Notice to applicant

Central Administration of pharmaceutical Products (CAPP)
General Administration For Human Pharmaceuticals Registration (GA-Hum-PR)

Guidance for In-vitro Studies Submission for Imported / Local human Pharmaceutical Products

Year 2025

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OVERVIEW

Bioequivalence Unit is pleased to submit this guidance to support your company in achieving the goals of your in-vitro studies. Our aim is to improve customer satisfaction by providing clear templates, guidance, and requirements that will streamline your fulfillment process. This will enable us to enhance our assessment process, ensuring greater accuracy and consistency within defined timeframes

Main Components of the study folder

- Folder #1: Administrative Documents Folder
- Folder #2: Technical Folder

Folder #1: Administrative Documents Folder (Registration Part)

A. Imported Pharmaceutical Products

- Application form stamped and signed: Kindly find the required template in the following link https://docs.google.com/document/d/1FqhCavQx7jiCnX_7txuw2zpVeq_H-Gz0/edit?usp=sharing&ouid=101281260984690515723&rtpof=true&sd=true
- Payment Receipt
- Valid Certificate of Pharmaceutical Product (CPP) issued by Competent Authorities in Country of Origin
- Composition attached to CPP
- Bioequivalence center license (where the study performed) – in case of the study is performed at Center (if any).
- Scan of Inner and Outer packages and inner leaflet of reference & Applicant drug products on which the study was performed. The scan should show all the data mentioned on all sides of the pack
- Bioequivalence approval for using Innovator product or scientific references, such as FDA Orange Book, ANSM, etc. websites). (In case of inquiring about the reference product)

A. For Under- Registered Imported Pharmaceutical Products

- Registration request approval (Action letter)
- Trade Name approval
- Pricing approval (if any) / mail or document proving receipt of the file from pricing administration
- Pharmacovigilance approval (if any)
- Bioequivalence unit decision for the type of study required (if any)

B. For Registered Imported Pharmaceutical Products

- Registration license (the latest)

* In case of Preliminary Registration License has been expired, an approval for its renewal must be submitted or Preliminary approval for the re-registration (in case of expired RL) + Approval for decision no. 150/2022 (if any)

- Variation approval for Registered Pharmaceutical Products on any change occurred (valid) – if any
- Composition certificate approved by EDA – if any

B. LOCAL Pharmaceutical Products

- Application form: Kindly find the required template in the following link https://docs.google.com/document/d/1FqhCavQx7jiCnX_7txuw2zpVeq_H-Gz0/edit?usp=sharing&ouid=101281260984690515723&rtpof=true&sd=true
- Payment Receipt
- Sample withdrawing report issued by the EDA inspectors mentioning the following:
- Trade name, concentration and dosage form -The factory name.
- The name of the bioavailability and Bioequivalence Center in which the study will be conducted.
- Type of batch (1st production batch - Pilot Batch - production batch -1st production batch after new change (new supplier -new composition ..etc).
- Batch number, Production date and expiration date.

- Names of raw materials suppliers on which the batch was produced. - The composition on which the batch was produced
- Composition certificate approved by EDA (for the batch on which the study will be performed on)
- Scan of Inner and Outer packages and inner leaflet of reference & Applicant drug products on which the study was performed. The scan should show all the data mentioned on all sides of the pack
- Bioequivalence approval for using Innovator product or Scientific references (such as FDA Orange Book, ANSM, etc. websites). (In case of * inquiring about the reference product)

A. For Under- Registered Local Pharmaceutical Products

- Registration request approval (Action letter)
- Trade Name approval
- Pricing approval (if any) / mail or document proving receipt of the file from pricing administration
- Pharmacovigilance approval (if any)
- Bioequivalence unit decision for the type of study required (if any)
- The production plan for the sources of the active raw materials. Or the importation approval for the active raw materials of the drug product to prove the name of the supplier of the raw material.

B. For Registered Local Pharmaceutical Products

- Registration license (the latest)

In case of Preliminary Registration License has been expired, an approval for its renewal must be submitted or Preliminary approval for the re-registration (in case of expired RL) + Approval for decision no. 150/2022 (if any)

- Variation approval for Registered Pharmaceutical Products on any change occurred (valid) – if any
- Composition certificate approved by EDA – if any

Folder #2: Technical Folder (Technical Part)

N.B. Kindly name each file or folder with its headline content without abbreviations or symbols.

- File #A: Study Summary
- File #B: Study protocol / report
- File #C: Protocols of Validation & verification of the study tests
- File #D: Study chromatograms or charts.

Please note that File #D is required. If you cannot fulfill this, kindly provide a justification.

