Registration Department  
Jordan Food & Drug administration

Registration Requirements for Pharmaceutical Finished Product according to CTD Format
**Introduction:**

1- The CTD (Common Technical Dossier) provides a format for the submission of information to regulatory authorities.

2- The required data for each application will differ, depending on the drug submission type (originator/new drug, Biological & Bio-similar drugs, Generic Drugs and Radiopharmaceuticals, However, all the required data should be in accordance with the CTD structure.
FIRST: Module 1→Administrative Documents:

1- Drug Registration Form, no. (LF4/RDP/7/2008):
   Should be filled, signed & sealed from the marketing authorization holder or
   the manufacturer on each page……..The Form is attached.

2- Summary of product characteristics (SPC):
   From the product packaging material such as leaflet, label, outer box….etc.
   You must attach original packaging material in English with this summary as:
   2.1 Twenty leaflets
   2.2 Ten labels
   2.3 Five outer boxes
   2.4 Artwork of the packaging material

3- Mock-up (Packaging material Artwork) such as: outer box, label & inner-
   insert….kindly note the following concerning the Mock-up:
   3.1 The artwork must be colored original copy for the same outer-box that you
   will use for the goods in Jordan after registration.
   3.2 You must mention product trade name, generic name, mfg. date, exp.date,
   batch number, storage condition, barcode, manufacturer name & address and
   MHA Company & address in the outer box.
   3.3 You must mention product trade name, generic name, mfg. date, exp.date,
   batch number, storage condition, manufacturer name & address and MHA
   Company & address in the label.
3.4 You must mention product trade name, generic name, storage condition, manufacturer name & address and MHA Company & address, revision date & number in the leaflet.

4- Declaration letters form the manufacturer:

4.1 To specify the product type as: Originator or Generic or Biosimilar..etc…..and to declare the product active substance name, pharmaceutical form, strengths, therapeutic indications, route of administration……..etc.

4.2 To specify Information for Product submission type (Technology Transfer, under license …..) if applicable.

5- Declaration for Pharmacovigilance System:

Detailed description of the Pharmacovigilance system must be provided this should include proof that the applicant has the services of a qualified person responsible for Pharmacovigilance and the necessary means for the notification of any adverse reaction, and to be signed by the qualified person.

6- Declaration for Risk-management System (plan):

A detailed description of the risk management system which the applicant will introduce should be provided, and to be signed by the qualified person
7- Other Information:

7.1 List of similar product available in Jordan market…to be done by Nobles.

7.2 Detailed comparison between Generic & Originator leaflet…this is requested only for Generic products…you must attach copy of your product insert plus copy of the originator insert.

7.3 Declaration from the manufacturer about the ingredient/s from human or animal origin included in the composition of the product and their source and the related certificates (TSE /BSE).

7.4 List from manufacturer to declare the worldwide registration status: (registered\Marketed (date & number), under registration and rejected (with reason)).

7.5 Technical Manufacturer Contract (Open part) in case of contract manufacturing….with clear clarification for:
   a) Manufacturing company or (Contract executor) agreed on to the(Contract giver) about the possibility to inspect or check the production area, Quality control area, warehouses, manufacturing process, analysis process, batch record & other technical matters.
   b) The responsibility of each part of the manufacturing contract agreement about the manufacturing and quality control process.
   c) The name of the part responsible for the product batch release.
   d) Duration of the agreement.

7.6 Health authority approval of the latest Plasma master file (if the product Contain plasma derivatives).

NOTE; in case any of the above items is not applicable, kindly send declaration letter to justify its unavailability.
8- Requested Certificates by Jordan FDA:

8.1. Duly legalized Certificate of Pharmaceutical product (CPP) according to WHO form.

8.1.1 The CPP Certificate must contain the following:
- Trade name of the product
- Registration number at your health authority or Competent Authority
- Registration date at your health authority or Competent Authority
- Active ingredients qualitative and quantitative
- Inactive ingredients qualitative and quantitative
- You must say clearly that the product is currently sold in your country, it's not enough to say that it is authorized to sell.
- Name, address of marketing authorization holder and names, addresses of all of manufacturing sites and its activities.

8.1.2 In case that the products is not sold in the country of origin then you must explain why, and to submit one CPP certificate from (USFDA or Japan or EMA or Canada) or two CPP certificates from two of the following countries (UK, Germany, France, Belgium, Switzerland, Holland, Sweden, Austria, Fenland, Australia and Spain)....the CPP must be valid and to be for product from the same production line that will be registered in Jordan.

