



U.S. Food and Drug Administration

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# PET Drug Product BE Requirements for ANDA Submissions

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# Two Regulatory Pathways

- Waiver of in vivo BE studies (21 CFR § 320.22(b)(1))
- Providing evidence to establish bioequivalence (21 CFR § 320.24(b)(6))

# Biowaivers – IV solutions

- Set forth in 21 CFR §320.22(b)(1)
- A parenteral solution intended for injection, or an otic or ophthalmic solution
- Must contain the same active and inactive ingredients in the same amounts as the RLD
  - Quantitatively (Q1) and qualitatively (Q2) the same

# Biowaivers – IV solutions

- To be deemed suitable for a waiver of in vivo BE studies to the RLD, a generic and RLD solution must be Q1 and Q2 the same
- However, an ANDA may be submitted under 21 CFR §314.94 with the following exceptions
  - Buffers
  - Antioxidants
  - Preservatives
- So, if your PET drug is Q1 and Q2 the same as the RLD, you can request and receive a waiver of BE study requirements.
- Because of the nearly identical formulas, safety of the test and reference products are assumed to be the same
- If you are not Q1/Q2 the same, another approach must be used

# Other BE Approaches

- If you are not Q1 and Q2 the same as the RLD, section §320.24 provides alternative ways to demonstrate bioequivalence, including “**Any other approach deemed adequate by FDA.**”
- Since PET drug products are IV solutions, the bioequivalence of the active drug substance is considered “self-evident” and BE studies are generally not needed.
- However, since the inactive ingredients are not the same, the safety cannot be assumed to be the same between test and reference products.
- The inactive ingredients are reviewed by FDA for safety.
- If you have used an inactive ingredient never approved by FDA in another parenteral product or a large amount of a known ingredient (reference: Inactive Ingredient Guide), you may have to submit toxicology data (usually from the literature) to support the safety of that ingredient.

## BE Information Needed for ANDA Submission for PET Drug Product (Tables from OGD Website)

- Table 1. Submission Summary
- Table 6. Formulation
  - This information may be in CMC section but it should also be included in the BE section as well
- Both of these are submitted in 2.7.1.1 in CTD or Module 2 of eCTD