U.S. FOOD & DRUG ADMINISTRATION

Overview and Contents

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WEBINAR: A Deep Dive: FDA Draft Guidance on Statistical Approaches to Establishing Bioequivalence – March 14, 2023

Overview

- Compare Test and Reference drug products

- Bioequivalence (BE) assessments rely on
  - criterion
  - confidence interval for criterion
  - predetermined limit for concluding BE

Overview

- Describe ways to statistically compare Test and Reference drug products

- Encourage discussion with FDA as methods and technology evolve

- Includes most topics from 2001, plus additional innovations

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Study design

Experimental Design

- non-replicated, replicated,
- adaptive design
- sparse sampling

Sample Size determination

Data Preparation

Log-transformation and other data transformation

Missing data and intercurrent events

Outliers

General Considerations

Statistical models

Test hypotheses (TOST)

→ confidence intervals

→ mixed effects / two-stage linear models

Specific Situations

- In-vitro – population BE; In Vitro Release Test, In Vitro Permeation Test; abuse-deterrence formulations; dissolution similarity, profile comparisons

- Pharmacokinetic (PK) – Narrow Therapeutic Index, Highly Variable Drug products; multiple groups;

Specific Situations

- Pharmacodynamic (PD) – dose scale
- Comparative clinical endpoint
- Adhesion, irritation - transdermal systems

But wait, there's more….