Guideline

Regulatory Guideline of the Registration Procedures of the Innovative Products

2023

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Guideline Contents

1- Introduction:

The Purpose of issuing this regulatory guideline is to define the concept of the innovative products and to stipulate their registration procedures preparatory to their registration in the Arab Republic of Egypt.

2- Scope of Implementation:

This Guideline shall apply to locally manufactured medicinal or biological products that have not previously been registered in the Arab Republic of Egypt or abroad which apply for registration in order to add a new therapeutic advantage.

3- Definitions:

- **Innovative products ([1]):** They are locally manufactured medicinal or biological products that have not been previously registered in the Arab Republic of Egypt or abroad and that apply for registration in order to add a new therapeutic advantage. They may include the following:

- Breakthrough innovation: New molecular entity either single or in combination.

- Incremental innovation: Novel modification that is made to already registered products.

- **Therapeutic advantage** [(2)]: An advantage that is added by the innovative product. It includes any of the following advantages:

  - An innovative product which is more effective.
  - An innovative product which ensures greater safety.
  - An innovative product which has better pharmacokinetics.
  - An innovative product which improves patient's compliance to medication.
  - An innovative product which adds a new therapeutic option.

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[1]- These definitions are subject to continuous updating according to developments in science and international references, provided that a decision to that effect shall be issued by the Head of the Central Administration of Biological and Innovative Products and Clinical Studies.

[2]- The first stage of registration of innovative products includes human pharmaceutical products and biological products. The other pharmaceutical products shall be added at a later phase to be determined.

4- Registration procedures:

Article One

The applicant company requesting registration shall be committed to submit an inquiry request about the innovative product via the e-mail designated for that purpose (innov.reg@edaegypt.gov.eg) to Innovative Products' Registration Administration in the Central Administration of Biological and Innovative Products and Clinical Studies, which request shall be accompanied by the documents indicated in the Appendix No. (1), provided that the company shall be already enrolled in the Egyptian Drug Authority's electronic companies register, taking into account that a maximum of (2) inquiry requests shall be received for each factory and a maximum of (1) inquiry request for each Toll company per month, provided that the maximum number of inquiry requests shall be updated according to the developments.

** In the case that the company is desirous to obtain a protection period for the submitted innovative product (in case of new molecular entity either single or in combination only), it shall first apply to the Egyptian Patent Office for registering its idea and then it shall submit an inquiry request to the Egyptian Drug Authority. The Egyptian Patent Office shall bear the responsibility for whether or not the innovative product can be granted a protection period in accordance with the law regulating intellectual property protection and without any impact on the decision of registering the innovative product by Egyptian Drug Authority.

Article Two

The General Administration of Innovative Products shall review the inquiry request and notify the company of the status of the submitted request in terms of the acceptance or rejection within (30 working days) from the date of receiving the complete request. The company shall be committed to fulfill any required documents within (10 working days) from the date of being notified thereof; otherwise the inquiry request shall be considered null and void. In the case of accepting the inquiry request, the approval for the inquiry request shall be issued indicating the classification of the innovative product, taking into account that the innovative product may be presented to an ad hoc committee for the initial evaluation of the submitted idea.

Article Three

The company shall be committed to submit the scientific file of the innovative product to Innovative Products' Scientific Evaluation Administration of the General Administration of Innovative Products in accordance with Appendix No. (2) within (30 working days) from the date of issuing the approval of the inquiry request.

Article Four

The Scientific Evaluation Administration of the General Administration of Innovative Products shall review the scientific file submitted by the company to ensure its fulfillment to all the requirements, in addition to evaluating the status of the product in accordance with the available information.

** The company shall be committed to fulfill any documents required by the General Administration of Innovative Products within (20 working days) from the date of being notified thereof.

Article Five

The Central Administration for Pharmaceutical Care shall be addressed to prepare a report on the safety of the substance(s) used in the product composition if required. The company shall be also committed to submit the file of the vigilance system status in accordance with the requirements of the General Administration of Pharmacovigilance along with fulfilling any required documents.

