Arab Republic of Egypt

Ministry of Health and Population
The Minister

Rules and Procedures Attached to the Decree of the Minister of Health No. (425) of 2015

Article (1): For the purposes of implementing the provisions of this decree, the following terms shall have the meanings set out for each term hereunder:

- **Locally-Manufactured Pharmaceutical Products**: They are the pharmaceutical products that are manufactured in factories within the Arab Republic of Egypt.
- **Imported Pharmaceutical Products**: They are pharmaceutical products that are imported from abroad as finished products or those products which are manufactured abroad but packed and packaged in factories within the country.
- **The Company**: It is the applicant company requesting the registration of the product.
- **Site Master File**: It is the Factory Inspection file.
- **Pilot Batch**: It is the experimental batch.
- **R&D**: It is the batch of research and development
- **GSP**: It refers to Good Storage Practices.
- **GDP**: It refers to Good Distribution Practice.
- **Fast Track**: It is the Fast Track System of registration.
- **CPP**: It refers to Certificate of Pharmaceutical Product.

Article (2): The number of similars within each box consisting of a set of pharmaceutical dosage forms, including the innovator product of the active ingredient shall be determined as indicated in the Appendix No. (1). In the event of the emergence of new pharmaceutical dosage forms, the Appendix No. (2) shall be modified after being presented to the Technical Committee for Drug Control.

Article (3): The registration applicant shall be obligated to submit an inquiry request about the product submitted for local marketing in accordance with the Appendix No. (3) to the Human Pharmaceuticals Registration administration. This inquiry request shall be registered duly and completely in accordance with the date and time of its submission during the official working days and times. The applicant shall be notified of the status of the product whether it is accepted or rejected within twenty-one working days from the date of receiving the complete request, provided that the approval of the inquiry request of the local products that have a place in the box shall be issued within ten working days from the date when the applicant was notified of the status of the product. For products that are imported as finished products from abroad, those products which are manufactured abroad but packed or packaged locally, or those products that are locally manufactured with a license and which have a place in the box, the required documents in the Appendix No. (4) must be entirely submitted within a maximum of 60 working days, otherwise the registration request shall be canceled.

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The approval of the inquiry request shall be issued within ten working days from the date of fulfilling all the requirements, except in the cases to which the provision of Article (4), clause (B) applies. The company shall be obligated to pay the consideration of the product registration before heading for receiving the approval of the inquiry request.

In the event that there is no available place for the product in the box, the inquiry request shall be registered in the waiting record in accordance with the date and time of its submission until the product has an available place or in case any product of the registered or under-registration products is canceled for whatever reason removed from the box.

Multivitamin, minerals and amino acid products as well as distilled water and water for injection shall not be included in the boxes.

Article (4): (A) To issue a marketing authorization license for the of imported products, the product shall be marketed in the country of origin or any of the reference countries approved by the Minister Assistant for Pharmaceutical Affairs or authorized by the World Health Organization (WHO-Prequalified) for at least one year, provided that the registration applicant shall be permitted to submit the inquiry request within this period.

(B) For the products submitted for registration which are imported from non-reference countries and which are not marketed in any of the reference countries or not authorized by the World Health Organization, in the event that they have an available place in the box, the product shall be presented to the Technical Committee for Drug Control to take a decision either to reject or to refer to the specialized scientific committees and/or to demand that the Site Master File shall be submitted to the General Administration of Inspection.

The company shall be obligated to submit the required documents within a maximum of thirty working days from the date of notifying the company, otherwise the registration request shall be canceled.

The Technical Committee for Drug Control has the right to demand that a factory abroad be inspected. After the Technical Committee for Drug Control consent to proceed with the product registration procedures, the approval of the inquiry request shall be issued.

