Study Synopsis

Title	Pharmacokinetics and Bioequivalence Study of 450 mg Rifampicin Capsules in Healthy Thai Volunteers
Sponsor	The Government Pharmaceutical Organization
Clinical laboratory	Faculty of Pharmaceutical Sciences, Chulalongkorn University
Analytical laboratory	Faculty of Pharmaceutical Sciences, Chulalongkorn University
EC approval	Ethics committee of the Faculty of Pharmaceutical Sciences, Chulalongkorn University
Principal investigator	Associate Professor Ubonthip Nimmannit, Ph.D. Faculty of Pharmaceutical Sciences, Chulalongkorn University
Clinical investigator	Dr. Arkom Chaiwerawatana, M.D. Protect and Control Cancer Center, Chonburi
Analytical investigator	Ms. Mukdavan Prakobvaitayakit M. Pharm Ms. Atchara Maimansomsook B. Pharm
Objectives	To compare the bioavailability of new generic product of Rifampicin 450 mg capsules (Rifampicin GPO®, The Government Pharmaceutical Organization) fgwith the innovator product (Rifadin®, Hoechst Marion Roussel).
Study design	A randomized, open label, two treatment, two-period, two sequence, single dose crossover design with one week-drug free interval between the periods in 16 healthy male subject under fasting condition
Test product	Rifampicin 450 mg capsules, Lot. K430026 Mfg. 26 May 00, Exp. 26 May 03 Manufactured by GPO, Thailand
Reference product	Rifadin® 450 mg capsules, Lot. 384039 Mfg. 22 Apr 98, Exp. 22 Apr 01 Manufactured by Hoechst Marion Roussel
Study subjects	Sixteen healthy Thai male volunteers with aging between 20-45 years

Demographic data (n = 16)	Age: 32.63 ± 8.29 year Height: 168.19 ± 7.86 cm Weight: 59.38 ± 7.09 kg BMI: 20.94 ± 1.52 kg/m^2
Admission and confinement	Prior to all dosing events, subjects were fasted overnight at least 8 hours prior to study drug administration. On study day, a standardized light lunch was provided 4 hours post-dose.
Drug administration	Two capsules (450 mg) Rifampicin will be orally administered to all subjects with water (240 mL) in the fasted state during 2 separate periods.
Study period	Period I: 27 August 2000 Period II: 3 September 2000
Washout period	7 days from the first drug administration
Safety assessment	All adverse events, physical examination, laboratory tests and vital signs were recorded and evaluated.
Blood sampling schedule	In each period, a total of 15 blood samples (10 mL each) were collected up to 24 hours post-dose. The blood samples for pharmacokinetic analysis were collected at 0.0 (pre-dose sample), 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 5.0, 6.0, 8.0, 10.0, 12.0 and 24.0 hours (post-dose samples). The total volume of blood draw was 300 mL for each subject.
Blood sampling handling	The blood samples were placed in heparin tube, centrifuged, and separated plasma samples were stored below -20ºC, until analyzed.
Clinical sample storage	Stored below -20ºC until analyzed.
Bioanalytical methodology	Rifampicin plasma concentration was assayed using a validated HPLC-UV method.
Pharmacokinetic Parameters	Primary pharmacokinetic parameters (C_{max}, $AUC_{0\text{-}inf}$) and secondary pharmacokinetic parameters (T_{max}, k_{el}, $t_{1/2}$) will be determined from the plasma concentration data of analytes

Confidence Intervals	90% CI for geometric mean of test/reference ratio $AUC_{0\text{-}inf}$: 98.18-107.88 C_{max}: 98.27-104.31
Conclusions	The peak and total systemic exposure of Rifampicin 450 mg were similar between the 2 formulations. The 90% confidence intervals for the test/reference ratio were 98.18-107.88 for $AUC_{0\text{-}inf}$ and 98.27-104.31% for C_{max}. Since 90% confidence intervals for the parameters $AUC_{0\text{-}inf}$ and $C_{max}$and were within the bioequivalence range of 80-125%, it can be concluded that the Rifampicin 450 mg Capsules (Test formulation) is bioequivalent to Rifadin® 450 mg capsules (Reference formulation) under fasting condition.