8.1.3 The products must be registered and used in the country of origin at least for one year before the registering in Jordan.

8.2 Pricing certificate informing about the price in the country of origin (duly legalized) and must contain the following:
- Trade name, Generic name ,Dosage form, unit Pack.
- Ex. Factory (Ex. Work) price in the country of origin in the local currency and in USD when your local currency is not USD
- Wholesaler price in the country of origin in the local currency and in USD when your local currency is not USD (if it is applicable)
- Pharmacy price in the country of origin in the local currency and in USD when your local currency is not USD (if it is applicable)
- Public price in the country of origin in the local currency and in USD when your local currency is not USD (if vat is included, kindly specify)
Notes:

Concerning the pricing certificate, kindly send us the additional following documents:

a) A letter from your company (not legalized) saying that you will export to Jordan the goods as CIF price in USD when your local currency is not USD.

b) In case that the pricing certificate is not legalized from your health authority then we need a letter issued from your heath authority saying that (it has no stated that in (mention your country name) neither the health authority nor its local competent authorities do issue and legalize pricing certificate, official price approvals for pharmaceutical products are not required by law and the prices will be defined by the pharmaceutical industry at its sole discretion)… duly legalized.

c) Pricing certificate from the manufacturer to explain, the public price for this product in the following countries (United Kingdom, France, Spain, Italy, Belgium, Greece, Holland, Australia, Cyprus, Hangaria, Ireland, Newsland, Portugal, Czech, Croatia and Austria) if it is Applicable, if not, kindly send us a letter to clarify this matter this certificate does not need any legalization.

d) In case that your health authority only issuing a pricing certificate containing Ex. Factory price/Ex-work, pharmacy price, Wholesaler price and public price only), we want from you to provide us with pricing certificate from your company in their official paper (only signed and sealed by the company) for your suggested export price as CIF in USD to Jordan.

e) Export Price to Saudi Arabia (if marketed) if not, kindly send us a letter to clarify this matter (this does not need any legalization.)

f) In case that your health authority has website and publish the products prices in the website, then Jordan FDA will not request legalized price certificate, so we will need the price certificate without legalization.

8.3 Declaration letter from the manufacturer company to declare the following information:

a) The name of the manufacturing company and the address of the manufacturing site

b) The name and the address of the marketing authorization holder company.

c) The name and the address of the company that will issue the invoice.

d) The Export Center (The name of the city and the name of the Airport or the Seaport)

e) The name and the address of the company responsible about the product batch release.
SECOND: Module 2 → CTD summaries

2.1 CTD table of contents (Module 2-5)

2.2 CTD introduction

2.3 Quality Overall Summary

2.4 Non Clinical Overview

2.5 Clinical Overview

2.6 Non Clinical written and Tabulated Summary

2.7 Clinical Summary
THIRD: Module 3 → Quality:

Module 3 is composed of the following sections:

IMPORTANT NOTE: CONCERNING MODULE (3) QUALITY (SECTION 3.2.S DRUG SUBSTANCE…. ) Kindly note the following carefully;

1- All the documents requested in this section must be from the API manufacturer for the active drug substance and must be printed in their company official paper and must be signed and sealed on each page.

2- Section no; 3.2.S.2 (manufacturer…..) which considered as closed part . Kindly note that we need only the following documents;

I- declaration letter from you printed in your official paper to declare the name and the address of the API manufacturer that you used.
II- valid copy of certificate of suitability (CEP) from EDQM for the active substance from each supplier OR valid GMP certificate (copy) sealed & singed from the health authority or notarized copy.
III- we need letter of access from the API manufacturer of the active substance addressed to Jordan fda.

I- 3.2.S DRUG SUBSTANCE (Active Pharmaceutical Ingredient-API)

Valid European Certificate of Suitability (CEP/ COS) with all appendices (copy) for drug substance manufacturer. The Drug Substance sections should refer to the Certificate of Suitability in the relevant sections in Module 3.2.S , the Certificates of Suitability are deemed to replace the data of the corresponding sections(S.2.2 , S.2.3, S.2.4 and S.2.6) and therefore in principle no further additional information is necessary except concerning technical characteristics of the substance where not covered by the Certificate of Suitability (e.g. when the Certificate of Suitability does not describe a specific technical grade, information and data for the re-test period).

