Regulatory Guideline of Mechanisms and Rules of Implementing the Decree of Egyptian Drug Authority's Chairman No. (343) of 2021

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1. Introduction

This regulatory guideline sets the regulating rules and procedures for registration of biological products within Egyptian drug authority (EDA) in accordance with the decision of EDA chairman No. 343 of 2021.

This guideline applies to biological products manufactured locally in the Arab Republic of Egypt or imported as either finished products, or bulk for primary and/or secondary packaging inside the Arab Republic of Egypt.

2. Scope

This guideline applies to locally manufactured or imported biological products submitted for registration within the Arab republic of Egypt.

3. Abbreviation

BioInn	Central Administration of Biological and Innovative Products and Clinical Studies	**MAH**	Market Authorization Holder
CAO	Central administration of operation	**PIL**	Patient Information Leaflet
CAP.Care	Central administration of pharmaceutical care	**PMF**	Plasma Master File
COO	Country Of Origin	**PSMF**	Plasma Site Master File
CPP	Certificate of Pharmaceutical Product	**PSSF**	Pharmacovigilance Sub-System Master File
CTD	Common Technical Document	**PSUR**	Periodic Safety Update Report
DS	Drug Substance	**PV**	Pharmacovigilance
DP	Drug Product	**RMP**	Risk Management Plan
EDA	Egyptian Drug Authority	**SMF**	Site Master File
EU	European union	**SmPc**	Summary of Product Characteristic
GMP	Good Manufacturing Practices	**SOP**	Standard Operating Procedure
GVP	Good Pharmacovigilance Practice	**TSE**	Transmissible Spongiform Encephalopathies
GSP	Good Storage Practice	**USP**	United States Pharmacopeia
GDP	Good Distribution Practice	**WDs**	Working days
ICH	International Council for Harmonization	**WHO**	World health organization

4. Definitions

Biological products: Products containing one or more active ingredient produced or derived from a biological source, including but not limited to human vaccines, serum, blood and plasma products and derivatives, also products manufactured using biotechnology and the like, as well as, any products or substances that may be created based on science update and/or international standard and reference.

Imported products: are biological products whether fully manufactured abroad or manufactured abroad and secondary packaged in factories within the Arab Republic of Egypt

Locally manufactured products: are biological products manufactured in factories inside the Arab Republic of Egypt or the products imported in bulk form that are formulated and/or primary filled in the Arab Republic of Egypt.

5. Main topic

5.1 . Inquiry request steps:

The applicant is requested to submit an inquiry of the product through the appropriate electronic program on EDA website. The request shall be accompanied by the documents mentioned in **Annex I.** The applicant will be notified of the inquiry status within **10 working days (WDs)** of receiving the inquiry. In case of missed documents, the applicant is committed to completing the required documents within **20WDs** of the date of receiving the notification; otherwise, the inquiry shall be considered cancelled.

5.2. Pricing:

After obtaining the approval for an inquiry, the following steps shall be followed:

- The required documents for pricing shall be submitted to the central administration of pharmaceutical policies and market access within **30 WDs** of the inquiry approval date, otherwise, the approval is considered cancelled.
- The biological products shall be priced within a period of no more than **60WDs** of the date of receiving the complete pricing file.

5.3. Procedures for registering locally manufactured products:

Registration procedures of locally manufactured products shall be completed in accordance with the following steps:

1. Active ingredient and bulk manufacturers from non-reference countries shall be inspected in case of registration for first time after submitting the site master file and obtaining approval from central administration of operations (CAO) “Administration of Inspection for biological sites” and shall be added to the risk-based inspection plan at reregistration. The inspection report shall be presented to the inspection higher committee and the committee resolution

should be communicated to central administration of biological and innovative products and clinical studies BioInn. Manufacturers who are world health organization (WHO) prequalified or authorized by one of the reference authorities are excluded from this requirement.

