

# **Human Studies**

## a. Pharmacokinetics

### 1. Method of Analysis

- LC-MS/MS (Liquid Chromatography-Mass Spectrometry)
- Bioanalytical Method Validation
- Chromatography Techniques
- Quantitative Assay
- Sensitivity and Specificity
- Non-compartmental Analysis
- Compartmental Modeling
- Software (e.g., Phoenix WinNonlin)

### 2. Absorption

- Bioavailability
- First-pass Metabolism
- Gastric pH Influence
- Gastric Emptying Time
- Intestinal Transit Time
- Drug Solubility and Permeability
- Transporter Proteins (e.g., P-glycoprotein)
- Formulation Effects

### 3. Distribution

- Volume of Distribution (Vd)
- Plasma Protein Binding
- Tissue Penetration
- Blood-Brain Barrier
- Lipophilicity
- Tissue Binding
- Body Composition Effects

#### 4. Metabolism

- Hepatic Metabolism
- Cytochrome P450 Enzymes (CYP450)
- Phase I and Phase II Metabolism
- Enzyme Induction/Inhibition
- Metabolite Profiling
- Genetic Polymorphisms

#### 5. Excretion

- Renal Clearance
- Biliary Excretion
- Glomerular Filtration Rate (GFR)
- Tubular Secretion and Reabsorption
- Half-life
- Elimination Rate Constant

#### 6. Pharmacokinetics in Special Populations

- Pediatric Pharmacokinetics
- Geriatric Pharmacokinetics
- Pregnancy Pharmacokinetics
- Renal Impairment
- Hepatic Impairment
- Age-related Physiological Changes
- Polypharmacy Effects
- Dose Adjustment

#### 7. Pharmacokinetics Drug Interaction

- Drug-Drug Interaction
- Enzyme Induction/Inhibition
- Transporter-Mediated Interaction
- Pharmacokinetic Interaction Mechanisms
- Clinical Significance of Interactions
- Therapeutic Drug Monitoring

b. Pharmacodynamics

1. Related to Proposed Indications

- Dose-Response Relationship
- Receptor Binding
- Receptor Sensitivity
- Agonist / Antagonist
- Efficacy
- Potency
- Therapeutic Index
- Mechanism of Action
- Target Tissue
- Post-Receptor Effects
- Signal Transduction
- Pharmacologic Effect
- Clinical Biomarkers
- Therapeutic Window
- Receptor Selectivity

2. Pharmacodynamic Drug Interaction

- Receptor Competition
- Synergistic Effect
- Antagonistic Effect
- Additive Effect
- Drug Interaction Mechanism
- Receptor Modulation
- Enzyme Inhibition / Induction (as PD mechanism)
- Toxicodynamic Interaction
- Therapeutic Drug Monitoring
- Drug Resistance
- Altered Signal Transduction

c. Efficacy

## 1. Placebo-Controlled Studies

- Randomized Controlled Trial (RCT)
- Placebo Group
- Double-Blind
- Blinding
- Control Group
- Treatment Effect
- Statistical Significance
- Intention-to-Treat Analysis
- Relative Risk Reduction (RRR)
- Absolute Risk Reduction (ARR)
- Number Needed to Treat (NNT)

## 2. Active-Controlled Studies

- Active Comparator
- Non-Inferiority Trial
- Equivalence Trial
- Head-to-Head Comparison
- Superiority Trial
- Dose Comparison
- Efficacy Endpoint
- Comparative Effectiveness
- Treatment Arms

## 3. Uncontrolled Studies

- Open-Label Study
- Single-Arm Study
- Observational Study
- Case Series
- Pilot Study
- Exploratory Study
- Historical Controls

#### 4. Efficacy in Paediatrics

- Pediatric Population
- Age Stratification
- Developmental Pharmacology
- Pediatric Dose Adjustment
- Growth and Maturation
- Pediatric Clinical Trials
- Safety and Efficacy in Children

#### 5. Dosage

- Dose-Response Relationship
- Therapeutic Dose
- Dose Escalation
- Maximum Tolerated Dose (MTD)
- Dose Optimization
- Dosing Regimen
- Steady-State Concentration
- Pharmacodynamics (PD) Correlation

#### d. Safety

##### 1. Adverse Drug Reactions (ADR)

- Adverse Event (AE)
- Serious Adverse Event (SAE)
- Side Effect
- Dose-Related Toxicity
- Hypersensitivity Reactions
- Idiosyncratic Reaction
- Causality Assessment
- Pharmacovigilance
- Risk Management
- Safety Signal Detection

##### 1.1 Special Warnings and Precautions

- Contraindications
- Black Box Warning
- Risk Minimization Measures
- Monitoring Parameters
- Drug Safety Alerts
- Precautionary Statements
- Warning Labels
- Risk-Benefit Analysis

## 2. Pregnancy and Lactation

### 2.1 Pregnancy

- Teratogenicity
- Embryotoxicity
- Pregnancy Exposure Registry
- Fetal Risk
- Pregnancy and Lactation Labeling Rule (PLLR)
- Gestational Timing of Exposure
- Maternal-Fetal Drug Transfer
- Reproductive Toxicology

### 2.2 Breast-feeding

- Drug Transfer into Breast Milk
- Milk-to-Plasma Ratio
- Infant Exposure
- Lactation Risk Assessment
- Neonatal Toxicity
- Breastfeeding Safety

### 2.3 Fertility

- Reproductive Toxicity
- Infertility Risk
- Gametotoxicity
- Fertility Studies

### 3. Overdose

- Toxic Dose
- Poisoning
- Acute Toxicity
- Overdosage Management
- Antidote
- Supportive Care
- Dose-Limiting Toxicity

### 4. Post-marketing Surveillance

- Pharmacovigilance
- Adverse Event Reporting System (AERS)
- Risk Evaluation and Mitigation Strategies (REMS)
- Signal Detection
- Real-World Evidence
- Safety Monitoring
- Post-Authorization Safety Studies (PASS)