Form no.1
(9 pages)

Jordan FDA Registration Requirements for Herbal medicine / Drug Product.

1-Herbal medicine/herbal drug JFDA definition as; Every pharmaceutical dosage form contain one medical plant/many medical plants or plant extract/extractions and have medical claims/indications and may be contains vitamins and or minerals.

2-Submit product classification request to the JFDA…the classification request documents as;

I- Product composition certificate containing the active and inactive substances and its concentration & activity function…this certificate must be in English and to be printed in the manufacturer company official paper then sign and sealed by the company seal and must carry revision number & date.

II- 3 pcs of the product packaging material such as (outer box, label , insert) in English ...incase that you don't have English packaging material then English color art work packaging material is accepted.

III- Finished product specification and analysis certificate in English.

IV- 5 pcs of the original product good in English packaging material …you can apply item no; III.

Note;

The classification fee is 36 US and it takes (2-4 weeks.)

3- The manufacturer should fill the attached form *(product registration form).*

This form should be sealed by company seal and signed from the manufacturer only, by Technical Director on each page.

4-- The manufacturer should provide the *CPP Certificate* (duly legalize) according to WHO forms.

<u>The CPP Certificate must contain the following:</u>

- Trade name of the product
- Registration number & date at the health authority or the Competent authority in the country of origin.
- Active ingredients & in active substances and its concentration.
- You must say clearly that the product is currently sold in your country, its not enough to say that it's authorized to sell.
- Name, address of marketing authorization holder and names, addresses of all of manufacturing sites and its activities.

5- The following documents should be submitted to Jordan FDA for each product:

a- List of the countries names that the product was registered and used, and to mention the registration number and date … if this is applicable.

b- List of countries names that the product is under registration…if this is applicable.

c- List of the countries names that refused the registration of the product and to mention the reason of the refusing … if this is applicable.

d- If items no. (a, b & c) are not applicable , kindly send a letter addressed to the following address:

Jordan FDA
Drug Directorate
Registration Dept.

To clarify the situation... this letter to be printed in your company official paper and to be signed by the authorized person and sealed by the company seal … this letter doesn't need any legalization.

6-List of substances from human origin or animal origin that interred in the product formulation and the origin countries of these substance with the requested related certificates for that…if it is not applicable you must send a letter (from your company) certifying that the product dose not contain any substance from human origin or animal origin. And certificate to prove (BSE) free.

7-The manufacturer shall provide a pricing certificate informing about the price in the country of origin (duly legalized) as follows:

- Trade name
- Generic name
- Dosage form
- Unite 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 or Euro.
- Public price in the country of origin in the local currency and in USD when your local currency is not USD or Euro.
- Pharmacy price in the country of origin in the local currency and in USD when your local currency is not USD or Euro.
- C&F price to Jordan in the USD when your local currency is not USD or Euro.

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 C&F prices 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 Ex. Factory price, the C&F price, the pharmacy price and the public price for this product in the following countries (United Kingdom, France, Spain, Belgium Greece, Holland, Australia, Cyprus Hangria, Ireland, News land, Portugal, Czech, Carotia, Austria and Saudi Arabia) <u>if it is applicable</u> … if not, kindly send us a letter to clarify this matter this certificate dose not need any legalization.

d) In case that your health authority only issuing a pricing certificate contain (Ex. Factory price, pharmacy 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 C&F in USD to Jordan.

8-Declaration letter from the manufacturer company to declare the following information:

<u>a)</u> The name of the manufacturing company and the address of the manufacturing site

<u>b)</u> The name and the address of the marketing authorization holder.

<u>c)</u> The name and the address of the company that will issue the invoice.

<u>d)</u> The Export Center (The name of the city and the name of the Airport or the Seaport.

9-Leaflet in English (in case that the mother language of the country of origin is English) and this leaflet must be legalized from the competent authority, and in case that the mother language of the origin country is not English you will submit the following:

a) The translation copy (English copy) must be legalized from notary public and then from chamber of commerce, foreign affairs ministry and Jordan Embassy.

b) The origin country language leaflet copy must be original copy (not photocopy) and must be legalized from your health or Competent Authority, Chamber of Commerce, Foreign Affairs and Jordan Embassy.

c) In case that your product is generic product Jordan FDA requires original copy of the Leaflet in English for the originator if it is available in your country or for the market leader product in case that the originator is not available in your country.

NOTES;

Your Generic product leaflet that you want to register in Jordan must be same as the originator product leaflet for the following information: (Indication, contraindication, warning, precaution, side effects or adverse effects, dosage and administration.)

10-Good agricultural and collection practices certificate (GACP) duly legalized.

11-Mention each medical plant inter in the product composition with the scientific name as (Genus, species, variety and author) the plant part in Latin (English name & part used of the plant).

12-Analysis certificate to declare that the product is free from the microbial organism that may will be harmful.

13-Analysis certificate to declare that the product is free from heavy minerals such as (Lead, Mercury, Arsenic, Cadmium…etc) and free from insecticide material & irradiation materials and particles.

