Regulatory Guideline

Executive Procedures for Regulating Registration/Re-registration Procedures for Herbal Pharmaceutical Products acc. to Decision of Technical Committee for Drug Control at 23/01/2020

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Introduction

All locally manufactured herbal medicinal products, locally manufactured products with a approval from abroad, imported products, and locally manufactured products for export only are subject to registration at the Egyptian Drug Authority (EDA) in accordance with the following procedures.

Scope

Herbal medicinal products are registered at the General Administration for Registration of Herbal Products affiliated with the Central Administration for Pharmaceutical Products (CAPP) at EDA, by using the links designated for this on the website.

Abbreviations

CPP: Certificate of Pharmaceutical Product

Free sale: A certificate for free circulation and selling

Toll: A local product manufactured by another party

F-Toll: A local product manufactured by another party

Under license product: A local product manufactured with license from abroad

EDA: Egyptian Drug Authority

CAPP: Central Administration for Pharmaceutical Products

CAPA: Central Administration for Pharmaceutical Affairs

CAO: Central Administration of Operations

Definitions

1. Herbal medicine: A fully manufactured pharmaceutical product that is administered orally, rectally, inhaled, or for external use. It contains in its active ingredients one or more herbal substances, one or more herbal formulas, or one or more herbal substances in combination with one or more of these herbal formulas. A herbal medicine may contain conventional excipients , in addition to its active ingredients of plant origin. The herbal medicine may also contain in some formulas natural organic or inorganic ingredients of non-plant origin or some vitamins and

minerals as complementary materials that have an auxiliary effect to the active herbal materials according to the indications for use. Herbal teas for medicinal purpose as well can be accepted as herbal medicine.

Herbal medicine may also include products where chemically defined substances are added to their active ingredients, such as synthetic compounds or components isolated from herbal substances like atropine and diosgenin, which are not considered as herbal medicine.

2. Company: A company is the entity requesting product registration and owns all legal rights of the product.

3. Factory: A factory is the entity manufacturing pharmaceutical products and is licensed in accordance with applicable laws, and conforms to the good manufacturing requirements approved by the EDA.

4. CPP and Free Sale certificates: A certificate containing the data of a product for export issued by the competent authority in the exporting country and addressed to the importing country.

5. Reference countries:A list of Countries for which a decision is issued by the Technical Committee for Drug Control .

6. Scientific Committee: A specialized scientific committee for herbal medicines.

Locally manufactured herbal medicinal products include the following:

- A local product:

It is a product owned by a company that owns a factory licensed by the EDA and is manufactured in the same factory.

- A local product manufactured by a third party (Toll)

It is a product owned by a company registered in the EDA's third-party register and is manufactured in a factory licensed by the EDA, with a production line available through a manufacturing contract.

- A local product manufactured by a third party (F-Toll)

It is a product owned by a company that owns a factory licensed by the EDA and is manufactured in third-party factory licensed by the EDA in the Arab Republic of

Egypt, with a production line available through a factory-to-factory manufacturing contract.

- A local product manufactured with a license from abroad (Under license)

It refers to a product that is manufactured in a factory licensed by the EDA with permission from a foreign company that owns the name and composition of the product. The foreign company might be located in one of the reference countries or a non-reference country. The product is traded in a reference country through a contract between the company granted registration and manufacturing rights in the Arab Republic of Egypt and the foreign company abroad.

Locally manufactured products with approval from abroad are required to fulfill the following conditions:

1. The composition of the product submitted for registration must be the same as the composition of the product circulated in the reference country or modified in accordance with the EDA's regulations.

2. The pharmaceutical raw materials included in the formula of the product must be from the same source as the product circulating in the reference country, or the company granted the registration and manufacturing rights with approval in the Arab Republic of Egypt must have an authorization to import from another source with the same specifications as the pharmaceutical raw materials.

3. The product submitted for registration must have the same name as the product traded in the reference country, provided that it does not conflict with the name of another product available in the local market.

4. In case of non reference country, a CPP or a Free Sale certificate from the country of origin or from a reference country should be submitted, provided that all data provided in the CPP by the reference country is adhered to. The certificate must include a statement of composition for the product circulating in the reference country and/or the product packaging, and it must be issued by the competent authority in the reference country, authenticated and certified by the Egyptian embassy or consulate in the reference country, as applicable.