If the Certificate of Suitability (CEP/COS) is not available, all the sections of 3.2.S for the Drug Substance in Module 3 should be full-filled & a valid copy of GMP certificate (for drug substance manufacturer/s) should be included.

The information from the Open Part of the DMF (Drug Master File) should be provided in drug submission. The open part of the DMF should be including all the subsections of the section 3.2.S for Drug substance or Active Pharmaceutical Ingredient-API.
**COS or CEP: Certificate Of Suitability**: A Certificate issued from EDQM (European Directorate for the Quality of Medicine) to demonstrate the compliance of the substance used with the monograph of the European Pharmacopoeia. (not issued for biological)

**GMP certificate**: issued from health authorities, the firm follow GMP, should mention the name of drug substance.

**DMF**: drug master file.

### 3.2.S.1 General Information (name of the active ingredient, manufacturer)

Information on the nomenclature of the drug substance (INN), chemical name, USAN….), Structure (structural formula, molecular formula..).

General properties: A list should be provided of physicochemical and other relevant properties of the drug substance, including biological activity for biotech, should be specified.

### 3.2.S.2 Manufacture (name of the active ingredient, manufacturer)

#### 3.2.S.2.1 Manufacture name, address.

The name, address, and responsibility of each manufacturer should be provided. Name should comply with (CEP or GMP certificate provided).

#### 3.2.S.2.2 Description of Manufacturing Process & process controls.

The description of the drug substance manufacturing process represents the applicant’s commitment for the manufacture of the drug substance. Information should be provided to adequately describe the manufacturing process (flow diagram) and process controls.

**Filling, storage and transportation (shipping)**

A description of the filling procedure for the drug substance, process controls (including in-process tests and operational parameters), and acceptance criteria should be provided. (Details in 3.2.S.2.4.) The container closure system(s) used for storage of the drug substance (details in 3.2.S.6.) and storage and shipping conditions for the drug substance should be described.

#### 3.2.S.2.3 Control of Materials.

Materials used in the manufacture of the drug substance (e.g., raw materials, starting materials, solvents, reagents, catalysts) should be listed identifying where each material is used in the process. Information on the quality and control of these materials should be provided.
3.2.S.2.4 Control of Critical Steps & intermediates.
Critical Steps: Tests and acceptance criteria (with justification including experimental data) performed at critical steps identified in 3.2.S.2.2 of the manufacturing process to ensure that the process is controlled should be provided.
Intermediates: Information on the quality and control of intermediates isolated during the process should be provided.

3.2.S.2.5 Process Validation
Process validation and/or evaluation studies for aseptic processing and sterilization should be included.

3.2.S.2.6 Manufacturing Process Development.
A description and discussion should be provided of the significant changes made to the manufacturing process and/or manufacturing site of the drug substance used in producing nonclinical, clinical, scale-up, pilot, and, if available, production scale batches.

3.2.S.3 Characterization (name of the active ingredient, manufacturer)
3.2.S.3.1 Elucidation of Structure and other Characteristics.
Confirmation of structure based on e.g., synthetic route and spectral analyses should be provided. Information such as the potential for isomerism, the identification of stereochemistry, or the potential for forming polymorphs should also be included.

3.2.S.3.2 Impurities. Specify impurity profile.

3.2.S.4 Control of Drug Substance (name of the active ingredient, manufacturer):
3.2.S.4.1 Specification (name, manufacturer)
The specification for the drug substance should be provided as the below table:

<table>
<thead>
<tr>
<th>Test</th>
<th>Specification</th>
<th>Reference</th>
</tr>
</thead>
</table>

Note: If pharmacopoeial a copy of the monograph should be included.
3.2.S.4.2 Analytical Procedures (name, manufacturer)
The analytical procedures used for testing the drug substance should be provided.

3.2.S.4.3 Validation of Analytical Procedures (name, manufacturer)
Analytical validation information, including experimental data for the analytical procedures used for testing the drug substance, should be provided.

Verification used for Pharmacopoeial methods.
Validation used for Non-Pharmacopoeial methods.

3.2.S.4.4 Batch Analyses (name, manufacturer)
Description of batches and results of batch analyses should be provided as the below table:

<table>
<thead>
<tr>
<th>Test</th>
<th>Specification</th>
<th>Batch NO.</th>
<th>Batch NO.</th>
<th>Batch NO.</th>
</tr>
</thead>
</table>

a) Provide COA for each Batch.
b) Use the same batches that you use the stability study section 3.2.S.7

3.2.S.4.5 Justification of Specification (name, manufacturer)
Justification for the drug substance specification should be provided.

