REPUBLIC OF LEBANON
MINISTRY OF PUBLIC HEALTH

الجمهورية اللبنانية
وزارة الصحة العامة

Checklist for the Clinical Part Module 5: Bioequivalence

February 2022

Information/Document(s) required	File Description	Page
Letter from the company (signed and dated) explaining your application and describing the content of all submitted files.		
Study Protocol		
Amendment to the study protocol (if available).		
Study report		
Study duration		
Manufacturer/Sponsor		
Copy of all investigators CV		
Certificate of analysis for both reference and test products.		
Information about the Test Product [Brand Name, Dosage, Pharmaceutical form, Manufacturer, Batch number, Manufacturing date, Expiry date]		
Information about the Reference Product [Brand Name, Dosage, Pharmaceutical form, Manufacturer, Batch number, Manufacturing date, Expiry date]		
Evidence showing that the reference product is used according to FDA or EMEA lists.		
Therapeutic class		
Information about the CRO [Name, Country, Address, Clinical (hospital), Medical Laboratory (for screening examination), Analytical Facility, Pharmacokinetic studies, Statistical analysis].		
Study design		
Information showing if the study was conducted according to FDA/EMA/others guidelines.		
API Pharmacokinetic Properties		
Evidence that the Medical Laboratory (for screening examination) meets GLPs as certified by an authorative agency.		
Signed Informed consent form for all participants		
IRB protocol approval (Signed and dated)		
Official certificates of GCP and GLP compliances.		
Quality assurance audits performed by the CRO with dates and signatures.		
Sample size calculation and sample size recruited		
Screening examination data and individual Case Report Form (CRF) for all participants.		
List of all adverse events (AE) encountered		
Subjects demographic data (Gender, Age, Weight, Height, BMI, etc …)		
Period I and Period II description and Washout period		
Blood Samples description [Anticoagulant, number of samples and blood volume (per subjects and per period), storage conditions,		
***In vitro* Dissolution Profile** [Medium composition, Medium pH, Apparatus, Speed (rpm), Temperature (°C),		

Volume (mL), Duration, Difference factor (f1), Similarity factor (f2), dissolution plot].		
Analytical method [Analytical method and detector, materials, solvents and equipment used. Method of preparation of the stock solutions, calibration standards and sample handling].		
Analytical Validation method in stock solution and plasma samples [Linearity (Linearity zone, Standard curve equation, R^2), Recovery, Inter-day and Intra-day Accuracy, Inter-day and Intra-day Precision, Stability (Short term, Long term, Freeze/thaw stability, autosampler), Specificity, Robustness, Sensitivity (LLOD, LLOQ), Quality control samples (Low QC, Medium QC, High QC)		
Analytical spectrums for a minimum of 20% of all subjects		
Copy of chromatograms realized in analytical section (Analytical validation).		
Raw data (as Excel sheet) for all analytical validation method.		
Pharmacokinetic Parameter calculation (Cmax, $AUC_{0\rightarrow t}$, AUC $_{0\rightarrow\infty}$, Half-life ($t_{1/2}$), K_e, T_{max}) with 90% Confidence Interval, and Intra-subject variability for Cmax, $AUC_{0\rightarrow t}$, AUC $_{0\rightarrow\infty}$.		
Data related to plasma concentration for all subjects and at all time points (as excel sheet).		
The **mean** plasma concentration vs. time plot in <u>linear scale</u> (with SEM/SD error bars on each point).		
The **mean** plasma concentration vs. time plot in <u>semi-logarithmic scale</u> (with SEM/SD error bars on each point).		
Individual plasma concentration vs. time plot in <u>linear scale</u> for all subjects (no more than 2 plots per page is allowed).		
Individual plasma concentration vs. time plot in <u>semi-logarithmic scale</u> for all subjects (no more than 2 plots per page is allowed).		
In case the criteria are different than 80 – 125%, the sponsor should provide detailed explanation and provide additional references that allow such modification. Any intra-subject variability should also be discussed according to literature.		
Statistical analysis: ANOVA data (and p-value) for the different sources: Period, Subject within the sequence, Formulation, Sequence, performed on the different PK parameters (Cmax, $AUC_{0\rightarrow t}$, AUC $_{0\rightarrow\infty}$, etc…).		
Sponsor should provide explanation or additionnal tests in case any p-value in the statistical analysis section is < 0.05 (Statistically significant).		