Article (5): If the product does not have a scientific reference, it shall be referred to the scientific committees, provided that the company shall be obligated to submit the scientific files of the product to the scientific committees within thirty working days from the date of issuing the approval of the inquiry request, otherwise, the registration request shall be canceled. The scientific files of the product shall be presented to the scientific committees within sixty working days from the date of receiving the complete scientific file. In the case of an approval on a scientific basis, the applicant shall be notified to fulfill

the procedures of registering the product. In the case that the studies submitted by the company are required to be fulfilled, the company shall be granted another grace period of thirty working days and the scientific files of the product shall be re-presented to the scientific committees within thirty working days. In the case of a non-approval on a scientific basis, the General Administration of Registration shall present the matter to the Technical Committee for Drug Control to take the decision that it deems appropriate and to state the reasons in the case of rejecting the registration request.

Article (6): For the products submitted for local marketing, the company shall be obligated to submit the following:

(a) A list contains twenty-five proposed trade names for the product within a maximum of fifteen working days from the date of issuing the approval of the inquiry request or from the date of issuing the approval of the Scientific Committee as specified in Article (5), otherwise the registration request shall be canceled. The Naming and Labelling Department shall examine the list of trade names submitted by the company within fifteen working days from the date of receiving the tradenames list from the company. Then, a letter shall be issued to the company stating the approval of the product name or the rejection of the first list of names previously submitted. In the case of rejection, the company shall be obligated to submit another list within ten working days from the date of issuing the rejection letter, otherwise the registration request shall be canceled. The company shall be permitted to submit a maximum of four lists of the proposed names, including the first list of names. In the case of rejecting the four lists submitted by the company, an approval of the scientific name alongside the company name shall be issued in parallel with applying for pricing and for The Egyptian Pharmacovigilance Center.

(b) Documents required for pricing indicated in the Appendix No. (5) for the local products and those indicated in the Appendix No. (6) for the imported products shall be submitted to the Pricing Administration within 30 working days from the date of issuing the approval of the inquiry request or from the date of issuing the approval of the scientific committee as provided for in Article (5), otherwise the registration request shall be canceled. It is imperative that the pricing of the products, whether local or imported, shall be made within a maximum of 60 working days from the date of receiving the complete pricing file.

(c) Documents required by the Egyptian Pharmacovigilance Center indicated in the Appendix No. (7) shall be fully submitted within 30 working days from the date of issuing the approval of the inquiry request or from the date of the Scientific Committee approval as stated in the Article (5), otherwise the registration application shall be canceled.-It is imperative that the documents submitted by the company shall be evaluated within a maximum of 60 working days from the date of receiving the complete pharmacovigilance

documents. In the case of the approval by the Pharmacovigilance Center, the registration applicant shall be notified and the product registration procedures shall be completed. In the case that the company is required to fulfill documents, a grace period of a maximum 15 working days shall be granted to the company. The evaluation by the Center shall be completed within 15 working day of the date of receiving the fulfilled documents. In the event of non-approval or non-fulfillment of the documents, the General Administration of Registration shall be addressed to present the matter to the Technical Committee for Drug Control to take the decision that it deems appropriate and to state the reasons in the case of rejecting the registration request.

Article (7): (A) For locally manufactured products that are locally marketed, the registration procedures shall be completed in accordance with the following steps:

Pilot batch shall be produced in accordance with World Health Organization standards with a minimum of 10% of the production batch size in the presence of an inspector from the General Administration of Inspection, provided that this batch shall NEVER be marketed in the local market. The registration procedures shall be completed in accordance with the composition form on which the production is based in accordance with the following steps:

1- Samples shall be withdrawn by Pharmaceutical Inspection Department from the pilot batch to be analyzed at the National Organization for Drug Control and Research (Registration Division). The registration applicant shall adhere to submitting the analysis file to the aforementioned authority, which file shall contain the documents and attachments required for the analysis file described in the Appendix No. (8). The Authority shall be obligated to issue the analysis result within 60 working day from the date of fulfilling the complete analysis file.

2- The six months' accelerated stability on the pilot batch shall be submitted to be evaluated by the Specialized Scientific Committee of Evaluating Stability Studies, provided that the evaluation shall be within 60 working days from the date of submitting the complete stability study file.

