## Pharmacokinetic Parameters Calculation

* Cmax is the highest observed concentration in a concentration-time profile. If two peaks of identical height are observed, the first peak is considered the Cmax. It is used to assess peak exposure.
* Tmax is the time of the sample identified as Cmax.
* AUC0-t is the area under the plasma concentration – time curve from time 0 to the last measurable plasma concentration.
* AUC0-72 is the area under the plasma concentration – time curve from time 0 up to 72 hours.
* AUCextra or AUCt-∞ is the area under the plasma concentration – time curve from the time of the last measurable concentration extrapolated to infinite time.
* AUC0-∞ is the area under the plasma concentration – time curve from time 0 extrapolated to infinite time. It is the sum of AUC0-t & AUCt-∞.
* AUCextra/AUC0-∞ or % Extrapolated is the ratio of AUCextra to AUC0-∞.
* Ke is the elimination rate constant. It is the rate at which drug is cleared from the body.
* t1/2 is the half-life of the drug in plasma which is the time taken for the concentration of the drug to decrease by 50%.
* The pharmacokinetic parameters of Sildenafil were estimated using standard non-compartmental methods.
* The maximal plasma concentration was taken directly from the measured data. The area under the plasma concentration–time curve (AUCt) was calculated from measured data points from the time of administration to the time of last quantifiable concentration (Clast) by the linear trapezoidal rule.
* The area under the plasma concentration–time curve extrapolated to infinity (AUC∞) was calculated according to the following formula:
* AUC0-∞=AUC0-t Clast/[ln (2)/t½], where Clast is the last quantifiable concentration.

## Graphical Abstract

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| **Name of the Finished Products** | Test Product: Satenafil 100 mg Film Coated Tablets, Batch No.: T30046, manufactured by Organo for Pharmaceutical & Chemical Industries (Organo Pharma) For Helwan pharmaceutical (Expiry date: 04/2018) |
| Reference Product: VIAGRA® 100 mg Film Coated Tablets, Batch No. 6702, manufactured by Pfizer Egypt S.A.E Cairo A.R.E under License of Pfizer –Inc., USA and its Subsidiary in UK (Expiry date: 01/2018 respectively) |
| **Name of Active Ingredients** | Sildenafil 100 mg |
| **Study Design** | A randomized, open-label, single-dose, three-period, three-treatment, six-sequence crossover design under fasting conditions. |
| **Objective of the Study** | This bioequivalence study aimed to investigate the rate and extent of absorption of Sildenafil through measurement of Sildenafil from, Satenafil 100 mg Film Coated Tablets manufactured by Organo for Pharmaceutical & Chemical Industries (Organo Pharma) For Helwan pharmaceutical and VIAGRA® 100 mg Film Coated Tablets manufactured by Pfizer Egypt S.A.E Cairo A.R.E under License of Pfizer –Inc., USA and its Subsidiary in UK |
| **Study Center** | Makin Research Center, Bldg. no. 4, Block 46, branched from Abdel Aziz Issa St., behind El Manhal School, in-front of the Standard Religious Institute, 9th zone, Mostafa El Nahas St., Nasr City, Cairo, Egypt |
| **Number of Subjects** | Planned: 30 (minimum 30)  Completed all study phases: 30  Analyzed: 30  Pharmacokinetics calculations & statistical analyses: 30 |
| **Diagnosis and Main Criteria for Inclusion** | Healthy male subjects (ages: 18-55 years), non-smokers or mild smokers with BMI of 30 or less and pass all physical and laboratory examinations. |
| **Dosage & Administration** | Single oral dose of 100 mg Sildenafil of both Satenafil 100 mg Film Coated Tablets manufactured by Organo for Pharmaceutical & Chemical Industries (Organo Pharma) For Helwan pharmaceutical and VIAGRA® 100 mg Film Coated Tablets manufactured by Pfizer Egypt S.A.E Cairo A.R.E under License of Pfizer –Inc., USA and its Subsidiary in UK |
| **Methodology** | Eligible subjects received test and reference products as a single oral dose on two different occasions. Blood samples were collected at zero, 5 min, 10 min, 0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 2.5, 3, 4, 6, 8, 12 & 24 hours after dosing. Zero-hour blood sample (start) was taken before dosing. Sildenafil concentrations in blood samples were determined by a validated LC.MS.MS assay method. |
| **Storage Period of Incurred Samples** | 200 days |
| **Analytical Method** | A validated LC.MS.MS assay method for the determination of Sildenafil was conducted with lower limit of quantification (LLOQ) of 25 ng/ml. |
| **Criteria for Evaluation** | Efficacy: Not applicable  Pharmacodynamics: Not applicable  Pharmacokinetics: AUC0-t , AUC0-∞ , Cmax , Tmax & t1/2 |
| **Statistical Methods** | The statistical analysis was performed according to the method of Schuirmann (1987) \*. The assessment of bioequivalence between the test and the reference products was based on the ratios of the mean pharmacokinetic parameter AUC0-t, AUC0-∞, Cmax, Tmax & t1/2. The Bioequivalence (BE) was concluded if either tail probability did not exceed the 90 % confidence limit and was completely contained in the 0.80 - 1.25 ranges for AUC0-t, AUC0-∞ and in the 0.80 -1.25 range for Cmax. Analysis of variance (ANOVA) is performed on pharmacokinetic parameters AUCs, Tmax & Cmax. |
| **Safety** | Pre-study: Vital Signs, Laboratory screening tests  Throughout the study: Vital signs and adverse events |
| **Conclusion** | The Test product, Satenafil 100 mg Film Coated Tablets manufactured by Organo for Pharmaceutical & Chemical Industries (Organo Pharma) For Helwan pharmaceutical is bioequivalent to the reference drug, VIAGRA® 100 mg Film Coated Tablets |