Work Plan & Methodology

- Literature survey
- Design & Development of study protocol, ICF, CRF
- Generation of TMF
- Ethics committee approval for the propose phenotyping study
- Procurement of study drugs and reference standards
- Method development and validation for analysis of drug
- Study subject recruitment
- Drug dosing to subjects and sample collection
- Sample processing and analysis
- Data collection and reanalysis (if required)
- Statistical analysis
- Related review and research article publications
- Report and thesis submission

METHODOLOGY

Subjects & Method

Study Subjects: One hundred and eight healthy, male, human subjects from Maharashtra region with age ranging between 18-45 years will enroll in this Phenotyping study. The screening consent & study consent shall be taken respectively before drug application. Thereafter subject’s medical records will be documented and physical examination will be conducted. The subject’s health status will be endorsed by medically qualified expert study personnel.

Study Design: This study will carried out as per the ICH (Step 5), ‘Guidance for Good Clinical Practices (GCP)’ and the principles of Declaration of Helsinki (Scotland, October 2000). The Independent Ethics Committee will review the protocol and the inform consent form for this study. A single dose, CYP2D6 enzyme Phenotyping study using healthy human subject of Maharashtra region will conduct.
**Clinical Method:** A single oral dose of Venlor XR (37.5 mg) tablet shall be administered to the study subjects at a pre-decided time. The dose shall be administered with 250 ml of water. No water and food of any kind will be allowed for 2 hours post dose. After 2 hours post dose, the subjects will be allowed food and water ad libium.

**Sampling Schedule:** Single blood sample of 7 ml will be collected two hours post dose:

**Blood Loss:** The total volume of blood withdrawn from each subject will not exceed 7 ml throughout the study.

**Washout Period:** There will be no washout period for this study.

**Safety Assessments:** Subjects will be monitored during the entire clinical period of the study for the evidence of any ADR they may experience or any adverse event they may get as a part of study procedure.

**Bio-analytical Procedure:** Blood samples (1x 7 ml) will be collected in vacutainers containing EDTA solution after 2 hours of drug administration. Each blood sample will be placed into a pre-labeled vacutainer containing EDTA solution. The samples collected from each volunteer will be centrifuged at 4000-rpm at 5°C to separate plasma, and divided in two aliquots immediately after receiving the blood samples from all the subjects. The separated plasma samples will then be transferred to deep freeze in pre-labeled tubes at or below –20°C for storage. A validated HPLC method will be employed for the estimation of Venlafaxine and its metabolite ortho-desmethylvenlafaxine in human plasma.

**Statistical Analysis:** calibration curve and QC standard distributed throughout each batch. Whenever possible, samples from each subject will be analyzed on the same standard curve. Samples with drug concentration greater than upper limit of the validated range of the analysis will be either diluted with the appropriate drug free biological fluid or such samples will be processed again with partial volume and reanalyzed. Samples, which are below the lower limit of quantification, will be set to zero for the phenotyping evaluation. Also samples will be reanalyzed in case of poor Chromatography. Based on the statistical analysis the population will be classified into poor, extensive or ultra extensive metabolizer.