Article Six

The product shall be presented to the Innovative Products' Scientific Evaluation Committee within (20 working days) from the date of receiving the Pharmaceutical Vigilance report. The company shall be notified of the committee's decision by a letter issued by the General Administration of Innovative Products within a period not exceeding (5 working days) from the issuance date of the committee's decision. In the case that the committee required that submitted documents shall be fulfilled, the company shall be granted another grace period (30 working days) and the matter shall be re-presented to the Innovative Products' Scientific Evaluation Committee within (30 working days) from the date of fulfilling the requirements.

Article Seven

In the event that Innovative Products' Scientific Evaluation Committee asks the company to submit studies and the company is desirous to price its product before starting these studies, the company has the right to obtain a report prepared by the General Administration of Innovative Products explaining the classification of the innovative product, degree of innovation, its importance and the nature of the required studies, provided that the company shall submit this report within (30 working days) from the issuance date of the letter of the decision of Innovative Products Scientific Evaluation Committee sent to the Pricing Policies Administration of the Central Administration of Drug Policies and Market Support.

** In the event that the product therapeutic advantage intended by the company has not been achieved after finishing the evaluation of the required studies by the Innovative Products' Scientific Evaluation Committee, the product shall be re-presented to the Pricing Policies Administration once again to evaluate the price before issuing the registration license.

Article Eight

In the event that a clinical trial is requested by the Innovative Products' Scientific Evaluation Committee, the following procedures shall be implemented:

- The Central Administration of Operations shall be addressed to ensure that the manufacturing conditions of the innovative product fulfill the basic requirements for conducting the required clinical study.
- The Innovative Products' Scientific Evaluation Committee is entrusted with determining the objective of the study, which includes the recommendations of the committee. Then, Innovative Products' Scientific Evaluation Committee shall transfer the matter to the General Administration of Clinical Studies to conduct the study in accordance with this objective and the recommendations included therein, in a manner that does not contradict the laws and regulations governing the conduct of clinical trials within the Arab Republic of Egypt and the international standards.
- The clinical trial results shall be evaluated by the General Administration of Clinical Studies then the Innovative Products' Scientific Evaluation Committee shall be provided with the results of that evaluation along with the decision of the General Administration of Clinical Studies. After that, the Innovative Products' Scientific Evaluation Committee shall consider

whether or not the product can be registered based on all available scientific evidence, including the results of the clinical study.

Article Nine

In the event that the Innovative Products' Scientific Evaluation Committee rejects the submitted product, the petitions may be received from the company within (60 working days) from the date when the product rejection letter is issued by the committee in the case that the company has new developments that deserve to be re-examined or re-presented to the Innovative Products' Scientific Evaluation Committee, after paying the specified service fees, provided that the petition shall be submitted in the first time to the General Administration of Innovative Products' and in the second and last time to the Head of the Central Administration of Biological and Innovative Products and Clinical Studies.

Article Ten

In the event that the product is finally rejected from a scientific point of view, a decision shall be issued by the Head of the Central Administration of Biological and Innovative Products and Clinical Studies, indicting the rejection reasons.

Article Eleven

In the event that the Innovative Products' Scientific Evaluation Committee approves the product submitted for registration, the company shall, within (30 working days) from the issuance date of the approval letter of the Innovative Products' Scientific Evaluation Committee, submit a list of proposed commercial names for the product to the General Administration of Innovative Products after the company revises the names they proposed on the Egyptian Drug Authority program (EDA naming checker), in order to ensure the initial compatibility of the proposed names with the product names available in the Egyptian Drug Authority database. Then, the General Administration of Innovative Products shall issue to the company a letter of acceptance of the product commercial name, as per the applicable rules.

