminants, residual organic solvents, elemental impurities and leachables, should meet compendial acceptance criteria and toxicological limits. If non-peptide process-related impurities meet these criteria and limits, and aggregation profiles are comparable to that of the RLD, applicants should not conduct in vitro innate immune testing.

[5] For any inquiries regarding the use of non-clinical assays to assess risk in recombinant generic peptides, please submit pre-ANDA product development meeting requests. For additional information, refer to the most recent version of the guidance for industry on *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*.

Document History: Recommended May 2024; Revised December 2025

Unique Agency Identifier: PSG_206321

[a] For the most recent version of a guidance, check the FDA guidance website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.