Note: if pharmacopoeial a copy of the monograph should be included.

3.2.S.5 Reference Standards or Materials (name of the active ingredient, manufacturer)
Standard name and its manufacturer (provide COA of API reference standard).

3.2.S.6 Container Closure System (name of the active ingredient, manufacturer)
Mention the type of the container, closure.

3.2.S.7 Stability (name of the active ingredient, manufacturer)
Results of the stability studies (e.g., forced degradation studies and stress conditions) should be presented in an appropriate format such as tabular, graphical, or narrative. Conclusions with respect to storage conditions and retest date or shelf-life, as appropriate. Include stability data minimum of: 6 months at accelerated conditions and 12 months at long term conditions for three batches, and if applicable to enclose Post-approval Stability protocol & Commitments.
II- 3.2.P  DRUG PRODUCT (NAME OF THE FINISHED PRODUCT, DOSAGE FORM)

3.2.P.1 Description and Composition of the Drug Product

A description of the drug product and its composition should be provided. List of all components of the dosage form, and their amount on a per-unit basis (including overages, if any) the function of the components, and a reference to their quality standards (e.g. compendia monographs or manufacturer’s specifications)

<table>
<thead>
<tr>
<th>NAMES OF INGREDIENTS</th>
<th>UNIT FORMULA</th>
<th>Percentage formula</th>
<th>FUNCTION</th>
<th>REFERENCE TO STANDARDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ACTIVE SUBSTANCE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 EXCIPIENTS (Inactive)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: The composition formula has to carry a number and to be dated

3.2.P.2 Pharmaceutical Development(name of the finished product, dosage form)

This section should contain information on the development studies conducted to establish the dosage form, the formulation, manufacturing process, container closure system, microbiological attribute, usage instructions.

3.2.P.2.1 Components of the Drug Product (name of the finished product, dosage form)

3.2.P.2.1.1 Drug Substance (name of the finished product, dosage form)

The compatibility of the drug substance with Excipients should be justified. Physicochemical characteristics for Drug Substance that can influence the performance of the drug product should be discussed (e.g., water content, solubility, particle size distribution or polymorphic form).

3.2.P.2.1.2 Excipients (name of the finished product, dosage form)

The functions of Excipients, their concentration and their characteristics that can influence the drug product performance should be discussed for each Excipient.
3.2.P.2.2 Drug Product (name of the finished product, dosage form):

3.2.P.2.2.1 Formulation Development (name of the finished product, dosage form)
A brief summary describing the development of the drug product, including pre formulation studies or justification if not needed.

3.2.P.2.2.2 Overages (name of the finished product, dosage form)
Any overages in the formulation should be justified.

3.2.P.2.2.3 Physicochemical and Biological Properties (name of the finished product, dosage form)
Parameters relevant to the performance of the drug product, such as pH, ionic strength, dissolution, redispersion, reconstitution, particle size distribution, aggregation, polymorphism, rheological properties, biological activity or potency, and/or immunological activity, to be addressed if needed.

3.2.P.2.3 Manufacturing Process Development (name of the finished product, dosage form)
- Specify the critical steps of Manufacturing
- Any differences between pivotal clinical batches and the production batches should be mentioned with its justification (ex: scaling up from pilot to production).

3.2.P.2.4 Container Closure System (name of the finished product, dosage form)
The suitability of the container closure system (described in 3.2.P.7) used for the storage, transportation (shipping) and use of the drug product should be discussed. e.g., choice of materials, protection from moisture and light, compatibility of the materials of construction with the dosage form (including sorption to container and leaching) safety of materials of construction, and performance (such as reproducibility of the dose delivery from the device when presented as part of the drug product).

3.2.P.2.5 Microbiological Attributes (name of the finished product, dosage form)
Where appropriate, the microbiological attributes of the dosage form should be discussed, including, for example, the rationale for not performing microbial limits testing for non sterile products and the
selection and effectiveness of preservative systems in products containing antimicrobial preservatives.
For sterile products, the integrity of the container closure system to prevent microbial contamination should be addressed.