Article Twelve

If the company has not applied for pricing its product after its product has been presented to the Innovative Products' Scientific Evaluation Committee, the company shall submit a report to the Pricing Policies Administration in the Central Administration of Drug Policies and Market Support. This report, which shall be prepared by the General Administration of Innovative Products, shall indicate the

classification of the innovative product, degree of innovation, its importance and the extent to which the therapeutic advantage is proven. The company, within (30 working days) from the issuance date of the approval letter of the Innovative Products' Scientific Evaluation Committee, shall submit this report to the Pricing Policies Administration, so that the product can be priced.

** If the company is desirous to re-evaluate the price of its product in the case that new data is emerged, the company may apply to review the product price before issuing the registration license.

Article Thirteen

The registration procedures shall be completed within 36 months from the issuance date of the approval letter of the Innovative Products' Scientific Evaluation Committee, in accordance with the following procedures:

- In the case of innovative biological products, inspection shall be conducted of the factory of active ingredients or bulk products in the case that they are imported from one of non-reference countries following the submission of the site master file to the General Administration of Factories Inspection and obtaining the approval of this administration for this site master file. The authorized factories of one of the reference countries, which have the World Health Organization approval or the Good Manufacturing Practices Certificate from FDA or EMA, shall be excluded. The inspection report shall be presented to the Inspection Higher Committee for the approval and the Central Administration of Biological and Innovative Products and Clinical Studies shall be corresponded with to be informed of the committee decision. In the case of innovative medicinal products, the rules and procedures for enrolling the active raw materials of the medicinal products, which are applicable by the Egyptian Drug Authority, may be applied.
- The registration file (Common Technical Document) shall be prepared in accordance with the rules of the International Council for Harmonization. The complete registration file shall be submitted in accordance with Appendix No. (3) to the Innovative Products' Registration Administration within a maximum of 36 months from the issuance date of the approval letter of the Innovative Products' Scientific Evaluation Committee, otherwise the registration request shall be considered null and void. The company shall be notified of the status of the submitted file within (15 working days) from the date of receiving the complete file, in preparation for its evaluation by all concerned departments.

- The Central administration of Operations shall be notified of the number of samples required for analysis by the Central Administration of Biological and Innovative Products and Clinical Studies. The company shall submit the samples from one batch of the finished product within (60 working days) from the issuance date of the letter specifying the number of samples. This period may be renewed for only once.

Article Fourteen

- If the raw material, the bulk material or the solvent are manufactured in more than one manufacturing site and they are assessed within the product technical file during the registration and only one batch of one of these manufacturers is analyzed, it is required in the Marketing Authorization License that analysis shall be conducted for samples from the rest of manufacturers mentioned in the Marketing Authorization License, as per the applicable rules of the Egyptian Drug Authority.
- In case of manufacturing a pilot batch of an innovative product from an imported raw material, the Central Administration of Operations shall control the raw material by monitoring the quantities which are manufactured and shall ensure that they are used for their intended purposes.

Article Fifteen

After submitting the complete registration file to Innovative Products' Registration Administration, the following materials shall be evaluated by the concerned entities, all within its competent jurisdiction:

- The file of laboratory and quality evaluation in order to issue of the technical assessment report and ensure the registration analysis of the product conformity.
- Inspection file by the Administration of Factories Inspection of the Central Administration of Operations.
- Pharmacovigilance files by the General Administration of Pharmacovigilance of the Central Administration of Pharmaceutical Care.
- Stability study of the product.
- Studying the bioequivalence or in-vitro dissolution, as required by the cases.
- In cases that require clinical trials, the clinical trials file shall be evaluated by the General Administration of Clinical Studies.
- The inner and external packaging of the product.

- Documents related to the medical leaflet proposed by the Administration of Leaflets in the Central Administration of Pharmaceutical Care.

The medical leaflet shall be evaluated after receiving the approval for the stability study of the product, the approval for the study of bioequivalence or in-vitro dissolution as required by the cases and the approval of the General Administration of Clinical Studies (if the event that a clinical trial is required).

** In the event that the concerned authorities make any remarks, the company shall address the remarks within (60 working days). This period may be renewed only for once.