Imported herbal medicinal products include the following:

- Imported product (bulk):

It is a product that is manufactured outside the Arab Republic of Egypt in one of the reference countries or in a non-reference country and is traded in a reference country and is packed and/or packaged in a factory licensed by the EDA.

- Finished imported product:

It is a product that is manufactured, packed and packaged outside the Arab Republic of Egypt and is imported completely manufactured from abroad from one of the reference countries or a non-reference country and is traded in a reference country.

Imported products are required to meet the following conditions:

A. The composition of the product submitted for registration must be the same as the formula circulating in the reference country or be modified in accordance with the EDA's regulations.

B. The product submitted for registration must have the same name as the product traded in the reference country, provided that it does not conflict with the name of another product available in the local market.

C. In case of non reference country , a CPP or a Free Sale certificate from the country of origin or from a reference country should be submitted, provided that all data provided in the CPP by the reference country is adhered to. The certificate must include a statement of composition for the product circulating in the reference country and/or the product packaging, and it must be issued by the competent authority in the reference country, authenticated and certified by the Egyptian embassy or consulate in the reference country, as applicable.

Locally manufactured herbal medicinal products for export only:

It is a product manufactured in an EDA-licensed factory solely for export and owned by a company that owns a factory or by a company listed on the EDA's third-party manufacturing registry.

Registration procedures at the CAPP

First: Registration procedures for a new product

1. Submit an inquiry request to approve the start of registration procedures:

A. The company submits an inquiry request about the product registration to the General Administration for the Registration of Herbal Products. The request will be presented to the Scientific Committee within a maximum of 30 (thirty) working days from the date of receipt of the complete inquiry request. The next similar formulations for which an inquiry request is submitted may be exempted from presentation to the Scientific Committee according to the following:

- The formulation must be similar in terms of active ingredients, concentrations and pharmaceutical form to one of the formulations previously approved by the Scientific Committee.

- The composition, in terms of active ingredients, concentrations, and pharmaceutical form, must be in one of the references mentioned in the registration regulations of herbal medicines, or it must be registered as a medicine in one of the reference countries.

If the studies submitted to the committee need further completions, the company will be given a grace period of 90 (ninety) days from the letter's date of issue, then the provided documents shall be presented to the Scientific Committee for a final decision.

B. If accepted, an approval to initiate the registration procedures valid for two years will be issued within 10 (ten) working days.

C. If rejected, a letter will be issued to the company informing it of the rejection and giving reasons.

2. Starting registration procedures

The company is obligated to submit the following within three months from the date of issuing the approval to initiate the registration procedures for products for local circulation:

A. Documents for checking the product's trade name.

B. Documents for pricing of the product.

3. Completing registration procedures:

The company completes the registration steps according to the following cases:

First: Locally manufactured products, locally manufactured and traded products with approval from abroad, and locally manufactured products for export and tenders:

The company shall:

A. Submit the analysis file for registration at the Central Administration for Pharmaceutical Affairs (CAPA) following the guidelines applied to a test or production batch within the first 18 (eighteen) months from the approval date to initiate the registration procedures.

B. Obtain the conformity analysis result accompanied by a statement of the composition on which the analysis was conducted.

C. Submit an accelerated stability study on its test or production batch for evaluation by the competent department within the first 18 (eighteen) months from the approval date apply final registration hard file.

D. Complete all registration requirements based on the approved composition statement to initiate the registration procedures after obtaining approval for the stability study.

Regarding products containing one of the plants mentioned in the Egyptian Herbal Monograph:

The company shall:

A. Submit an accelerated stability study on research samples for evaluation by the competent department within the first 18 (eighteen) months from the approval date to initiate the registration procedures.

B. Complete all registration requirements based on the approved composition statement to initiate the registration procedures after obtaining approval for the stability study.

C. Submit the analysis file for registration at the CADC, following the guidelines applied to the first production batch after obtaining a registration license. The

analysis results must match the approved specifications in order to approve the release of first production batch.

Note: It is permissible, upon the request of the company wishing to provide a production batch for analysis for registration - before the issuance of the registration license - to produce that batch, specifying the storage conditions, expiration date, and conditions of use, on the company's responsibility. The company commits to execute this production batch if it does not conform, is rejected, or the result of the stability study is changed, which requires a change in storage conditions and expiration date. It is approved to circulate this production batch provided that the registration license and the results of analysis and conformity are obtained from the CADC and that all required conditions and obligations are met. This will be followed up by the Central Administration of Operations (CAO).

