**ABSTRACT**

**Bioequivalence and Pharmacokinetic study of different Brands of formulations in biological matrices**

**Objective:** To examine the *in vivo* average bioequivalence of *Test* and *Reference* formulation and to evaluate the drug’s pharmacokinetics in biological matrices.

**Introduction:**

Studies to measure Bioavailability and/or establish Bioequivalence of a product are important elements in support of INDs, NDAs, ANDAs, and their supplements. As part of INDs and NDAs for orally administered drug products, Bioavailability studies focus on determining the process by which a drug is released from the oral dosage form and moves to the site of action. Bioavailability data provide an estimate of the fraction of the drug absorbed, as well as its subsequent distribution and elimination. Bioavailability can be generally documented by a systemic exposure profile obtained by measuring drug and/or metabolite concentration in the systemic circulation over time. The systemic exposure profile determined during clinical trials in the IND period can serve as a benchmark for subsequent Bioequivalence studies.

Studies to establish Bioequivalence between two products are important for certain changes before approval for a pioneer product in NDA and ANDA submissions and in the presence of certain post approval changes in NDAs and ANDAs. In
Bioequivalence studies, an applicant compares the systemic exposure profile of a test drug product to that of a reference drug product (RLD). For two orally administered drug products to be bioequivalent, the active drug ingredient or active moiety in the test product must exhibit the same rate and extent of absorption as the reference drug product.

Both Bioavailability and Bioequivalence studies are required by regulations, depending on the type of application being submitted. Bioequivalence information is required to ensure therapeutic equivalence between a pharmaceutically equivalent test drug product and a reference listed drug.

From a pharmacokinetic perspective, Bioavailability data for a given formulation provide an estimate of the relative fraction of the orally administered dose that is absorbed into the systemic circulation when compared to the Bioavailability data for a solution, suspension, or intravenous dosage form. In addition, Bioavailability studies provide other useful pharmacokinetic information related to distribution, elimination, the effects of nutrients on absorption of the drug, dose proportionality, linearity in pharmacokinetics of the active moieties and, where appropriate, inactive moieties. Bioavailability data can also provide information indirectly about the properties of a drug substance before entry into the systemic circulation, such as permeability and the influence of presystemic enzymes and/or transporters.
PLAN OF WORK

Phase-I
Selection of drugs
Selection of Subjects

Study Design:

- Single-dose, two-way crossover fasted
- Single-dose, two-way crossover fed
- Alternatives: Single-dose, Parallel, fasted
  Single-dose, replicate design
  Multiple-dose, two-way crossover, fasted

Clinical endpoint study

Collection and Storage of Samples

Phase-II
Method Development: Selection of suitable instrument,
Selection of chromatographic conditions, Instrument conditions,
Extraction Procedures, Regression
Method Validation: Selectivity (Matrix interference), Sensitivity,
Linearity,
Precision & Accuracy, Matrix effect, Recovery, Ruggedness.
Stability: Solution stability: Stock solution stability
  Plasma Stability: Bench top stability, Freeze thaw
  stability, Auto sampler stability,
  Re injection stability.

Phase-III
Analysis of drugs in Plasma Samples

Phase-IV
Pharmacokinetic Parameters and Statistical Analysis:

- $\text{AUC}_0-t$, $\text{AUC}_{0-\infty}$, $\text{C}_\text{max}$, $\text{T}_\text{max}$, $\text{K}_e$, and $t_{1/2}$
- Test/Reference values of $\text{AUC}_0-t$, $\text{AUC}_{0-\infty}$, and $C_{\text{max}}$. 