Article Sixteen

The General Administration of Innovative Products shall present the registration file of the product to the Technical Committee for Drug Control, in order to take the decision which it deems appropriate regarding the product registration within (20 working days) of receiving each of the following documents:

- The technical assessment report and the registration analysis of the product conformity.
- The approval of the submitted inspection file by the Administration of Factories Inspection of the Central Administration of Operations.
- The approval of the General Administration of Pharmacovigilance of the company's vigilance files in addition to submitting a statement on the status of the current vigilance system of the company owning the product.
- Approval of the stability study of the product.
- Approval of the external and internal labels (indicating the approved commercial name of the product as well as the logo of The General Administration of the Innovative Products).
- Approval of the medical leaflet of the product.
- The final pricing notification.
- The approval of the study of bioequivalence or in-vitro dissolution as required by the cases.
- The approval of the General Administration of Clinical Studies (if a clinical trial is required).

** In the event of the approval by the Technical Committee for Drug Control, a valid five-year registration license shall be issued indicating the type of innovation and therapeutic advantage. In the event of the rejection by the Technical

Committee for Drug Control, the company shall be notified of this decision by a reasoned letter. The company has the right to petition within (60 working days) from the issuance date of the decision to re-presentation only for once after paying an additional service consideration.

Article Seventeen

The company may file a grievance against the final decision issued by the Technical Committee for Drug Control within (60 working days) from the issuing date of the decision. The grievance shall be aired to the Grievance Committee formed in accordance with the Law on Establishing the Egyptian Drug Authority and shall be based on a reasoned request submitted to the committee and supported by the documents and information on which the company desires to rely when considering the grievance.

Article Eighteen

The products obtaining a registration license of an innovative product shall be published on the Egyptian Drug Authority's website within one month as from the license issuance date.

Article Nineteen

The product's owner shall be obligated to submit any variables to the Registration Administration in the General Administration of the Innovative Products to be evaluated after paying of the stipulated consideration.

Article Twenty

The product shall re-registered based on a request submitted by the product's owner during the last year of the validity of the registration license to the General Administration of Innovative Products, otherwise the registration license shall be regarded as a nullity. After that, a transfer letter shall be sent to the competent administration as per the nature of the product, provided that the General Administration of Innovative Products shall be notified of the material(s) confirming the approval of proceeding with re-registration procedures or the rejection of re-registration by those departments. The re-registration procedure shall comply with the regulations and rules governing the work of those administrations.

Article Twenty one

Importation and sealed medical customs release of pharmaceutical raw materials and packaging supplies used in manufacturing innovative products shall be permitted under the registration license or the approval of proceeding with the registration procedures issued by the Central Administration of Biological and Innovative Products and Clinical Studies, provided that the company shall be committed to submit the documents required to issue the import approval and the letter of Sealed Medical Customs Release in accordance with the regulatory guideline of the rules and procedures regulating importation and medical customs release of medicinal products, their raw materials and packing and packaging supplies.

Article Twenty two

The product's owner shall adhere to the following:

- Giving a pledge that he shall comply with the provisions of the Intellectual Property Rights Law no. (82) of 2002 and that he shall accept full liability if he is proven to violate this law. The Central Administration of Biological and Innovative Products and Clinical Studies has the right to nullify the track of registration procedures or to withdraw registration upon a recommendation of the Technical Committee for Drug Control.
- Writing the manufacturer name, the product-owning company, manufacturing date, expiry date, batch number, the barcode, registration number and price on the external package and printing the manufacturer name, manufacturing date, expiry date and batch number on the internal package.
- Making no changes to the product until refereeing the Central Administration of Biological and Innovative Products and Clinical Studies to submit the file of the variations which the product shall undergo so that they can be assessed in accordance with the rules approved by the Technical Committee for Drug Control and obtaining an approval for these changes from the Innovative Products' Registration Administration.
- Making the products that have been granted a Marketing Authorization License in accordance with this decree available within one and a half year of the date of issuing the Marketing Authorization License.
- Giving a pledge that all submitted data in the product registration file are correct and that he is fully responsible for them.

