2. SYNOPSIS

Generic Name: Levofloxacin **Test Product:** Levoflox GPO **Reference Product:** Cravit® Tab.500	**Sponsor Name:** The Government Pharmaceutical Organization
Study Title:	Bioequivalence study of Levofloxacin 500 mg tablet in Healthy Thai Volunteers
Investigators:	Principal Investigator and Study Director: Dr.Isariya Techatanawat., B.Pharm, Ph.D. Clinical Investigator: Dr.Archawin Rojanawiwat, M.D. Analytical Investigator: Mr. Wiwat Supasena, B.Sc PK & Statistic Investigator: Dr.Isariya Techatanawat, Ph.D Other Investigator: Ms.Achara Eksaengsri, B.Pharm
Protocol Number:	BE GPO 03/2009
Project Number:	53-01
IRC/Ethics Approval Date:	Institute for Development of Human Research Protection (IHRP) 18 May 2010
Objectives:	To compare the rate and extent of absorption of a generic Levofloxacin 500 mg tablets formulation with that of a reference formulation (Cravit® Tab.500) when given as equal labeled dose.
Dosage Regimen:	**Test Product:** Single dose, 500 mg of Levoflox GPO Tablet, Batch No. S530001 Mfd. 01/2010 Exp. 01/2012 **Reference Product:** Single dose, 500 mg of Cravit® Tab.500Tablet, Batch No. CTAGL17 Mfd. 12/2009 Exp. 12/2014

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Clinical Site:	Clinical Research Center, Department of Medical Sciences, Ministry of Public Health, 88/7 Tiwanond rd. Nonthaburi 11000, Thailand
Study Subjects:	No. of subjects planned: 26 (22+4) No. of subjects dosed in period 1: 26 No. of subjects dosed in period 2: 26 No. of subjects withdrawn: - No. of subjects dropped out: - No. of subjects completed: 26 No. of subjects analyzed: 26 No. of subjects included in pharmacokinetic and statistical analysis: 26
Demographic Data of Enrolled Subjects (N = 26):	Total of 26 subjects with average age = 23.38±4.27 years, Height = 171.48±4.75 cm, Weight = 62.71±7.31 kg, BMI = 21.29±2.03 kg/m^2 and physical examination were indicated that all participants were healthy.
Admission and Confinement:	Subjects were fasted overnight at least 10 hrs prior to study drug administration. Water was permitted ad-lib until 1 hour before dosing and 1 hour after dosing. Standard meals were provided to each subject 4 hrs post-dose. Subjects seated for the first 4-5 hours following drug administration and prohibited from any strenuous or athletic activity during housing period of the study. Subjects were discharged after 48 hrs after drug administration.
Drug Administration:	A single dose of Levofloxacin 500 mg tablet was administered along with 250 ml of water after an overnight fasting for at least 10 hours.

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Study Period:	Screening: 31 May - 2 June 2010 Period 1: 11-18 June 2010, Period 2: 18-25 June 2010
Washout Period:	7 Days from the first period
Blood Sampling Schedule:	A total of 16 blood samples (5 mL each) were collected at pre-dose (0 hour) and at 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10, 12, 24 and 48 hours after dosing in each period.
Blood Sampling Handling:	A blood samples were collected for 5 ml in K_3EDTA vacutainers from each subject for bioanalysis during the course of the study. After collection, the blood samples were centrifuged at 3,500 rpm for 10 minutes. The supernatant of each sample was divided into two aliquots and kept in labeled cryovials. All cryovials were immediately stored at -20 °C.
Clinical Sample Storage:	Bioequivalence Study Group, Research and Development Institute, The Government Pharmaceutical Organization
Analytical Site:	Bioequivalence Study Group, Research and Development Institute, The Government Pharmaceutical Organization
Bioanalytical Methodology:	Levofloxacin plasma concentrations were assayed using a validated HPLC with fluorescence detector. The lower limit of quantification was 50 ng/ml.
Analyte:	Levofloxacin in human plasma
Safety Evaluation:	Both treatments were well tolerated. No clinical significant or serious ADR was observed.
Primary Pharmacokinetic Parameters:	The primary pharmacokinetic parameter employed for Levofloxacin were C_{max}, $AUC_{0\text{-tlast}}$ and $AUC_{0\text{-}\infty}$.

