2. STUDY SYNOPSIS

Generic Name:	Levocetirizine 5 mg tablets	**Sponsor's Name:** The Government Pharmaceutical Organization
Test Product:	Levocetirizine GPO 5 mg tablets	
Reference Product:	Xyzal® 5 mg tablets	
Study Title:		Comparative Randomized, Single Dose, Two-Way Crossover, Open-Label Study to Determine the Bioequivalence of Levocetirizine Formulations, Levocetirizine GPO 5 mg Tablets and Xyzal® 5 mg Tablets, after Oral Administration to Healthy Thai Male Volunteers Under Fasting Conditions.
Investigators:		Study Director: Dr.Isariya Techatanawat Principal Investigator: Ms.Piengthong Narakorn Clinical Investigator: Dr.Archawin Rojanawiwat Analytical Investigator: Mr. Polsak Teerawonganan PK & Statistic Investigator: Ms.Piengthong Narakorn
Protocol Number:		005-12
Project Number:		005-12
IRC/Ethics Approval Date:		Institute for the Development of Human Research Protections (IHRP) Approval Date 18 Jul 2012 , 9 Aug 2012 (1st amendment)
Objectives:		To compare the rate and extent of absorption of levocetirizine from levocetirizine 5 mg tablets formulation with that of reference formulation. To investigate the safety and tolerability of the formulations on the basis of clinical and laboratory examinations at the beginning and at the end of the trial and registration of adverse events and/or adverse drug reactions.

2. STUDY SYNOPSIS (Cont.)

Generic Name: Levocetirizine 5 mg tablets **Test Product:** Levocetirizine GPO 5 mg tablets **Reference Product:** Xyzal® 5 mg tablets	**Sponsor's Name:** The Government Pharmaceutical Organization
Dosage Regimen:	Test Product: Single dose, 5 mg of Levocetirizine GPO tablets. Batch No. S540451 Mfg. Date 23 Jan 2012 Exp. Date 23 Jan 2014 Name and address of manufacturer: The Government Pharmaceutical Organization 75/1 Rama VI Road Ratchathewi Bangkok 10400 Thailand Reference Product: Single dose, 5 mg of Xyzal® tablets. Batch No. 29281 Mfg. Date 30 Nov 2010 Exp. Date 28 Oct 2014 Name and address of manufacturer: UCB Farchim SA, Bulle-Switzerland Name and address of importer or authorization holder: GlaxoSmithKline (Thailand) Ltd., Bangkok.
Clinical Study Site:	Clinical Research Center, Department of Medical Sciences, Ministry of Public Health, Thiwanon Rd., Amphur Mueng, Nontaburi, Thailand 11000
Study Subjects:	26 subjects, selected randomly from healthy adult Thai male volunteers.
Demographic Data Enrolled and Completed Subjects (N=26):	Age = 30.19±8.02 year; Height = 172.42±7.37 cm; Weight= 66.81±7.95 kg, BMI= 22.44±1.95 kg/m^2
Admission and Confinement:	Subjects were admitted the night before study drug administration, supervised for at least 10 hrs overnight fasting and confined until collecting the 48 hrs sample.
Drug Administration:	Each subject randomly received a single dose of the assigned formulation, administered with 240 ml of water.

2. STUDY SYNOPSIS (Cont.)

Generic Name: Levocetirizine 5 mg tablets **Test Product:** Levocetirizine GPO 5 mg tablets **Reference Product:** Xyzal® 5 mg tablets	**Sponsor's Name:** The Government Pharmaceutical Organization
Study Period:	Screening: 21-24 Aug 2012 Enrollment: 30 Aug 2012 – 9 Sep 2012 Period I: 30 Aug 2012 – 2 Sep 2012 Period II: 6 Sep 2012 – 9 Sep 2012
Washout Period:	7 days
Blood Sampling Schedule:	22 blood samples were drawn at 0.000 (pre-dose sample) and 0.167, 0.333, 0.500, 0.667, 0.833, 1.000, 1.250, 1.500, 1.750, 2.000, 2.500, 3.000, 4.000, 6.000, 8.000, 10.000, 12.000, 16.000, 24.000, 36.000 and 48.000 hours (post-dose). The total volume of blood draw did not exceeded 120 ± 10 mL.
Blood Sampling Handling:	The blood samples for levocetirizine were placed in K_2EDTA tubes, centrifuged, and the separating plasma samples were immediately stored at -65 ± 10 °C until analyzed.
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:	Plasma samples of subjects were assayed for levocetirizine using a validated LC-MS/MS method. The LLOQ of method was 5.090 ng/ml.
Analyte:	Levocetirizine in human plasma
Safety Evaluation:	Both treatments were well tolerated. No clinically significant or serious ADR were observed
Surrogate Parameters:	Drug plasma concentrations to indicate clinical activity.