- Acknowledging the full responsibility for the storage of the raw material, the manufacturing phases of the product and the product conformity to the technical specifications up to its complete distribution.
- In the case of toll manufacturing, the manufacturing site is required to be licensed by the Egyptian Drug Authority and to abide by all obligations provided herein and by the good manufacturing practices.
- Undertaking to inform the General Administration of Pharmacovigilance of any adverse effects that are observed about the product and to implement all required vigilance activities in compliance with the applicable principles of good pharmacovigilance practices, as well as submitting the periodic safety update report for assessing the product benefits and risks to the General Administration of Pharmacovigilance in accordance with the pharmacovigilance rules and procedures mentioned in the guideline of the procedures of pharmacovigilance for innovative products, otherwise the product circulation shall be suspended based on a report by the Central Administration for Pharmaceutical Care.
- Submitting a statement (in the case of using a plasma derived product as excipient in an innovative biological product) proving that the supplier of this substance conforms with informing the registration-requesting person of any data pertaining to the safety and efficacy of this substance. This requirement applies to plasma derivatives which are not registered in the Arab Republic of Egypt.
- Notifying the Central Administration for Biological and Innovative Products and Clinical Studies of the names all of his authorized distributers and of any change that may be made to their data and ensuring that his authorized distributers implement good storage and distribution practices.
- Updating the electronic companies register (Company profile), which is available on the website of the Egyptian Drug Authority, in the event that there is any update in the data of the company owning the registration request.

Article Twenty three

The registration license of the innovative product shall be cancelled if the said product is not available on markets for one and a half year after issuing the final registration license or if the product is not produced and circulated before the last day of the expiry date of the last produced batch, based on a report submitted by the Central Administration of Operations.

The registration license shall be canceled by a decree of the President of the Egyptian Drug Authority based on an explanatory memorandum that is presented by the Head of the Central Administration of Biological and Innovative Products and Clinical Studies and that is based on a recommendation by the Technical Committee for Drug Control. Any batch produced after this date shall be sealed and necessary disciplinary actions shall be taken in this regard.

Article Twenty four

In the event that the product registration validity period expires without submitting a re-registration application for the first time, the registration license shall be annulled. The annulment shall take effect by a decree of the President of the Egyptian Drug Authority based on an explanatory memorandum that is presented by the Head of the Central Administration of Biological and Innovative Products and Clinical Studies and that is based on a recommendation by the Technical Committee for Drug Control. Any batch produced after this date shall be sealed and necessary disciplinary actions shall be taken in this regard.

Article Twenty five

The President of the Egyptian Drug Authority has the right to issue any decision to suspend or cancel proceeding with registration procedures or to withdraw the registration of any innovative product which he considers its circulation to be harmful to public health, based on a technical memorandum supported by scientific evidence and market studies issued by the Central Administration of Biological and Innovative Products and Clinical Studies.

The registration application of the innovative product may also be canceled in the case of exceeding the dates and deadlines stipulated in this guideline, pursuant to a decision by the Head of the Central Administration of Biological and Innovative Products and Clinical Studies, based on reports sent by the relevant central administrations and after presenting the matter to the Technical Committee for Drug Control.

Article Twenty-six

In emergency cases, a product may be circulated and exceptionally exempted from some requirements contained in this decree, based on an integrated technical report of each case. This report shall be issued by The Central Administration of Biological and Innovative Products and Clinical Studies and it shall be approved by the Authority's President.

In such a case, samples of that product shall be withdrawn for analysis at the competent central administration as per the nature of product, provided that the concerned person shall present the registration file upon its completion.

5- References:

- European Medicine Agency (EMA)
- Food and Drug Administration (FDA)
- Italian Medicines Agency (AIFA)
- Decree of the President of the Egyptian Drug Authority No. (388) of 2023 Concerning Issuing the Rules of Innovative Products' Registration.

6- Appendixes:

- Appendix (1) Request inquiry for registration of innovative product.
- Appendix (2) Template for scientific evaluation of innovative product.
- Appendix (3) Documents required for an innovative product registration file.