14-Product Technical part must be as hard copy and sof copy and must contain the following information:

a) Formula certificate (must carry revision number & date) and method of manufacturing
b) Active ingredient specification and method of analysis
c) Inactive ingredient specification and method of analysis
d) Specification of the primary and secondary package and one sample of each (in English language).
e) Finished products method of analysis.
f) Validation of method of analysis.
g) Stability indicating method, degradation profile and the related component chromatograms
h) Certificate of analysis for the raw material of the active and inactive ingredient as follows:
    1- One certificate from the raw material manufacturer
    2- One certificate from the finished product manufacturer

i) Certificate of analysis for the finished product (for the same batch submitted for registration with Jordan FDA)
j) Finished product specification at batch release and shelf life and must carry revision date & number.
k) Stability studies :

I- ***Accelerated stability studies*** for the finished product at its marketing package at 40ºC ± 2 ºC and 75% ± 5% Humidity or alternative storage condition suitable for the nature of the product for duration of six months for **three batches as:**

Two pilot batch (10% of production batch) and **one** batch lab scale … 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.

NOTE.: Six months stability for shelf life as 24 months or more.

II- ***Real stability studies*** at (30ºC ± 2 ºC and RH 65%± 5%) as storage conditions for the whole shelf life.

P.S.:

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 declare that you will submit the complete results upon it finish.**
2- **Jordan according to the ICH Guidelines is consider as climate zone III, this mean that the storage condition for Jordan will be as store below 30ºC.**

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 it's required.

V- Conclusion of the stability studies and to confirm the shelf life, the storage condition and the primary packaging material used for the product during the stability study.

VI- Analytical method validation such as:

- Linearity
- Precision
- Accuracy
- Suitability
- Specificity

NOTE; you must attach the chromatograms of the analysis method for active substance and degraded substances for the whole shelf life.

VII- 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, in case the product has 24 months or more.**

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.

VIII- On going stability. .

NOTE; **Technical part must be in the manufacturer formal paper and to be sealed by company seal and signed on each page from the technical director and must be in English.**

15-Clinical studies as follows:

a) Clinical studies and Published scientific studies in international medical journal.
b) Periodic safety updated report (PSUR).

Periodic safety updated report (PSUR); this PSUR is must to be submitted with the registration documents for each product.
Putting in your consideration that according to ICH guidelines the PSUR must contain the following information:

1. The product trade name, generic name, all of it's strengths and dosage forms, plus the following information's:
   a. The period time that the report covered.
   b. The place and the date of product born.
   c. The name and the address of the manufacturing site plus the name of the agent in Jordan.
   d. The date of the submitting the report to Jordan FDA.
   e. The signature of the qualified pharmacovigilance person (QPP).

2. Product introduction, which include product summary (Name, Composition, dosage form, indication, therapeutic efforts....)

3. World wide marketing authorization status for the product.

4. Update actions that has been taken against the Health authorities or the manufacturer company since the product was registered as first time world wide or in Jordan.
5. Comparison of the new safety information with the reference safety information with the committed to use the originator leaflet information for the generic product leaflet.

6. Patient Exposure for:
   a. Clinical studies.
   b. Market exposure.

7. Individual case safety report (General consideration).

8. Post marketing studied that declare the safety which can be taken from scientific reference or the internet.

9. Any other related efficiency date.

10. over all safety evaluation for the product which contains:
    a. Line listing.
    b. Abuse.
    c. Side effect's regarding children and pregnancies.

11. Internal action plan to face any emergency action regarding the life threatening products.

12. Appendix such as:
    - CCDS
    - CCSI
    - SMPC
    - Leaflet
    - etc.

13. Scientific references.

16-Inside and outside packaging material requested information such as:

A- <u>Outer box carton</u>:

- Product trade name and concentration
- Product active substances and their concentrations.
- Product inactive substances and their concentrations.
- Dosages form and package size.
- Route of Administrations.
- Batch number.
- Manuf. Date.
- Expiration date (month & year).
- Storage conditions (as store below 30ºC)
- Manufacturing name and address (country and city or region)
- Marketing authorization holder name and address (country and city or region) if applicable.

B- <u>Bottle label: the same information of outer carton box</u>.

C- <u>Blister form:</u>

- Product trade name and concentration.
- Product active substance and concentration in case that the product contains one or two active substances.
- Expire date (month & year).
- Batch number.
- Marketing authorization holder name and/or manufacturer name.

D- <u>Leaflet attached with the product (if applicable):</u>

- Product trade name and concentration
- Product active substances and their concentrations.
- Product inactive substances and their concentrations.
- Indications
- Precaution
- Warnings
- Contraindication.
- Special instruction for the used of the product for children, pregnant, lactation, old patients….etc.
- Over dose and how to deal with.
- Route of administration (dose & duration).
- Side effects.
- Dosage form.
- Unite package size
- Marketing Authorization Holder and/or manufacturer name plus the address (country, city or region).
- The last revision date.

17- SMPC certificate and must be legalized.

18-(10) original labels in English

19-(10) original outer boxes (empty) in English

20- (10) Blister and Aluminum sheet (empty) in case of tab and cap form

21- (10) inner leaflet (original copies) in English

22-Raw Material supplier documents (Raw material master file):

a. Declaration letter from your company to determine the name and the address of the raw material manufacturing site (Maximum three manufacturing sites) that supply you with the raw material that you used for your manufacturing process of your finished products. And you must be committed to consider these manufacturing sites of the raw material as your accredited or confirmed suppliers for the raw material that you used.

b. Valid certificate of suitability (COS) for each active raw material (from each manufacturing site) issued by:
European Directorate for quality of medicines certification unite (EDQM) or copy of (COS)... in case the (COS) is not available so you can submit GMP(notarized copy) or GMO copy legalized from the Health or competent Authority in the country of origin of the raw materials manufacturer and must be valid and must be for each raw material manufacturing site.

c. Raw material specification and copy of reference specification in case that it is (USP or BP).

d. Raw material analysis certificate from the raw material manufacturing site and from the finished product-manufacturing site.

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