Study Synopsis

Title	Bioequivalence Study of 75 mg Oseltamivir Capsules in Thai Healthy Volunteers
Sponsor	The Government Pharmaceutical Organization
Clinical laboratory	Siriraj Clinical Research Center Faculty of Medicine, Siriraj Hospital, Mahidol University
Analytical laboratory	Department of Pharmacology Faculty of Medicine, Siriraj Hospital, Mahidol University
EC approval	Siriraj Ethics Committee
Principal investigator	Assoc.Prof.Supornchai Kongpatanakul, MD. Department of Pharmacology Faculty of Medicine, Siriraj Hospital, Mahidol University
Co-investigator	Dr.Somruedee Chatsiricharoenkul, MD. Department of Pharmacology Faculty of Medicine, Siriraj Hospital, Mahidol University
Analytical investigator	Piyapat Pongnarin Department of Pharmacology Faculty of Medicine, Siriraj Hospital, Mahidol University
Co-analytical investigator	Assoc.Prof.Polkit Sangwanit, PhD. Department of Chemistry, Faculty of Science, Chulalongkorn University
Pharmacokinetic and/or statistical investigator	Assoc.Prof.Korbtham Sathirakul, PhD. Department of Pharmacy, Faculty of Pharmacy, Mahidol University
Objectives	To compare the rate and extent of absorption of generic product of Oseltamivir 75 mg capsule (GPO-A-FLU™, Government Pharmaceutical Organization) with the innovator product (TAMIFLU®, Hoffmann-La Roche Limited).
Study design	A randomized, two treatment, two-period, two sequence, single dose crossover design with one week wash out period in 24 healthy Thai male and female volunteers

Test product	Oseltamivir 75 mg capsule (GPO-A-FLU™), Lot No. S490052 Mfd. 20/03/2006, Exp. 20/03/2008 Manufactured by GPO, Thailand
Reference product	TAMIFLU® 75 mg capsule, Lot no. B1084 Mfd. 10/2004, Exp. 10/2008 Manufactured by Hoffmann-La Roche Limited
Study subjects	Twenty three healthy Thai male and female volunteers with aging between 18-45 years
Demographic data (n = 23)	Age: 22.74 ± 4.57 year Height: 1.65 ± 0.09 m Weight: 57.01 ± 10.17 kg BMI: 20.70 ± 2.02 kg/m^2
Admission and confinement	Prior to all dosing events, volunteers 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	One 75 mg capsule of Oseltamivir was orally administered to all volunteers with water (240 mL) in the fasted state during 2 separate periods.
Study period	Period I: 8 - 30 August 2006 Period II: 16 August – 13 September 2006
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 (6 mL each) were collected up to 48 hours post-dose. The total volume of blood draw was 180 mL for each subject.
Clinical sample storage	The resulting plasma was transferred into cryovial tube and stored at -70°C until anaylsis.
Bioanalytical methodology	Osteltamivir carboxylate (active metabolite) plasma concentration was assayed using a validated LC-MS/MS method. The lower limit of quantification of osteltamivir carboxylate plasma concentration was 0.5 ng/mL.

Pharmacokinetic Parameters	Primary pharmacokinetic parameters (C_{max}, AUC_{0-t}, $AUC_{0-\alpha}$) and secondary pharmacokinetic parameters (T_{max}, k_{el}, $t_{1/2}$) were determined from the plasma concentration data of analytes.
Confidence Intervals	90% CI for geometric mean of test/reference ratio (ln-transformed data) C_{max}: 90.90-109.10 AUC_{0-t}: 90.90-109.10 $AUC_{0-\alpha}$: 90.92-109.08
Conclusions	The peak and total systemic exposure of Oseltamivir carboxylate 75 mg were similar between the 2 formulations. The 90% confidence intervals for the test/reference ratio were 90.90-109.10% for C_{max}, 90.90-109.10% for AUC_{0-t} and 90.92-109.08% for $AUC_{0-\alpha}$ (ln-transformed data). Since 90% confidence intervals for the parameters C_{max}, AUC_{0-t} and $AUC_{0-\alpha}$ were within the bioequivalence range of 80-125%, it can be concluded that the Oseltamivir 75 mg capsule (GPO-A-FLU™, Test formulation) is bioequivalent to TAMIFLU® 75 mg capsule (Reference formulation) under fasting condition.