File #A: Study Summary

- Kindly find the required template in the following link (from page 9 to 13) https://drive.google.com/file/d/1Ab3qzY1vhHaFQpnBHGLQgQKj49D5mgz_/view

File #B: Study protocol / report

- The study protocol should include three key tests: the potency test, the uniformity of dosage test, and the dissolution test. Each test should be detailed in five components:
- The methodology for preparing the standard and test (e.g., applicant product, innovator product, others)
- The parameters of the instrument used in dissolution apparatus and quantitative analysis for example: HPLC
- The equation for determining the final results.
- A table containing the peak area or response from the instrument printout, the practical weights taken, dilution factors, potency, and water content of the standard and final results (% assay, %release, f1 & f2)
- The acceptable limits for each test, along with evidence-based references for the applied methodology, such as the FDA or the US Pharmacopoeia (USP) ... etc

Suggested template for presenting each test in the study protocol:

- Name of test: ……
- Reference used: …….
- Methodology:

STANDARD SAMPLE PREPARATION METHOD

APPLICANT PRODUCT SAMPLE PREPARATION METHOD

INNOVATOR PRODUCT SAMPLE PREPARATION METHOD

- The parameters of the instrument used:

For dissolution test	
Apparatus	
Rate of rotation	
Dissolution media	
Volume	
Temperature of dissolution	
Number of dosage units	
Time Interval for Sampling	

Example for HPLC	
Mobile phase	
Detector	
Column	
Flow rate	
Injection volume	

- Equation applied: ……

1.2 Tabulated results (Example for assay test)

Required Items	Standard	Applicant product batch number:…….	Innovator product batch number:…….
Peak area or response (at least 3 readings for the each sample)			
Weight taken of samples			
Average weight of the product dosage form			
Potency and water content of the standard			
Final results			

- N.B. In case of uniformity of dosage, at least 10 readings are required.

Tabulated results in case of dissolution test

Tablet NO.	**Peak Area of (sample name) dissolved in (medium name) after different time intervals Duration**					
	Time 1		Time 2		Time 3	
	Test	Ref	Test	Ref	Test	Ref.
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Mean						
STDEV						
RSD %						

Tablet NO.	**%Release of (sample name) dissolved in (medium name) after different time intervals Duration**					
	Time 1		Time 2		Time 3	
	Test	Ref.	Test	Ref.	Test	Ref.
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Mean						
STDEV						
RSD %						

Time	Rt	Tt	|Rt-Tt|	|Rt-Tt|^2
Time 1				
Time 2				
Time 3				
sum |Rt-Tt|^2				
n				
Similarity factor F2				
F1				

N.B. Calculation of F1 & F2 is according to EMEA guideline & Egyptian guideline.

File #C: Protocols / reports of Validation & verification

- The protocol should include methodology of each validation item and tabulated instrument response and results (For example: %RSD, % Recovery, %pooled RSD, ….. etc)

File #D: Study chromatograms or charts

- Please submit the chromatograms or charts for each test in a separate PDF.
- If the charts are submitted in any language other than English, please ensure that the file is translated into English.
- Each chromatogram /chart should clarify the following:

1. Sample Name: include the name of product and batch number
2. Name of the solvent in which the sample is dissolved
3. Type of detector and wavelength
4. System suitability parameters (Tailing factor, Resolution and No. of theoretical plates)

- Each chromatogram /chart should have appropriate scale that shows the peak clearly

Please note this guidance is provided to help make your submission process smoother and reduce missing information. When you submit your study, it is essential to follow the instructions in the following links listed in the Google form and submit the documents in the specified order exactly as instructed.

How to Submit Your Application:

1. **COMPLETE THE REGISTRATION FORM**
   To begin the submission process, please complete the registration form available through the following link:
   https://docs.google.com/forms/d/e/1FAIpQLSfLDD999ziozYC62BO9ELpBtU17s4hc0zGr8senDkwnJ0ciLA/closedform

2. **SUBMIT THE REQUIRED DOCUMENTS**
   The registration form includes separate instructions on submitting two essential components of your application

A. Registration Part:
   https://drive.google.com/file/d/1Ht1uNKF2Y13Q3gCGJ1ech60Vt54uNMOZ/view?usp=sharing

B. Technical Part:
   Format and Content of **Comparative In Vitro Dissolution Study** Report
   https://drive.google.com/file/d/1Ab3qzY1vhHaFQpnBHGLQgQKj49D5mgz_/view?usp=sharing
   Or Format and Content of **Dissolution Profile Study** Report
   https://drive.google.com/file/d/1fIzW3BQ2cGoVv0scrus3NSOmVkW6ADOB/view?usp=sharing

We appreciate your attention to detail and look forward to receiving your submission.