2. STUDY SYNOPSIS (Cont.)

<table>
<tr><td>Generic Name:</td><td>Levocetirizine 5 mg tablets</td><td rowspan="3">Sponsor's Name:
The Government Pharmaceutical Organization</td></tr>
<tr><td>Test Product:</td><td>Levocetirizine GPO 5 mg tablets</td></tr>
<tr><td>Reference Product:</td><td>Xyzal® 5 mg tablets</td></tr>
<tr><td colspan="2">Primary Pharmacokinetic Parameters:</td><td>The primary pharmacokinetic parameter employed for levocetirizine was $AUC_{0\text{-}tlast}$, $AUC_{0\text{-}\infty}$ and C_{max}.
The mean ± SD values of primary pharmacokinetic parameters of levocetirizine for Test Product-T and Reference Product-R for twenty-six subjects were summarized in the following table :
<table>
<tr><th rowspan="2">Parameters (Units)</th><th colspan="2">(Un-transformed data)</th></tr>
<tr><th>Test-T</th><th>Reference -R</th></tr>
<tr><td>$AUC_{0\text{-}tlast}$ (ng.hr / mL)</td><td>1708.294 ± 372.0046</td><td>1739.707 ± 356.0465</td></tr>
<tr><td>$AUC_{0\text{-}\infty}$ (ng.hr / mL)</td><td>1830.174 ± 360.1070</td><td>1847.587 ± 344.0151</td></tr>
<tr><td>C_{max} (ng / mL)</td><td>222.414 ± 37.1886</td><td>220.950 ± 36.3423</td></tr>
</table></td></tr>
<tr><td colspan="2">Secondary Pharmacokinetic Parameters:</td><td>The secondary pharmacokinetic parameter employed for levocetirizine was T_{max} , λ_z , $t_{1/2}$, $AUC_{0\text{-}tlast}$/ $AUC_{0\text{-}\infty}$ and AUC_%Extrap_obs.
<table>
<tr><th rowspan="2">Parameters (Units)</th><th colspan="2">(Un-transformed data)</th></tr>
<tr><th>Test-T</th><th>Reference -R</th></tr>
<tr><td>T_{max} (hr)*</td><td>0.667 (0.500- 2.000)</td><td>0.667 (0.333- 1.250)</td></tr>
<tr><td>λ_z (1 / hr)</td><td>0.083 ± 0.0113</td><td>0.085 ± 0.0110</td></tr>
<tr><td>$t_{½}$ (hr)</td><td>8.451 ± 1.0917</td><td>8.276 ± 1.0283</td></tr>
<tr><td>AUC_%Extrap_obs (%)</td><td>6.995 ± 3.2581</td><td>6.137 ± 3.1377</td></tr>
<tr><td>$AUC_{0\text{-}tlast}$ / $AUC_{0\text{-}\infty}$</td><td>0.930 ± 0.0326</td><td>0.939 ± 0.0314</td></tr>
</table>
*T_{max} was represented in median (Min, Max) value.</td></tr>
</table>

2. STUDY SYNOPSIS (Cont.)

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<tr><td>Test Product:</td><td>Levocetirizine GPO 5 mg tablets</td></tr>
<tr><td>Reference Product:</td><td>Xyzal® 5 mg tablets</td></tr>
<tr><td colspan="2">PK Confidence Intervals:</td><td>The 90% parametric confidence intervals were calculated for the ln-transformed primary pharmacokinetic parameters, $AUC_{0\text{-tlast}}$, $AUC_{0\text{-}\infty}$ and C_{max} of levocetirizine and presented as below.
<table>
<tr><th>Parameter</th><th>Ratios</th><th>90% CI</th></tr>
<tr><td>ln $AUC_{0\text{-tlast}}$</td><td>98.1</td><td>94.60-101.72</td></tr>
<tr><td>ln $AUC_{0\text{-}\infty}$</td><td>99.0</td><td>95.81-102.31</td></tr>
<tr><td>ln C_{max}</td><td>100.6</td><td>95.56-105.89</td></tr>
</table></td></tr>
<tr><td colspan="2">Conclusion:</td><td>The Test Product-T (Levocetirizine GPO 5 mg tablets – Manufactured by: GPO, Thailand. / Batch Number – S540451) when compared with the Reference Product-R (Xyzal® 5 mg tablets– Manufactured by: UCB Farchim SA, Switzerland/ Batch No.29281) met the bioequivalence criteria with respect to the rate and extent of absorption of levocetirizine as set in the Protocol.</td></tr>
<tr><td colspan="2">Date of Report:</td><td>28 Jun 2013</td></tr>
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