STUDY SYNOPSIS

Generic Name: Sildenafil **Test Product:** Sidegra **Reference Product:** Viagra®	**Sponsor Name:** The Government Pharmaceutical Organization
Study Title:	Bioequivalence study of Sildenafil 100 mg tablet in healthy Thai volunteers
Investigators:	Principal Investigator: Dr. Isariya Techatanawat., B.Sc. (Pharm), Ph.D. Clinical Investigator: Dr. Archawin Rojanawiwat, M.D. Analytical Investigator: Mr. Ashutosh Pudage, M.Sc. PK & Statistic Investigator: Ms. Jyoti Kadam, M.Sc. Other Investigator: Ms. Achara Eksaengsri, B.Sc. (Pharm)
Protocol Number	BEGPO 05/2010
Study Number	BEGPO-02/2011
IRC/Ethics and Approval Date	Institute for Development of Human Research Protection, Thailand 19 Oct 2010, 4 April 2011 (1st amendment)
Objectives:	To compare the rate and extent of absorption of a sildenafil 100 mg tablet formulation with those of a reference formulation (Viagra®) when given a single dose under fasting conditions.
Dosage Regimen	**Test Product:** Single dose, 100 mg of Sidegra tablet, Batch No. S530454 Mfd. 15 Sep 2010 Exp. 15 Sep 2012 **Reference Product:** Single dose, 100 mg of Viagra® tablet, Batch No. 101483122 Mfd. Mar 2010 Exp. Mar 2015

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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Study Subjects	No. of subjects enrolled: 32 No. of subjects dropped out/withdrawn: Nil No. of subjects completed: 32 No. of subjects analyzed: 32 No. of subjects included in pharmacokinetics and statistical analysis: 32
Demographic Data of Enrolled Subjects (N = 32)	Total of 32 subjects with average age = 27.06 ± 6.03 years, Height = 171.50 ± 7.30 cm, Weight = 65.98 ± 8.33 kg, BMI = 22.39 ± 2.12 kg/m^2 and physical examination were indicated that all participants were healthy.
Admission and Confinement	Subjects were fasted overnight at least 10 hours before dosing and 4 hours after dosing. Subjects were discharged after 24 hours after drug administration.
Drug Administration	In each of the 2 study periods, a single dose of Sildenafil 100 mg tablet of test or reference product was administered along with 240 mL of drinking water after an overnight fasting of at least 10 hours.
Study Period	Screening : 5 April 2011 - 7 April 2011 Clinical study : 18 April 2011 – 30 April 2011 Period I : 18 April 2011 – 23 April 2011 Period II : 25 April 2011 – 30 April 2011
Washout Period	7 days from the first period

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Blood Sampling Schedule	A total of 19 blood samples (6 mL each) were collected pre-dose (0 hour) and at 0.16, 0.33, 0.5, 0.67, 1.0, 1.25, 1.5, 1.75, 2.0, 2.5, 3.0, 3.5, 4.0, 6.0, 8.0, 10.0, 12.0 and 24.0 hours post dose in each period.
Blood Sampling Handling	A total of 19 blood samples were collected for 6 mL in vacutainers containing K_3EDTA from each subject for bioanalysis during the course of the study in each period. After collection, the blood samples were centrifuged at 3,500 rpm under refrigeration at 4° C for 10 minutes. The resulting plasma from each blood sample was divided into two aliquots and stored in suitably labeled microcentrifuge tube maintained below -50° C or colder, pending assay.
Clinical Sample Storage	-50° C or colder
Analytical Site	Accutest Research Laboratories (I) Pvt. Ltd., Mumbai, India.
Bioanalytical Methodology	Plasma samples of subjects were assayed for Sildenafil and its N-desmethyl metabolite using a LC-MS/MS method as per in-house SOPs.
Analyte	Sildenafil and its metabolite N-desmethyl Sildenafil in human plasma
Safety Evaluation	A total of 22 adverse events during study periods such as blurred vision for 9 volunteers which relates to test product or reference product, dizziness, and flushing which were probably and possibly related to test product or reference product. The other one adverse event, which was skin rash after scratching, was not related to test product or reference product. Clinical