3.2.P.2.6 Compatibility (name of the finished product, dosage form)

The compatibility of the drug product with:
- The reconstitution diluent(s) or
- Dosage devices (e.g., precipitation of drug substance in solution, sorption on injection vessels, stability)

3.2.P.3 Manufacture (name of the finished product, dosage form)

3.2.P.3.1 Manufacturer(s) (name of the finished product, dosage form)
The name, address, and responsibility of finished product manufacturer, including contractors, and each proposed production site or facility involved in manufacturing and testing should be provided.

3.2.P.3.2 Batch Formula (name of the finished product, dosage form)
A batch formula should be provided that includes a list of all components of the dosage form to be used in the manufacturing process and their amounts on a per batch basis.

3.2.P.3.3 Description of Manufacturing Process and Process Controls (name, dosage form)
A flow diagram should be presented giving the steps of the process and showing where materials enter the process.
The critical steps and points at which process controls, intermediate tests or final product controls are conducted should be identified.
A narrative description of the manufacturing process, including packaging, that represents the sequence of steps undertaken and the scale of production should also be provided.
Equipment should, at least, be identified by type (e.g., tumble blender, in-line homogenizer) and working capacity, where relevant. Steps in the process should have the appropriate process parameters identified, such as time, temperature, or pH. Associated numeric values can be presented as an expected range. Numeric ranges for critical steps should be justified in Section 3.2.P.3.4. In certain cases,
environmental conditions (e.g., low humidity for an effervescent product) should be stated.

3.2.P.3.4 Controls of Critical Steps and Intermediates (name of the finished product, dosage form)
Critical Steps: Tests and acceptance criteria should be provided (with justification, including experimental data) performed at the critical steps identified in 3.2.P.3.3 of the manufacturing process, to ensure that the process is controlled.
Intermediates: Information on the quality and control of intermediates isolated during the process should be provided.

3.2.P.3.5 Process Validation and/or Evaluation (name of the finished product, dosage form).
Process validation protocol (should outline the formal studies planned for the production scale batches) or / and Process Validation Report should be provided. (Which include Description, documentation, and results of the validation studies for critical steps or critical assays used in the manufacturing process).
Validation of the sterilization process or aseptic processing or filling should be provided.

3.2.P.4 Control of Excipients (name of the finished product, dosage form)
3.2.P.4.1 Specifications (name of the finished product, dosage form)
The specifications for excipients should be provided.
(if compendial provide the monographs).

3.2.P.4.2 Analytical Procedures (name of the finished product, dosage form)
The analytical procedures used for testing the excipients should be provided (if compendial provide the monographs).
Also provide Certificate of Analysis of each excipient.
3.2.P.4.3 Validation of Analytical Procedures (name of the finished product, dosage form)
For Pharmacopoeial Excipients (Not Applicable).
For non-compendial excipients, Analytical validation information, including experimental data, for the analytical procedures used for testing the excipients should be provided, where appropriate.
3.2.P.4.4 Justification of Specifications (name of the finished product, dosage form)
For Pharmacopoeial Excipients (Not Applicable).
For non-compendial excipients, Justification for the proposed excipient specifications should be provided, where appropriate.

3.2.P.4.5 Excipients of Human or Animal Origin (name of the finished product, dosage form)
For excipients of human or animal origin, EDQM certificate of TSE/BSE free certificates or certificate from health authorities should be provided.

3.2.P.4.6 Novel Excipients (name of the finished product, dosage form)
If included in the drug formula (full details if used for the first time in a drug product.)

3.2.P.5 Control of Drug Product (name of the finished product, dosage form)
3.2.P.5.1 Specification(s) (name of the finished product, dosage form)

The specification for the drug product should be provided and to carry a number and to be dated.

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>SPECIFICATIONS</th>
<th>METHOD &amp; REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.2.P.5.2 Analytical Procedures (name of the finished product, dosage form)
The analytical procedures (Method of Analysis) used for testing the drug product should be provided.

