**Abstract**

Bioequivalence studies play an important role in the development of new drug and the generic drugs, and thus attract considerable attention globally. It is a strategy to introduce equivalent drugs of same quality, efficacy and safety as that of brand-name drugs (innovator drugs) to lower the cost of medication. Bioequivalence studies compare both the rate and extent of absorption of test drug formulations with the innovator product, on the basis of similar plasma/blood concentration-time profiles. The purpose of current pilot study was to demonstrate the equivalence by comparing open label, randomized, balanced, single oral dose, two-treatment, two-period, two-sequence, two-way, cross over bioequivalence study of sulfamethoxazole and trimethoprim oral suspension, USP 200 mg/40mg per 5ml, in 12 healthy, adult, human subjects under fasting conditions with a 07 days of wash out period. Twenty five (25) blood samples (1x5 mL) will be collected in pre labeled K2EDTA vacutainers. Single venous blood sample will be withdrawn at pre-dose (0.00 hour) sample will be collected within 01 hour prior to drug administration and the post dose samples will be collected at 0.16, 0.33, 0.50, 0.75, 1.00, 1.33, 1.67, 2.00, 2.33, 2.67, 3.00, 3.33, 3.67, 4.00, 4.50, 5.00, 5.50, 6.00, 8.00, 12.00, 16.00, 24.00, 36.00 and 48.00 hours post-dose. sulfamethoxazole and trimethoprim will be estimated in plasma using a validated LC-MS/MS method.

Primary pharmacokinetic parameters Cmax, AUC0-t, and secondary pharmacokinetic parameters AUC0-∞, tmax, t1/2, kel and residual area will be estimated for sulfamethoxazole and trimethoprim by using Phoenix® WinNonlin® Version 6.3.

At least 11.00 hours before dosing to 24.00 hours after drug administration the study participants will be housed. The clinical duration of the study is approximately 07 days from the day of period I check-in to 24.00hrs post dose of period-II.

Summary statistics, ANOVA, intra subject variability, 90% confidence intervals and power will be calculated using SAS version 9.2

Based on statistical results of the 90% confidence intervals for the geometric least square mean ratio (T/R) of Cmax and AUC0-t conclusions will be drawn whether the test formulation is bioequivalent to reference formulation under fasting conditions. The acceptance range for bioequivalence is 80.00-125.00% for the 90% confidence intervals of the geometric least square mean ratio of log transformed Cmax and AUC0-t for sulfamethoxazole and trimethoprim.

statistics was calculated and statistical analysis was performed by using ANOVA on in transformed pharmacokinetic parameters by using SAS software for sulfamethoxazole and trimethoprim.(ANOVA will be performed on log transformed pharmacokinetic parameters Cmax AUC0-t, AUC0-∞, and on untransformed pharmacokinetic parameters Tmax) based on the obtained results on applying ANOVA the test product of sulfamethoxazole and trimethoprim is not bioequivalent to the reference product sulfamethoxazole and trimethoprim.

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# Abbreviations

|  |  |  |
| --- | --- | --- |
|  |  |  |
| **ADR** | **:** | Adverse Drug Reaction |
| **AE** | **:** | Adverse Event |
| **ALP** | **:** | Alkaline Phosphatase |
| **ALT** | **:** | Alanine Transaminase |
| **ANOVA** | **:** | Analysis of variance |
| **AST** | **:** | Aspartate Transaminase |
| **AUC** | **:** | Area under the plasma concentration versus time curve |
| **AUC0-t** | **:** | Area under the plasma concentration versus time curve from 0 to the last measurable concentration (t) |
| **AUC0-inf** | **:** | Area under the plasma concentration versus time curve from 0 to infinity |
| **BAA** |  | Breath Alcohol Analysis |
| **BE** | **:** | Bioequivalence |
| **BLQ** | **:** | Below Limit of Quantification |
| **BMI**  **eCTD** | **:**  **:** | Body Mass Index  Electronic Common Technical Document |
| **CDSCO** | **:** | Central Drugs Standard Control Organization |
| **CFR** | **:** | Code of Federal Regulations |
| **Cm** | **:** | Centimeter |
| **Cmax** | **:** | Maximum measured analyte concentration in the biological fluid |
| **COA** | **:** | Certificate of Analysis |
| **CPU** | **:** | Clinical Pharmacology Unit |
| **CRF** | **:** | Case Report Form |
| **DBP** | **:** | Diastolic Blood Pressure |
| **ECG** | **:** | Electrocardiogram |
| **FDA** | **:** | Food and Drug Administration |
| **GCP** | **:** | Good Clinical Practice |
| **g/Dl** | **:** | Gram/Deciliter |
| **Hb s Ag** | **:** | Hepatitis B surface antigen |
| **HCV** | **:** | Hepatitis C virus |
| **HIV** | **:** | Human immunodeficiency virus |
| **hrs** | **:** | Hours |
| **ICF** | **:** | Informed Consent Form |
| **ICH** | **:** | International Conference on Harmonisation |
| **ICMR** | **:** | Indian Council of Medical Research |
| **ICU** | **:** | Intensive Care Unit |
| **IP** | **:** | Investigational Product |
| **IRB** | **:** | Institutional Review Board |
| **IUD** | **:** | Intrauterine device |
| **IV** | **:** | Intravenous |
| **K2EDTA** | **:** | Di Potassium Ethylene Diamine Tetra Acetic acid |
| **kel** | **:** | Elimination rate constant |
| **Kg** | **:** | Kilogram |
| **LC-MS/MS** | **:** | Liquid Chromatography-Mass Spectrometry / Mass Spectrometry |
| **LSM** | **:** | Least-square means |
| **mg** | **:** | Milligram |
| **mL** | **:** | Milliliter |
| **mm/Hg** | **:** | Millimeter of Mercury |
| **MSE** | **:** | Mean Square Error |
| **NA** | **:** | Not applicable |
| **OTC** | **:** | Over the Counter |
| **PI** | **:** | Principal Investigator |
| **PK** | **:** | Pharmacokinetic |
| **R** | **:** | Reference |
| **RPM** | **:** | Rotations per Minute |
| **RPR** | **:** | Rapid Plasma Reagin |
| **SAE** | **:** | Serious Adverse Event |
| **SAS** | **:** | Statistical Analysis System |
| **SD** | **:** | Standard Deviation |
| **SGOT** | **:** | Serum Glutamic Oxaloacetic Transaminase |
| **SGPT** | **:** | Serum Glutamic Pyruvic Transaminase |
| **SOP** | **:** | Standard Operating Procedure |
| **T** | **:** | Test |
| **t1/2** | **:** | Elimination half-life |
| **UDS** | **:** | Urine Drug Screening |
| **U/L** | **:** | Units per Liter |
| **VDRL** | **:** | Venereal Disease Research Laboratory |
| **WMA** | **:** | World Medical Association |
| **XX** | **:** | Current Version |