<table>
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<tr><td>Safety Evaluation (cont.)</td><td>laboratory evaluation at the end of the study was shown to be safe for all participants.</td></tr>
<tr><td>Primary Pharmacokinetic Parameters</td><td>The primary pharmacokinetic parameters employed for Sildenafil were C_{max}, $AUC_{0\text{-}tlast}$ and $AUC_{0\text{-}\infty}$.
The mean ± SD values of primary pharmacokinetic parameters of Sildenafil for Test Product-A and Reference Product-B for 32 subjects are summarized in the following table:
<table>
<tr><th>Parameters (Units)</th><th>Test Product-A</th><th>Reference Product-B</th></tr>
<tr><td>C_{max} (ng/mL)</td><td>602.09±196.17</td><td>652.74±301.36</td></tr>
<tr><td>$AUC_{0\text{-}tlast}$ (ng.hr/mL)</td><td>1401.77±506.74</td><td>1445.16±512.68</td></tr>
<tr><td>$AUC_{0\text{-}\infty}$ (ng.hr/mL)</td><td>1477.76±533.16</td><td>1520.82±532.54</td></tr>
</table>
The mean ± SD values of primary pharmacokinetic parameters of N-desmethyl Sildenafil for Test Product-A and Reference Product-B for 32 subjects are summarized in the following table:
<table>
<tr><th>Parameters (Units)</th><th>Test Product-A</th><th>Reference Product-B</th></tr>
<tr><td>C_{max} (ng/mL)</td><td>434.23±128.62</td><td>434.63±165.51</td></tr>
<tr><td>$AUC_{0\text{-}tlast}$ (ng.hr/mL)</td><td>1306.35±431.84</td><td>1325.95±481.68</td></tr>
<tr><td>$AUC_{0\text{-}\infty}$ (ng.hr/mL)</td><td>1449.10±492.31</td><td>1462.89±521.31</td></tr>
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<tr><td>Test Product: Sidegra</td></tr>
<tr><td>Reference Product: Viagra®</td></tr>
<tr><td>Secondary Pharmacokinetic Parameters</td><td colspan="2">The secondary pharmacokinetic parameters employed for Sildenafil were T_{max}, λz, $t_{1/2}$ and AUC_%Extrap_obs.
The mean ± SD values of secondary pharmacokinetic parameters of Sildenafil for Test Product-A and Reference Product-B for 32 subjects are summarized in the following table:
<table>
<tr><th>Parameters (Units)</th><th>Test Product-A</th><th>Reference Product-B</th></tr>
<tr><td>T_{max} (hr)</td><td>0.72±0.48</td><td>0.78±0.56</td></tr>
<tr><td>λ_z (1 / hr)</td><td>0.34±0.10</td><td>0.35±0.09</td></tr>
<tr><td>$t_{1/2}$ (hr)</td><td>2.23±0.79</td><td>2.19±0.88</td></tr>
<tr><td>AUC_%Extrap_obs (%)</td><td>5.32±3.05</td><td>5.10±2.78</td></tr>
</table>
The mean ± SD values of secondary pharmacokinetic parameters of N-desmethyl Sildenafil for Test Product-A and Reference Product-B for 32 subjects are summarized in the following table:
<table>
<tr><th>Parameters (Units)</th><th>Test Product-A</th><th>Reference Product-B</th></tr>
<tr><td>T_{max} (hr)</td><td>0.88±0.49</td><td>0.89±0.55</td></tr>
<tr><td>λ_z (1 / hr)</td><td>0.23±0.06</td><td>0.22±0.05</td></tr>
<tr><td>$t_{1/2}$ (hr)</td><td>3.29±0.90</td><td>3.29±0.83</td></tr>
<tr><td>AUC_%Extrap_obs (%)</td><td>9.70±4.19</td><td>9.51±3.80</td></tr>
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<tr><td>Reference Product: Viagra®</td></tr>
<tr><td>90% Confidence Intervals</td><td>The 90% parametric confidence intervals were calculated for the ln-transformed primary pharmacokinetic parameters, C_{max}, $AUC_{0-tlast}$ and $AUC_{0-\infty}$ of the Sildenafil and are presented as below.
<table>
<tr><th>Parameters (Units)</th><th>90% Confidence Interval (Parameter)</th></tr>
<tr><td>C_{max} (ng/mL)</td><td>87.80-108.48</td></tr>
<tr><td>$AUC_{0-tlast}$ (ng.hr/mL)</td><td>91.09-103.23</td></tr>
<tr><td>$AUC_{0-\infty}$ (ng.hr/mL)</td><td>91.78-102.96</td></tr>
</table></td></tr>
<tr><td>Conclusion</td><td>The Test Product-A (single dose, 100 mg of Sidegra Tablet–Manufactured by The Government Pharmaceutical Organization, Bangkok, Thailand / Batch No. S530454) when compared with the Reference Product-B (single dose, 100 mg of Viagra® Tablet–Manufactured by: Pfizer Australia Pty Limited, NSW, Australia / Batch No. 101483122) meets the bioequivalence criteria with respect to the rate and extent of absorption of Sildenafil as per the criteria set in the Protocol.</td></tr>
<tr><td>Date of Report:</td><td>31 Aug 2011</td></tr>
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