Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Olive Oil; Soybean Oil

November 2025

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Active Ingredients:	Olive oil; Soybean oil
Dosage Form:	Emulsion
Route:	Intravenous
Strength:	16% (160 g/1000 mL); 4% (40 g/1000 mL)
Recommended Studies:	Two options: (1) one in vitro bioequivalence study with comparative characterization studies, or (2) one in vivo bioequivalence study with pharmacokinetic endpoints

To demonstrate bioequivalence using the studies recommended in this guidance, the test product[1] should be qualitatively (Q1)[2] and quantitatively (Q2)[3] the same as the reference listed drug (RLD).

I. Option 1: One in vitro bioequivalence study with comparative characterization studies

1. Type of study: Globule size distribution (GSD)
   Design: In vitro bioequivalence study on at least three batches of both test product and the reference standard (RS)
   Strength: 16%; 4%

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

Additional comments: The sample preparation and particle sizing methods should be adequately optimized and validated to demonstrate the adequacy of the selected method in accurately and reliably identifying and measuring the globule size and size distribution. Prospective applicant should perform size characterization at different dilution conditions as part of method development to demonstrate the impact of dilution. Full GSD profiles representative of all test product and RS batches tested should be submitted as supporting information.

Parameters to measure: Z-average size and polydispersity index (PDI) or D_{50} and SPAN [$(D_{90}-D_{10})/D_{50}$], as appropriate

Bioequivalence based on (95% upper confidence bound): Population bioequivalence (PBE) analysis of the Z-average size or D_{50}. Prospective applicants should provide no less than 10 data sets from three batches of both the test product and the RS for PBE analysis. Refer to the section of "Recommendation Related to the PBE Statistical Analysis Procedure" in the most recent version of the FDA product-specific guidance on *Budesonide Inhalation Suspension* (NDA 020929)[a] for additional information regarding PBE computation.[4] Comparable SPAN or PDI should be provided as supporting evidence for bioequivalence.

Comparative characterization studies:

The comparative studies should be performed on at least three exhibit batches of the test product[5] and three batches of the RS and should include:

a. Viscosity
b. pH
c. Zeta potential
d. Osmolality

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

1. Type of study: Bioequivalence study with pharmacokinetic endpoints
   Design: Single-dose, randomized, two-way crossover
   Strength: 16%; 4%
   Subjects: Males and non-pregnant, non-lactating females, general population
   Additional comments:
   a. The subjects should be encouraged to remain sedentary.
   b. Pharmacokinetic parameters should be computed from the individual baseline-adjusted measurements.

Analytes to measure (in appropriate biological fluid): Triglycerides in serum

Bioequivalence based on (90% CI): Triglycerides in serum

[4] The recommendation on collecting data on different life stages is NOT applicable.
[5] The manufacturing process for the exhibit batches should be reflective of the manufacturing process to be utilized for commercial batches.

Additional information:

Device:
The RLD is presented in an intravenous (IV) bag with two ports. The IV bag with ports 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:

- Features of the ports

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.