<table>
<tr><td>Generic Name: Levofloxacin
Test Product: Levoflox GPO
Reference Product: Cravit® Tab.500</td><td>Sponsor Name:
The Government Pharmaceutical Organization</td></tr>
<tr><td></td><td>The mean ± SD values of primary pharmacokinetic parameters of Levofloxacin for Test product and Reference product for 26 subjects were summarized in the following table:
<table>
<tr><th>Parameters (Units)</th><th>Test Product-T</th><th>Reference Product-R</th></tr>
<tr><td>C_{max} (ng/mL)</td><td>5345.10±1525.07</td><td>5016.25±1590.74</td></tr>
<tr><td>$AUC_{0\text{-}tlast}$ (ng.hr(s)/mL)</td><td>35612.66±6399.70</td><td>35396.28±6333.57</td></tr>
<tr><td>$AUC_{0\text{-}\infty}$ (ng.hr(s)/mL)</td><td>38519.38±6693.58</td><td>38136.27±6545.13</td></tr>
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<tr><td>Secondary Pharmacokinetic Parameters:</td><td>The secondary pharmacokinetic parameter employed for Levofloxacin were t_{max}, λz, $t_{1/2,}$ ($AUC_{0\text{-}tlast}$ / $AUC_{0\text{-}\infty}$) and AUC_%Extrap_obs. The mean ± SD values of secondary pharmacokinetic parameters of Levofloxacin for Test product and Reference product for 26 subjects were summarized in the following table:
<table>
<tr><th>Parameters (Units)</th><th>Test Product-T</th><th>Reference Product-R</th></tr>
<tr><td>T_{max} (hr(s))</td><td>0.990 ± 0.510</td><td>1.450 ± 0.650</td></tr>
<tr><td>λz (K_{el}) (1 / hr)</td><td>0.106 ± 0.017</td><td>0.110 ± 0.020</td></tr>
<tr><td>$t_{1/2}$ (hr(s))</td><td>6.720 ± 1.119</td><td>6.500 ± 1.200</td></tr>
<tr><td>$AUC_{0\text{-}tlast}$ / $AUC_{0\text{-}\infty}$</td><td>92.40 ± 3.09</td><td>92.76 ± 3.19</td></tr>
<tr><td>AUC_%Extrap_obs (%)</td><td>7.602 ± 3.094</td><td>7.244 ± 3.194</td></tr>
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<tr><td>90% Confidence Intervals:</td><td>The 90% confidence intervals were calculated for the ln-transformed primary pharmacokinetic parameters, C_{max}, $AUC_{0\text{-}tlast}$ and $AUC_{0\text{-}\infty}$ of the Levofloxacin and presented as below.</td></tr>
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<tr><th>Parameters (Units)</th><th>Ratio of Least Square Mean (T/R)%</th><th>90% Confidence interval</th></tr>
<tr><td>C_{max} (ng/mL)</td><td>100.87%</td><td>96.48-120.17%</td></tr>
<tr><td>$AUC_{0\text{-}tlast}$ (ng.hr(s)/mL)</td><td>100.05%</td><td>98.02-103.19%</td></tr>
<tr><td>$AUC_{0\text{-}\infty}$ (ng.hr(s)/mL)</td><td>100.09%</td><td>98.50-103.48%</td></tr>
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<tr><td>Conclusion:</td><td>The Test Product-T (Single dose, 500 mg of Levofloxacin GPO Tablet – Manufactured by The Government Pharmaceutical Organization, Bangkok, Thailand / Batch No. S530001) when compared with the Reference Product-R (Single dose, 500 mg of Cravit® Tablet – Manufactured by: InterThai PharmaceuItical Manufacturing Ltd., Thailand licensed by Daiichi Pharmaceutical Co., Ltd., Tokyo Japan / Batch No. CTAGL17) meet the bioequivalence criteria with respect to the rate and extent of absorption of Levofloxacin as per the criteria set in the Protocol.</td></tr>
<tr><td>Date of Report:</td><td>18 Nov 2011</td></tr>
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