6.0 SUMMARY AND CONCLUSION

The present study was undertaken to determine the rate and extent of sertraline between the test formulation, SERLIFT 100 (contains Sertraline hydrochloride equivalent to 100 mg sertraline) and the reference formulation, ZOLOFT (each tablet contains sertraline hydrochloride equivalent to 50 mg sertraline; total dose 100 mg) in healthy, adult, human subjects under fasting conditions and to assess the safety profile of SERLIFT and ZOLOFT during the course of study.

The study was carried out in accordance with ICH Good Clinical Practices. The study protocol and the informed consent form were approved by the Jamia Hamdard Institutional Review Board.

Each of the subjects was required to read and understand the information before giving his consent to participate in the study by signing the informed consent form. The signed original copy was retained and one signed copy was given to the study subject for the record. The study was conducted by using an open label; balanced, randomized, cross over design in healthy, male volunteers under fasting conditions. The order of receiving the test and reference products for each subject was determined according to a SAS generated randomization schedule. The clinical study was carried out in accordance with ICH Good Clinical Practices. The SOP’s of the clinical pharmacology unit (CPU) and Clinical Pharmacology and Pharmacokinetics (CPP), Ranbaxy have been adhered to in the clinical, bioanalytical, pharmacokinetic and statistical analysis.

Eighteen (18) subjects were enrolled into the study. Seventeen (17) subjects completed both the periods of the study. Subject number 17 was withdrawn from the study on period II admission due to failure to comply with the requirements of the study (Subject was found to be positive for cannabinoids in urine drugs of abuse, screened at admission of period II)

The washout period maintained between the periods was of twenty one days. Safety of the subjects was assessed throughout the study. Vital signs (oral temperature, sitting blood pressure and radial pulse) were found to be normal for all the subjects.
during the course of the study. The clinical examinations of all subjects were found to be normal. Adverse event monitoring was done throughout the study.

There were no serious adverse events during the conduct of the study. The Test (T) and Reference (R) products were well tolerated by the study subjects. Two adverse events including one laboratory adverse event was reported during the study.

One adverse event of nausea was reported post-dose period II in reference group. The event had possible relationship to the study drug and recovered without sequelae. The event was mild and not serious in nature.

One laboratory adverse event of raised eosinophils was reported at the end of study safety assessment in test group. The event had unlikely relationship to the study drug and recovered without sequelae. The event was moderate and not serious in nature.

A high performance liquid chromatographic tandem mass spectrometric method was developed for the estimation of sertraline in human plasma. The method was validated in terms of selectivity, precision, accuracy, linearity, recovery, dilution integrity, ruggedness and stability studies. Before the initiation of unknown plasma samples of the biostudy, validation was completed. All validation parameters met the pre-defined acceptance criteria. The validated method was used for the analysis of subject samples. Pharmacokinetic and statistical evaluation was done on the concentration data obtained after analysis of subject samples.

Bioequivalence was assessed by measuring the pharmacokinetic parameters namely $C_{\text{max}}$, $AUC_{0-t}$ and $AUC_{0-\infty}$. The bioequivalence criteria used were 90% confidence intervals of ratios of LSM of log transformed data for $C_{\text{max}}$, $AUC_{0-t}$ and $AUC_{0-\infty}$.

The following conclusions were drawn from the study:

90% confidence intervals for the ratios of Test (T) and Reference (R) product averages (least-squares means) derived from the analysis of log transformed pharmacokinetic parameters $C_{\text{max}}$, $AUC_{0-t}$ and $AUC_{0-\infty}$ were within 80-125% for Sertraline.
Based on these results, tablet of SERLIFT 100 mg tablet (contains Sertraline hydrochloride equivalent to 100 mg sertraline) of Ranbaxy (M) SDN BHD and two tablets of ZOLOFT (contains sertraline hydrochloride equivalent to 50 mg sertraline; total dose 100 mg) of Pfizer (Malaysia) SDN BHD., are bioequivalent in healthy, adult, male human subjects under fasting conditions.

The test and reference drug products were well tolerated by the study subjects.