Second: Imported products:

During the first 18 (eighteen) months from the approval date to initiate the registration procedures, the company is required to submit the following:

A. A stability study of the product conducted abroad, subjected to evaluation by the competent department to obtain approval for the study. This must be accompanied by a statement of the approved composition.

B. An analysis file for registration with the CAPA, following its regulations for imported products.

Third: Locally manufactured products for export only:

A. The company submits the analysis file for registration with the CAPA in accordance with its regulations for research samples within the first 18 (eighteen) months from the approval date to initiate the registration procedures.

B. The analysis result proving conformity will be issued with a statement on the composition upon which the analysis was conducted.

C. The company submits an accelerated stability study on research samples for evaluation by the competent department within the first 18 (eighteen) months from the approval date to initiate the registration procedures.

D. Completing all registration requirements in accordance with the approved composition statement to initiate the registration procedures on which a stability study was conducted.

Note: The company may submit the required studies on samples from a test or production batch based on a request submitted by the company.

4. Submit the final registration file to obtain a registration license:

A. The company sets a date to submit the final registration file within a maximum of 3 (three) months from the issue date of the conformity analysis result or the decision of the Scientific Committee for Stability, whichever is later.

B. The company submits the final registration file on the specified date. If some documents are required, the company will be given 30 (thirty) days to fulfill them.

5. Presentation to the Technical Committee for Drug Control:

The product shall be presented to the Technical Committee for Drug Control within 10 (ten) working days of fulfilling the final registration file in order to make the final decision.

A. If the Committee approves the registration of the product, the following will be required:

- The competent administration shall issue a registration license for a period of 10 (ten) years, calculated from the date of approval by the Technical Committee for Drug Control.

The following are required for the registration license when applying for re-registration:

1. Provide the analysis result for registration with the CAPA in accordance with its regulations. This will be carried on its first production batch in the case of locally manufactured products, locally manufactured and locally traded products with approval from abroad, and products manufactured for export and tenders with regard to products containing one of the plants mentioned in the Egyptian Herbal Monograph. It is a prerequisite for obtaining release that the analysis results match the approved specifications.

2. Submit a long-term stability study for locally manufactured products, locally manufactured and locally traded products with approval from abroad, and products manufactured for export and tenders.

3. Submit the pharmacovigilance report in accordance with applicable regulations.

B. If the committee refuses to register the product, the company will be notified by a letter explaining the reasons for the rejection.

Second: Re-registration procedures

1) For the pharmaceutical products registered at CAPP and whose registration license is still valid at the time of issuing the decision and the requirements for registering herbal medicinal products apply to them, the following are required:

A. The products shall be re-registered as herbal medicinal products based on an application submitted by the product owner, including the documents required for the re-registration file, during the last year of the license's validity.

B. The request should be submitted to the Scientific Committee within a maximum of 30 (thirty) working days from the completion of the re-registration request. The formulations for which a re-registration request has been submitted may be exempted from presentation to the Scientific Committee, as previously mentioned regarding new products.

C. If accepted, an approval will be issued for the product to initiate the re-registration procedures as a herbal medicine, valid for 3 (three) years from approval to set a date for submitting the final re-registration file after completing the rest of the documents on the date specified for review.

- If some documents are required, the company will be given 30 (thirty) days to submit them and complete the re-registration file.

D. The product should be presented to the Technical Committee for Drug Control within 10 (ten) working days from the date of completing the registration file in order to take the final decision regarding re-registering the product.

- If the committee approves the re-registration of the product, the following will be required:

1. A new registration license with a new registration number will be issued for the product as herbal medicine for a period of 10 (ten) years, calculated from the expiration date of the previous registration license.

2. The re-registration license requires the completion of the pharmacovigilance assessment report in accordance with the regulations followed in this regard (if it has not been submitted earlier), provided that it is submitted when applying for re-registration.

- If the Technical Committee refuses to re-register the product, the company will be notified via a letter explaining the reasons for the rejection.