3.2.P.5.3 Validation of Analytical Procedures (name of the finished product, dosage form)
-Validation of method of analysis, including experimental data, for the analytical procedures used for testing the drug product, should be provided (Assay, impurities, dissolution..) with related chromatograms

Note: if the analytical procedures used in the control of the drug product are Pharmacopoeial then verification is required which include:
- System suitability (tailing factor, resolution, stability of solution, theoretical plates,..).
- Linearity & Accuracy
3.2.P.5.4 Batch Analysis (name of the finished product, dosage form)

1- Description of batches analysis in a tabular form, including the following:
   - Drug Name & Concentration (Trade Name and Generic Name)
   - Batch no., batch type, batch size
   - Manufacturing and Expiration Dates
   - Package Type
   - Storage Conditions

2- Batch analysis Result:

<table>
<thead>
<tr>
<th>Test Parameters</th>
<th>BATCH NO.</th>
<th>BATCH NO.</th>
<th>BATCH NO.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptance criteria</td>
<td>Results</td>
<td>Results</td>
<td>Results</td>
</tr>
</tbody>
</table>

Note:

a) A copy of the original analysis certificates for all these batches to be included.

b) Use the same batches that you used in the stability study (section 3.2.S.8)

3.2.P.5.5 Characterization of Impurities (name of the finished product, dosage form)

Information on the characterization of impurities should be provided, it could be referred to Module 3, Drug substance section "3.2.S.3.2 Impurities".

3.2.P.5.6 Justification of Specification(s) (name of the finished product, dosage form)

Justification for the proposed drug product specification should be provided (if not compendial).

3.2.P.6 Reference Standards or Materials (name of the finished product, dosage form)

Refer to Module 3, section "3.2.S.5 Reference Standards or Materials".

3.2.P.7 Container Closure System (name of the finished product, dosage form)

A description of the container closure systems should be provided (and critical dimensions, with drawings where appropriate), along with specification and Method of Analysis (Where appropriate).

For non-functional secondary packaging components (e.g., those that neither provide additional protection nor serve to deliver the product), only a brief description should be provided.

For functional secondary packaging components, additional information should be provided.
3.2.P.8 Stability (name of the finished product, dosage form)

3.2.P.8.1 Stability Summary and Conclusion (name of the finished product, dosage form)
The types of studies conducted (Accelerated, Long term…), protocols used, and the results of the studies should be summarized. The summary should include conclusions with respect to storage conditions, primary packaging material and shelf-life that will be applied on the product intended to be marketed in Jordan. And, if applicable, in-use storage conditions and shelf life. Provide Special stability tests for different dosage forms (e.g. inverted stability study, ….) if applicable.
Summarize Forced degradation studies and stress condition (i.e. Photo stability studies) if applicable.

3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment (name of the finished product, dosage form)
The post-approval stability protocol and stability commitment should be provided:
1- To Complete Real Stability Data (to cover shelf life) on pilot batches (if not completed at time of submission) and Real Stability Data on production batches (if not submitted with file) once they are available as annual report.
2- Ongoing stability (Real data as annual report) for the goods from the market.

3.2.P.8.3 Stability Data (name of the finished product, dosage form)

I- Accelerated stability studies for the finished product at its marketing package at 40°C ± 2 °C and 75% ± 5% Humidity or alternative storage condition suitable for the nature of the product for duration of six months for three pilot or production batches manufactured at the same manufacturing site plant, these stability studies will decide the shelf life also you must provide results statistical analysis for the stability.

II- Real stability studies at (30°C ± 2 °C and RH 65%± 5%) as storage conditions for the whole shelf life….Jordan climate zone is considered as ( zone III) according to ICH guidelines.
NOTES:

1- In case that you don’t have complete real stability for the whole shelf life, in this case you can submit the results that you have (at least for one year) plus declaration letter to commit that you will submit the complete results upon it finish.

2- Jordan according to the ICH Guidelines is considered as climate zone III, this mean that the storage condition for Jordan will be as store below 30ºC.

3- It is favorable that the accelerated and long-term stabilities to be on the same batches if possible.

III – Description of the used stability batches (Batch size, Batch type, Batch No, Manufacturing date, Exp date, package type and the storage conditions).

IV- Batch analysis for all the Batches used in the A/M stability studies… Evaluation of the result of the a/m stability studies…Scientific justification if its required, plus original copy of analysis for certificate for the batches used in the stability.

IV- Clear and addressed chromatograms for the stability study for both (Real and accelerated stability).

Kindly note the following about the chromatograms:

1. Clearly labeled chromatograms during the period of the stability study should be presented.
2. Chromatograms that indicate the blank, the standard and the standards of related substances (if applicable) must be presented which should be clearly labeled.
3. Internal standards used in HPLC analysis should be stated and the relative retention times (retention time of the compound / retention time of the internal standard) should be reported.
4. All the peaks on the chromatograms should be labeled clearly (including the solvent peak) or listed in clearly in a form of a table.
Note: 1. For accelerated stability the chromatograms interval must be for zero time and six months time.