3- In the cases that require conducting a study of bioavailability, bioequivalence, or In-vitro dissolution in accordance with the rules and procedures regulating the conduct of studies of bioavailability, bioequivalence and In-vitro dissolution studies, samples shall be withdrawn by the General Administration for Pharmaceutical Inspection to be sent to centers of bioavailability and bioequivalence that are licensed and approved by the Central Administration for Pharmaceutical Affairs. The study shall be evaluated within 30 working days from the date of submitting the fulfilled study.

(B) For imported products, the registration procedures shall be completed in accordance with the following steps:

1- The analysis file including the documents and attachments required for the analysis file described in the Appendix No. (8) shall be submitted to the National Organization for Drug Control and Research (Registration Division). The results of the analysis shall be issued by the National Organization for Drug Control and Research within 60 working days from the date of fulfilling the complete analysis file.

For the products that have a registration and marketing certificate from one of the reference countries approved by the Technical Committee for Drug Control, the analysis file of the first incoming consignment after the issuance of the final marketing authorization license may be submitted to the National Organization for Drug Control and Research (Registration Division), which file shall include the documents and attachments required for the analysis file described in the Appendix No. (8).

The first incoming consignment shall not be released except after the analysis result is received from the National Organization for Drug Control and Research within 21 working days. Next, the General Administration for Pharmaceutical Inspection shall withdraw random samples from the incoming consignments to be analyzed in accordance with the followed rules.

2- The documents required for the product in accordance with the rules approved by the Stability Department shall be submitted for evaluation within 60 working days from the date of submitting the complete documents.

3- In the cases that require a study of bioavailability, bioequivalence or In-vitro dissolution in accordance with the rules and procedures regulating the conduct of studies of bioavailability, bioequivalence and In-vitro dissolution studies, the study shall be evaluated within 30 working days from the date of submitting the fulfilled study.

(C) For locally manufactured products that are submitted to be marketed for export and tender or for export only, the following steps shall be followed:

An application to start the procedures of the product registration shall be submitted by the company via e-mail in accordance with the Appendix No. (9) to the Administration of Human Drugs Registration, provided that the company shall be notified with the acceptance or rejection within fifteen working days from the date of receiving the complete and correct application. In case of acceptance, the Registration Administration shall issue an approval letter for the application submitted by the company, provided that the company shall adhere to paying the registration consideration before receiving the approval of the application from the Registration Administration. Then the product shall

be presented to the scientific committees as described in Article (5), provided that the procedures of registering the products submitted for export and tender shall be fulfilled in accordance with the following steps: The required documents shall be submitted to the Egyptian Pharmacovigilance Center in accordance with Article (6), clause (C), then the procedures shall be completed as specified in Article (7), item (A).

Procedures of registering products submitted for export only shall be completed in accordance with the following steps: The six months' accelerated stability study or the long-term study on three (R&D) batches shall be submitted by the company to be evaluated by the committee of stability within 60 working days from the date of submitting the complete stability study file. The analysis file shall be submitted to the National Organization for Drug Control and Research (Registration Division) regarding the (R&D) samples, including the documents and attachments required for the analysis file described in the Appendix No. (8). The analysis result shall be issued by the National Organization for Drug Control and Research within 60 working days from the date of fulfilling the complete analysis file. The Products registered for export only shall be exempted from conducting a study on bioavailability, bioequivalence or In-vitro dissolution.

(D) The company shall be obligated to send an email to set a date for submitting the marketing authorization file to the Central Administration for Pharmaceutical Affairs within the following:

- A maximum of twenty-one months as from the date of the issuance of the pricing certificate or the approval of the Egyptian Pharmacovigilance Center for the locally manufactured products that are locally marketed, provided that the documents specified in the Appendix No. (10) shall be included.
- A maximum of six months for imported products as from the date of the issuance of the pricing certificate or the approval of the Egyptian Pharmacovigilance Center, provided that the documents specified in the Appendix No. (11) shall be included.
- A maximum of twelve months for the products submitted for export only as from the date of issuing the request approval by the Registration Administration, provided that the documents specified in the Appendix No. (10) shall be included.
- A maximum of twenty-one months for products submitted for export and tender as from the date of the issuance of the approval of the Egyptian Pharmacovigilance Center, provided that the documents specified in the Appendix No. (10) shall be included.