In cases where applicable registration licenses issued by CAPP fall under the classification of herbal medicinal products according to the prevailing regulations, companies have the option to request the conversion of the registration license to that of a herbal medicinal product.

2. Pharmaceutical products registered as herbal medicinal products:

A. Re-registration shall be done based on a request submitted by the company, including the documents required for the re-registration file, during the last year of the license's validity.

- If completions are required, the company will be given 30 (thirty) days to submit them and complete the re-registration file, and the products will be evaluated in accordance with the decisions valid on the date thereof.

B. The product is presented to the Technical Committee for Drug Control within a maximum of 10 (ten) working days from the date of completing the re-registration request in order to make the final decision regarding the product re-registration.

- If the committee approves the re-registration of the product, a re-registration license with the same previous registration number will be issued and will be valid for 10 (ten) years, calculated from the expiration date of the previous registration license.

- If the committee refuses to re-register the product, the company will be notified of this via a letter explaining the reasons for the rejection.

Third: Regarding pharmaceutical products submitted for registration or re-registration as herbal medicine at CAPP before the commencement of this decision and when the registration requirements are applicable

For new products:

1. For products with valid approvals: Companies must submit an inquiry request about the classification of the product. If the product is approved as a herbal medicinal product, it will be given a deadline ending on December 31st, 2023 in order to complete the registration procedures as herbal medicinal product in accordance with the abovementioned. The registration procedures and the studies conducted by the company are taken into account.

2. For products with expired approval of initiating the registration procedures without applying to complete the registration procedures: The approval of initiating the registration procedures will be invalid and a registration request must be submitted again. If the procedures are about to be completed, the company may submit a request to extend the deadline of the approval. These products will be given a deadline ending on December 31st, 2023 in order to complete the registration procedures as herbal medicinal product in accordance with the abovementioned. The registration procedures and the studies conducted by the company will be taken into account.

For re-registration of products with valid approvals without submitting a final registration file:

3. As for the products that obtained the CAPP approval to initiate the re-registration procedures before the implementation of this decision, while being subjected to the conditions required for registering herbal medicines: The company shall complete the registration procedures, and the product shall be evaluated as herbal medicine after submitting the final registration file. During this period, the company may submit an inquiry request to have the product evaluated in order to obtain a three-year approval, starting from the committee approval date, to complete the re-registration procedures and set a date for submitting the final re-registration file.

4. As for the products that obtained approval to initiate the re-registration procedures as herbal medicines before the implementation of this decision: The company shall comply with the validity period of the re-registration approval determined at the time of approval (three years from the approval date) to complete the re-registration procedures and set a date for submitting the final re-registration file.

The rest of the procedures must be completed as previously mentioned in Clause 2.

1. As for the products whose approval of initiating the registration procedures has expired: The company must comply with the decisions of the Technical Committee for Drug Control regarding the re-registration procedures.

Fourth: Names and cards

Names

A list of 20 trade names should be submitted and assessed and reviewed based on the database in terms of pronunciation and spelling in both Arabic and English. The overall structure, pronunciation, and rhyme should be distinct from names already registered with the EDA. However, the scientific name of the active ingredient can be used in a product, followed by the company name if used independently.

For imported products, the name should be verified based on the data provided in the CPP certificate. If there is any conflict with names of other products listed in the EDA database, it must be referred to the Technical Committee for Drug Control for further evaluation.

Cards

All data should be written in Arabic and English on the outer and inner cover of the package. This includes trade name, active ingredients, pharmaceutical form, number of units composing the package, storage conditions, company name, factory, address, telephone number, company logo, registration number with EDA, batch number, manufacturing date, expiry date, and the price on the outer box. Graphics on the box are allowed. It is enough to write the product name, the pharmaceutical form, and the company name or logo if the inner cover is made of aluminium.

As for finished imported products, the packaging should be checked according to the data provided in the CPP, with pledges to add the importer's name, address and telephone number in Arabic, the price and registration number with the EDA, in addition to batch number, manufacturing date, and expiry date.

Fifth: Pricing

Pricing is determined based on the price proposed by the company, which submits a request to have the product priced after receiving approval to initiate the registration procedures as a herbal medicinal product from the competent administration. The pricing request includes the selling price to the public, with the determination of the pharmacist's profit and the distributor's profit in accordance with applicable laws and decisions.