2. For real stability the chromatograms interval must be for zero time, 12 months time, 18 months time & 24 months time in case the product has 24 months as shelf life, and for zero time, 12 months time, 18 months time, 24 months time & 36 months …, in case the product has 36 months or more as shelf life.

Important Note:
Technical part must be in the manufacturer formal official paper and to be sealed by company seal and signed on each page from the technical director and must be in English, and must be provided as hard and soft (CD) Copies.
FORTH : Module 4 → Nonclinical Study Reports

A. For Generic Product:

Module 4 (Not applicable)

B. For Originator Product:

4.1 TABLE OF CONTENTS
A Table of Contents should be provided that lists all of the Nonclinical Study Reports and gives the location of each study report in the Common Technical Document.

4.2 STUDY REPORTS
The study reports should be presented in the following order
4.2.1 Pharmacology
4.2.2 Pharmacokinetics
4.2.3 Toxicology

4.3 LITERATURE REFERENCES
FIFTH: Module 5 → Clinical Study Reports as Hard copy & Electronic copy

A. For Generic Product:
(As solid dosage form like tablet, capsule, susp……..) you must submit:
   1- Bioequivalence Study
   2- Comparative dissolution study.
   3- In some cases JFDA asked for Pharmacodynamics End Point Study to improve Safety & Efficacy….this maybe requested when we submit the registration dossier to JFDA.

• Comparative Dissolution Study: for the low concentration (in case that you want to register high & low concentration) and the dissolution study must be as:
  i. Your product (low concentration) compared with your product (high concentration).
  ii. Your product (low concentration) compared with the originator (low concentration).

The both studies should be performed on 12 tabs. At 0,5,10,15,20,30,45 and 60 minutes, in three different acidic media that are 0.1 N HCl, pH 4.5, pH 6.8. We need you to calculate the mean and the relative standard deviation (RSD). RSD should not exceed 20% at the first point, while after that it shouldn’t exceed 10%. We need the similarity factor ($F_2$) value to be calculates as well.

Note:
For class I highly permeable product: that didn’t need BE study, JFDA NEEDS;
I- Comparative dissolution on 12 tablets, mean & relative standard deviation in Three Medias (0.1 N HCl, pH 4.5 & pH 6.8). Two speeds 50 & 75 rpm. Analytical method & its validation, ($F_2$) value unless release is more than 85% after 15 min.
Submit scientific documents as supportive data.
II- Pharmacodynamics End Point Study to improve Safety & Efficacy.

Module 5 should be submitted first & then after approval of the Bioequivalence studies all the modules 1,2,3 should be submitted & a copy of JFDA committee approval of the B.E or the Comparative Dissolution Profile should be provided in the file.

4- Incase the bioequivalence study not requested, you must submit the Following reports:
3.1 Reports of Human Pharmacokinetic (PK) Studies including:
   3.1.1 Healthy Subject PK and Initial Tolerability Study Reports
   3.1.2 Patient PK and Initial Tolerability Study Reports
   3.1.3 Intrinsic Factor PK Study Reports
   3.1.4 Extrinsic Factor PK Study Reports
3.1.5 Population PK Study Reports

3.2 Reports of Human Pharmacodynamic (PD) Studies including:
   3.2.1 Healthy Subject PD and PK/PD Study Reports
   3.2.2 Patient PD and PK/PD Study Reports

B. For Originator Product:

1. Bioavailability (BA) Study Reports
2. Clinical Study Report
3. Published scientific study in international medical Journals.
4. Periodic Safety Updated Report
5. Cost effectiveness Study
**Important Notes:**
1. Once the above requirements are completed by the manufacture, we will submit the 
documents to Jordan FDA for the registration.

2. All the signs from the manufacturer should be done by the technical director.

3. When there are no Jordan Embassy you can legalized from any Jordan Embassy in 
the nearest country to your country.

4. All the registration requirement should be applied for each item and each dosage 
form.

   e.g.: If you have for one item three dosage forms, so we need the registration 
   requirements for each dosage form alone (one registration documents set for each 
   form)

5. From each product registration documents we want two copies (one original copy as 
hard copy and one copy as soft copy), the hard copy to be in one file and to be arranged 
well with separators and clear indexing.

6. You are kindly requested to send us one draft copy of the registration documents 
before legalization in order to check it (in order to save time and money) and we 
will return it back to you very soon.

7. If the product contains any plasma derivatives, you must submit plasma master file