In the event of non-compliance with the aforementioned deadlines, the registration application shall be cancelled.

The registration applicant shall be notified of the status of the file within 60 working days from the date of receiving the complete marketing authorization file, provided that the

required documents shall be fully submitted within 60 working days from the date of notifying of the registration applicant. This period is renewable only for one time, otherwise the registration request shall be canceled.

The registration request shall be presented to the Technical Committee for Drug Control within 30 working days from the date of fulfilling the complete file by the registration applicant in order to take the appropriate decision whether to register the product or not. In case of the Technical Committee for Drug Control approval, a final marketing authorization license with a ten years validity shall be issued, provided that the company shall be obligated to submit accelerated and long-term stability studies on the first three production batches together for the locally manufactured products that are locally marketed or for the products submitted for export and tender within five years from the date of issuing the final marketing authorization license, otherwise the authorization license shall be canceled. In the case of rejecting the product registration by the Technical Committee for Drug Control, the registration applicant shall be notified by a letter including the decision of the Technical Committee for Drug Control alongside the reasons for rejection.

Article (8): Pharmaceutical products shall be re-registered each ten years upon a request submitted by the product owner to the General Administration for Registration. The request shall include the documents required for the re-registration specified in the Appendix No. (12) as well as the requirements of the Egyptian Pharmacovigilance Center specified in the Appendix No. (13). Re-registration requirements shall be submitted in the last year of the marketing authorization license validity, provided that the company shall fulfill re-registration requirements within a maximum period of two years as from the expiry date of the registration validity. During this period, the product is permitted to be marketed with a temporary license from the General Administration of Registration, otherwise the product registration shall be canceled.

The product shall be referred to the scientific committees as specified in Article (5). In the event of non-approval, the product shall be submitted to the Technical Committee for Drug Control to take the decision that it deems appropriate and to state the reasons in the case of rejecting the re-registration request.

The re-registration procedures shall be completed, the inner leaflets shall be updated and the evaluation of stability study of the product shall be completed within 60 working days from the date of submitting the complete stability study file. The studies of bioavailability, bioequivalence, or in-vitro dissolution shall be evaluated within 30 working days from the date of submitting the fulfilled study in the cases that require conducting these studies in accordance with the rules and procedures regulating conducting the studies of bioavailability, bioequivalence, or in-vitro dissolution, provided that samples shall be

withdrawn by the General Administration for Pharmaceutical Inspection in the event of a request for a bioequivalence study.

Then the re-registration file shall be presented to the Technical Committee for Drug Control within 60 working days from the date of fulfilling the re-registration file. In the case of approval, the registration shall be renewed for another ten years with the same registration number if no variation in the quantity or quality of any of the active ingredients has occurred. However, if a variation in the quantity or quality of any of the active ingredients has been made by the company, all the procedures required for registration shall be conducted as a new product.

In the event that the registration period of the product expires without submitting the re-registration file during the last year of the marketing authorization license validity, the product registration shall be canceled.

Article (9): The owner of the product shall adhere to the following:

1- Making an undertaking specified in the Appendix No. (14) that he shall comply with the provisions of the Intellectual Property Rights Law No. (82) of 2002 and its executive regulations without any responsibility on the the Ministry of Health.

2- Printing the name of the manufacturer, its address, the name of the license holder, the production date, the expiry date, the batch number, the registration number and the price on the outer package and making no changes to the product without obtaining the approval of the Central Administration for Pharmaceutical Affairs.

In the case of imported products, the name of the license holder could be replaced by printing the name of the marketing authorization holder in accordance with the submitted Certificate of Pharmaceutical Product.

