REPUBLIC OF LEBANON
MINISTRY OF PUBLIC HEALTH

الجمهورية اللبنانية
وزارة الصحة العامة

Self-Assessment for the Efficacy Module 5: Bioequivalence

February 2022

Section I – Generalities

1. Study Title	
2. Name of the generic product	
3. Name of the active ingredient(s)	
4. Manufacturer/Sponsor	
5. Therapeutic class	
6. Information about the Test Product	
6.a. Brand Name	
6.b. Dosage	
6.c. Pharmaceutical form	
6.d. Manufacturer	
6.e. Batch number	
6.f. Manufacturing date	
6.g. Expiry date	
7. Information about the Reference Product	
7.a. Brand Name	
7.b. Dosage	
7.c. Pharmaceutical form	
7.d. Manufacturer	
7.e. Batch number	
7.f. Manufacturing date	
7.g. Expiry date	
8. Drug half-life	
9. Information about the CRO	
9.a. Name	
9.b. Country	
9.c. Address	
9.d. Clinical (hospital)	
9.e. Medical Laboratory (for screening examination)	
9.f. Analytical Facility	
9.g. Pharmacokinetic studies	
9.h. Statistics	
10. Study design	
11. Fasting / Fed condition	
12. IRB Protocol Approval (day/month/year)	
13. Protocol study number	

Section II – Clinical Part

1. Sample size	
1.a. Subjects recruited (Male / Female)	☐ Male ☐ Female ☐ Both
1.b. Number of subjects included	
1.c. Number of subjects who completed both periods of the study	
1.d. Age (mean ± SD) (years)	
1.e. Age (youngest age – oldest age)	
1.f. Height (mean ± SD) (cm)	
1.g. Weight (mean ± SD) (kg)	
2. Informed Consent signed by applicants on	
3. Date of the screening examination	
4. Period I started on (day/month/year)	
5. Period I ended on (day/month/year)	
6. Wash out period (number of days)	
7. Period II started on (day/month/year)	
8. Period II ended on (day/month/year)	
9. Blood Samples	
9.a. Number of blood sample per subject	
9.b. Time period for each blood sample	
9.c. Total volume of blood drawn per subject and per period	
9.d. Anticoagulant used in blood test tube	
9.e. First blood sample (period I) was taken on	
9.f. Last blood sample (period II) was taken on	
10. Samples storage temperature	
10.a. at clinical site	
10.b. at analytical site	
11. Study Duration	
11.a. For the clinical part	
11.b. For the bio-analytical part	
11.c. For the statistical part	
12. Study report released on	
13. Name of clinical investigator and title	
14. GCP issued from (and date of issuance)	

Section III – *In vitro* Dissolution Profile

	Medium 1	Medium 2	Medium 3
Medium composition			
Medium pH			
Apparatus			
Speed (rpm)			
Temperature (°C)			
Volume (mL)			
Duration			
Difference factor (f1)			
Similarity factor (f2)			

Attach in the space below the dissolution plot:

Section IV – Analytical Validation method

1. Sample preparation and drug/metabolite extraction method used	
2. The analytical method used to quantify the analyte (with detector)	
3. Analyte (drug or metabolite) measured	
4. Analyte (drug or metabolite) measured in	☐ Plasma ☐ Urine
5. The internal standard used	
6. Biological matrix used in the preparation of the standard curve	
7. Linearity	
7.a. Linearity zone	
7.b. Standard curve equation	
7.c. R^2	
8. Recovery	
8.a. for the active ingredient	
8.b. for the internal standard	
9. Accuracy	
9.a. Inter-day Accuracy	
9.b. Intra-day Accuracy	
10. Precision	
10.a. Inter-day Precision	
10.b. Intra-day Precision	
11. Stability	
11.a. Short term Stability (period at different temperature)	
11.a.1. In stock solution	
11.a.2. In human plasma	
11.b. Long term stability (period at different temperature)	
11.b.1. In stock solution	
11.b.2. In human plasma	
11.c. Freeze/thaw stability (Temperature and number of cycle)	
11.d. In autosampler	
12. Specificity	
13. Robustness	
14. Sensitivity	
14.a. Lowest limit of detection (LLOD)	
14.b. Lowest limit of quantification (LLOQ)	
15. Quality control samples	
15.a. Low QC	
15.b. Medium QC1	
15.c. Medium QC2 (if available)	
15.d. High QC	