Sixth: Petitions

The company has the right to appeal the final decision issued by the Technical Committee for Drug Control within 60 (sixty) days from the decision's issue date. The appeal should be accompanied by a reasoned request supported by the documents and information that the company wishes to rely on during the review. The appeal is presented to the Technical Committee, which will make the appropriate decision after considering the grievance.

Seventh: Extending deadlines

If the company fails to adhere to the specified procedures or deadlines outlined in this executive decision, the deadline may be extended for similar periods upon payment of the prescribed fees. Otherwise, the registration application will be considered invalid. Failure to comply with the re-registration of products will lead to the issue being referred to the Technical Committee for Drug Control for a decision.

Eighth: Fast-Track Registration

Companies may apply to register products with the Fast-Track Registration system in accordance with the announced mechanisms.

Ninth: Study of stability for re-registration

*** Products are exempted from submitting a stability study for re-registration if the product:**

- Was re-registered at least once and obtained a stability study evaluation report for re-registration.

- Fulfilled all data necessary for a previously issued stability approval to complete the re-registration file.

*** In case that the company has not completed the stability study for re-registration:**

A re-registration license may be issued based on a request submitted by the company, on the condition that a stability study for re-registration should be submitted for evaluation by the specialized scientific committee to assess the stability study within a maximum period of 3 (three) years from the license issue date. Otherwise, production will be held until the evaluation of the stability study is complete so that the company can re-register the product.

Tenth: Variation

Variation rules and standards apply to registered pharmaceutical products.

Eleventh: Modifying the composition statement

1. Any modification in the active ingredients, whether quantitatively or qualitatively, will be subject to all registration procedures as a new herbal medicine. The exception to this is that the modification is based on the decisions of the specialized committees or the decisions of the Technical Committee for Drug Control. If additional studies or requests are required, the company will be given a period of time to complete them.

2. If modifications involve inactive ingredients, the rules and standards governing variations will be applied to registered pharmaceutical products regarding obligations and deadlines for completion.

*** A re-registration license is issued in accordance with the rules and procedures stated in the statement of the approved composition if it has completed all studies and there is no decision from the Technical Committee for Drug Control to cancel one of the substances and not to produce it.**

- There should be a pledge to complete all studies on the new composition statement after issuing the license according to the prescribed deadlines.

Twelfth: Intellectual property

The company shall comply with the provisions of the Intellectual Property Protection Law promulgated by Law No. 82 of 2002 and its executive regulations, with no liability on the part of EDA.

Thirteenth: Adverse effects

The company shall inform the Central Administration of Pharmaceutical Care of any serious adverse effects detected on the product within 15 (fifteen) days. It shall also submit the Periodic Safety Update Report as approved by the Egyptian Pharmacovigilance Centre.

Appendixes

The following is a table of fees for one-time extension services in accordance with Clause 7 and based on the approval of the EDA Chairman.

Deadline to be extended	**Deadline granted in the procedures that will be extended for a similar period from the expiry date of the previous deadline**	**Fees for extending deadlines**
Scientific Committee requests the company to complete the studies submitted	Company is granted 90 (ninety) days as grace period from the notice letter's issue date	EGP 1,000
For a product submitted for local circulation, submit a review of the name and pricing	Within three months from the issue date of the approval to initiate the registration procedures	EGP 1,000
Company completes the registration procedures by submitting an analysis and a stability study	Within 18 (eighteen) months from the issue date of approval to initiate the registration procedures	EGP 5,000
Request to schedule an appointment to submit the final registration file	Within a maximum of three months from the issue date of the conformity analysis result, issuance of approval for the stability study, or issuance of the pricing notice - whichever is later	EGP 2,000
Apply for re-registration as herbal pharmaceutical product based on a request submitted by the product owner	During the last year of the license's validity	EGP 3,000

Approval to initiate re-registration procedures as a herbal medicine	Valid for three years	EGP 3,000
Company may appeal the decision issued by the Scientific Committee or the final decision issued by the Technical Committee for Drug Control	This must be done within 60 (sixty) days from the decision's issue date	EGP 1,000
For pharmaceutical products submitted for registration at the CAPP before putting this decision into effect, and requirements for registering them as herbal medicines are applicable	Deadline ends on December 31st, 2023 to complete registration procedures as herbal medicines	EGP 5,000