3- Notifying the Central Administration for Pharmaceutical Affairs of all the names of his authorized distributers and of any change that may be made to their data and ensuring that his authorized distributers implement Good Storage Practices and Good Distribution Practices and that their follow-up actions are pursued by the General Administration for Pharmaceutical Inspection.

4- Manufacturing the product with the same supplier of the raw materials from which the Pilot Batch was made and on which all the required studies were conducted for the locally manufactured products that are submitted for local marketing or products for export and tender.

5- An undertaking that he may not change the suppliers of the raw materials without the approval of the General Administration of Registration, otherwise the marketing authorization license shall be cancelled.

6- Acknowledging full liability for the storage of the raw materials, all manufacturing phases of the product, the product conformity to the technical specifications and the storage of the product up to its complete distribution. In case of toll manufacturing, the manufacturer is required to be licensed by the Ministry of Health, to conform to all requirements specified in this decree, including abiding by Good Manufacturing Practices and the provisions stipulated in the Ministerial Decree No. (539) of 2007 regarding adopting the Egyptian guideline for good manufacturing practice for pharmaceuticals.

7- An acknowledgment that manufacturing place as well as the product ownership shall not be transferred except after obtaining an approval from the General Administration of Registration, otherwise the marketing authorization license shall be cancelled.

8- For locally manufactured products intended for local marketing, an undertaking shall be made to the effect that the product ownership shall not be transferred except after three years of marketing and after obtaining the approval by the General Administration of Registration, otherwise the marketing authorization license shall be cancelled.

9- A declaration that all data submitted in the analysis file of the product in the National Organization for Drug Control and Research are identical with the data submitted in the marketing authorization file at the General Administration of Registration and that all documents and data are correct and their full responsibility fall on him.

Article (10): The registration applicant may submit a grievance against the final decision issued by the Technical Committee for Drug Control, within 60 working days from the date of issuing the decision, based on a reasoned request submitted to the Committee and supported by the documents and information that s/he desires to draw upon when considering the grievance. The adjudication shall be within 60 working days as from the date of the grievance submission.

Article (11): The marketing authorization license shall be canceled by a decision of the Chairperson of the Central Administration for Pharmaceutical Affairs upon a recommendation of the Technical Committee for Drug Control, specifying the reasons for cancellation in the following cases:

1- If the locally manufactured products intended for local marketing are not produced within eighteen months from the issuance date of the final marketing authorization license as well as if the imported products that obtained a final marketing authorization license in the Egyptian markets are not imported within eighteen months from the issuance date

of the final marketing authorization license, in conformity with the report submitted by the General Administration of Pharmaceutical Inspection. An exception to this grace period shall be made for generic drugs, whose innovator products were granted Egyptian patents, until the expiry of the prescribed patent protection period.

2- If the production of the locally manufactured products intended for local marketing as well as the importation of the imported products ceases to take place on a continuous basis for a period of two years in a row as from the expiry date of the last production batch in accordance with the report submitted by the General Administration of Pharmaceutical Inspection. An exception to this grace period shall be made for generic drugs, whose innovator products were granted Egyptian patents, until the expiry of the prescribed patent protection period.

3- If the company fails to submit accelerated and long-term stability studies for the first three production batches together, for locally manufactured products intended for local marketing or for the products for export or tender within five years as from the issuance date of the final marketing authorization license.

Article (12): In emergency circumstances, a product may be marketed with the exception of some conditions mentioned in this decree based on a recommendation from the Assistant of the Minister of Health for Pharmaceutical Affairs. This recommendation shall be approved by the Minister of Health.

Article (13): It is permissible to register the products in the Fast Track system in accordance with the classification approved by the Technical Committee for Drug Control.

Article (14): In the event of non-compliance with the deadlines specified in this decree, the registration application shall be canceled by Chairperson of the Central Administration for Pharmaceutical Affairs upon a report submitted by the General Administration of Registration after follow-up with the various concerned administrations.