Contains Nonbinding Recommendations

Draft – Not for Implementation

Draft Guidance on Soybean Oil

November 2023

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic.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:	Soybean oil
Dosage Form:	Injectable
Route:	Injection
Strengths:	10%, 20%, 30%
Recommended Studies:	Two options: (1) one in vitro bioequivalence study with supportive comparative characterization studies, or (2) one in vivo bioequivalence study with pharmacokinetic endpoints

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

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

One in vitro bioequivalence study:

1. Type of study: Drug particle size distribution (PSD)
   Design: In vitro bioequivalence study on at least three batches of both test and reference standard (RS) products
   Strengths: 10%, 20%, 30%

[1] The manufacturing process for the exhibit batches should be reflective of the manufacturing process to be utilized for commercial batches.
[2] Q1 (Qualitative sameness) means that the test product uses the same inactive ingredient(s) as the RLD product.
[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 product.

Additional comments: The sample preparation method and selected particle sizing methodology should be adequately optimized and validated to demonstrate the adequacy of the selected method in accurately and reliably identifying and measuring the size of the drug particles without any interference from the sample concentration or any excipient particles that may also be suspended in the formulation. An orthogonal method may be required if the selected methodology is not sensitive to measure particles beyond a certain size range. Full PSD profiles representative of all test product and RS product batches tested should be submitted as supporting information.

Parameters to measure: D_{10}, D_{50}, and D_{90}

Bioequivalence based on (95% upper confidence bound): Population bioequivalence (PBE) analysis of the PSD D_{50} and SPAN [i.e., $(D_{90}-D_{10})/D_{50}$]. Refer to the most recent version of the FDA product-specific guidance on *Budesonide Inhalation Suspension* (NDA 020929)[a] for additional information regarding PBE.

Supportive characterization studies:

Comparative physicochemical characterization of the test and RS products. The comparative studies should be performed on a minimum of three exhibit batches of the test product and three batches of the RS product and should include:

a. pH
b. Zeta-potential
c. Osmolality
d. Viscosity profile as a function of applied shear

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

1. Type of study: Fasting
   Design: Single-dose, randomized, two-way crossover
   Strengths: 10%, 20%, 30%
   Subjects: Healthy males and non-pregnant, non-lactating females
   Additional Comments**:** (1) The subjects should be encouraged to remain sedentary to minimize the activity. (2) Pharmacokinetic parameters should be computed from the individual baseline-adjusted measurements. (3) Note that 30% strength (i.e., NDA 019942, Intralipid 30% pharmaceutical bulk package) is not intended for direct infusion. See the "mixing guidelines and limitations" section in the drug label for proper sample preparation and follow the administration instruction when performing the BE study for the 30% strength. (4) Note that 20% strength (i.e., NDA 019531, Nutrilipid 20% pharmaceutical bulk package) is not intended for direct intravenous administration. See the drug label for additional information.

Analytes to measure: Triglycerides in serum

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

Dissolution test method and sampling times: Not applicable

Additional comments:

Device:
The RLD is presented in an intravenous (IV) bag with a dual port. 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 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 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]

Revision History: Recommended February 2018; Revised November 2023

Unique Agency Identifier: PSG_017643

[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.