Section V – Pharmacokinetic Analysis Section

Software used to Calculate PK parameters	

Parameters	**Cmax**	**$AUC_{0\rightarrow t}$**	**$AUC_{0\rightarrow\infty}$**
Criteria	**80 – 125 %**	**80 – 125 %**	**80 – 125 %**
Mean			
90% Confidence Interval			
Intra-subject variability			

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 be discussed according to literature.**

Note: BE study will be rejected in absence of a**ny unjustified wideness of these criteria.**

Half-life ($t_{1/2}$)	
K_e	
T_{max}	

Please attach below the mean plasma concentration vs. time plot in both linear and semi-logarithmic scale (with SEM/SD error bars on each point).

Section VI – Statistical Analysis Section

Software used to do the ANOVA analysis	

	p values		
Source	**Cmax**	**$AUC_{0\rightarrow t}$**	**$AUC_{0\rightarrow\infty}$**
Period			
Subject (seq)			
Formulation			
Sequence			

Please provide below **explanation or additionnal tests in case any p-value in the statistical analysis section is < 0.05 (Statistically significant).**

Note: BE study will be rejected in absence of any explanation/justification.

<u>In addition, Sponsor should provide</u>:

1. Certificate of analysis for both reference and test products.
2. Evidence showing that the reference product is used according to FDA or EMEA lists.
3. Information showing if the study was conducted according to FDA/EMA/others guidelines.
4. Evidence that the Medical Laboratory (for screening examination) meets GLPs and procedures as <u>certified by an authorative agency.</u>
5. Copy of the study protocol.
6. Amendment to the study protocol (if available).
7. Copy of the informed consent form
Note: signed informed consent for all participants should be attached in BE report.
8. IRB protocol approval.
Note: Sponsor should attach the IRB approval document (dated with all committee members signatures).
9. Official certificates of GCP and GLP compliances.
Note: Date of certificates should fit the study period.
10. Quality assurance (QA) audits performed by the CRO with dates and signatures.
11. Official authorization (certificate) for laboratory where routine lab analysis had been done.
12. GMP (for the manufacturer).
13. Method used to calculate the minimum number (formula, and all numbers used in the formula**) of subjects** required to be enrolled in the study. Number of subjects who completed both periods should not be less than the minimum number of subjects calculated prior to beginning the study (as required above), or else the study will be rejected.
14. All screening examination data and individual Case Report Form.
15. Table with all adverse events and discuss it.
16. Certificate of analysis for the reference standards used in the analysis
17. A minimum of 20% of all subjects analytical spectrums should be provided in the BE report.
18. The materials, solvents and equipment used should be detailed. Method of preparation of the stock solutions, calibration standards and sample handling should be outlined in details.
19. All raw data related to plasma concentration (on excel sheet) for all subjects and at all time points. No scanned sheet is allowed.
20. The mean plasma concentration vs. time plot in both linear and semi-logarithmic scale (with SEM/SD error bars on each point).
21. Individual plasma concentration vs. time plot in both linear and semi-logarithmic scale for all subjects.
22. In case the criteria are different than 80 – 125%, the sponsor should provide detailed explanation and provide additional references that allow such modification. **Any unjustified wideness of these criteria will be rejected. Any intra-subject variability should be discussed according to literature.**
23. Sponsor should provide explanation or additionnal tests in case any p-value in the statistical analysis section is < 0.05 (Statistically significant). BE study will be rejected in absence of any explanation/justification.