2. The stability protocol shall be submitted for review and approval before starting the stability study by the stability unit. The review and approval is achieved within no more than of **30 WDs**
3. The complete common technical document (CTD) registration file shall be submitted in accordance with documents mentioned in **Annex II** to BioInn "administration of biological products registration" within a maximum of two years from the date of pricing of the product. Otherwise, the registration request shall be considered cancelled.
4. Within **20 WDs** of submitting the complete registration file, it shall be screened by the relevant administration within BioInn , CAO, and central administration of pharmaceutical care (CAP.Care) to ensure that the submitted file is complete, then the file could be received. The applicant shall be notified of the product status within **20 WDS** of the date of submitting the complete file.
5. CAO shall be notified of the number of samples required for analysis by BioInn. The company shall submit the analysis requirements and samples from one batch of the finished product within **60WDs** of the date of issuing the letter specifying the number of samples. This period may be renewed only once.
6. If any notes are provided by any of the assessment bodies, the applicant will be notified within **45 WDs** from the data of receiving the complete file and shall fulfill these notes within **60WDs**. This period may be renewed only once , otherwise, the registration request shall be considered cancelled.
7. The submitted replies from the applicant are reviewed for completeness within **5WDs.** The assessment of the registration file will not be resumed until all the required notes are completely submitted.
8. The assessment of the registration file shall be completed within **70WDs after submission of all requirements.**
9. The above-mentioned steps shall be completely finished within **120 WDs**
10. The product shall be presented to the technical committee for drug control within 20 **WDs** from the date of receiving the following:
    - The technical assessment report and analysis certificate of conformity.
    - The inspection administration of biological products factories approval for the submitted inspection file.
    - Approval for the product stability study.

- The report received from the general administration of pharmacovigilance (PV)
- Recommendation of the scientific committee for biological products.
- Approval for outer, inner labels and the package leaflet of the product.

The final resolution regarding the registration of the product shall be taken, In the case of refusal of the product registration, the applicant shall be notified by a written letter indicating the reason for the refusal. In the case of approval, the product shall be granted a marketing authorization license valid for five years.

5.4. Procedures for registering imported manufactured products after pricing :

The procedures of imported products' registration shall be completed after pricing in accordance with the following steps:

1. The complete CTD Registration File shall be submitted in accordance with documents mentioned in **Annex II** to the BioInn "administration of biological products registration" within **60 WDs** of the date of pricing of the product, otherwise, the registration request shall be considered cancelled. The applicant shall be notified of the product status within **20 WDS** of the date of submitting the complete file.
2. Within **20 WDs** of submitting the complete registration file, it shall be screened by the relevant administration within BioInn, CAO and CAP.Care to ensure that the submitted file is complete, then the file could be received. The applicant shall be notified of the product status within **20 WDS** of the date of submitting the complete file.
3. CAO shall be notified of the number of samples required for analysis by BioInn. The company shall submit the analysis requirements and samples from one batch of the finished product within **60WDs** of the date of issuing the letter specifying the number of samples. This period may be renewed only once.
4. If any notes are provided by any of the assessment bodies, the applicant will be notified within **45 WDs** from the data of receiving the complete file and shall fulfill these notes within **60WDs**. This period may be renewed only once , otherwise, the registration request shall be considered cancelled.
5. The submitted replies from the applicant are reviewed for completeness within **5WDs.** The assessment of the registration file will not be resumed until all the required notes are completely submitted.
6. The assessment of the registration file shall be completed within **70WDs after submission of all requirements.**
7. The above-mentioned steps shall be completely finished within **120 WDs.**

8. The product shall be presented to the technical committee for drug control within 20 **WDs** from the date of receiving the following:
    - The technical assessment report and analysis certificate of conformity.
    - The inspection administration of biological products factories approval for the submitted inspection file.
    - Approval for the product stability study.
    - The report received from the general administration of PV
    - Recommendations of the scientific committee for biological products.
    - Approval for outer, inner labels and the package leaflet of the product.

The final resolution regarding the registration of the product shall be taken, In the case of refusal of the product registration, the applicant shall be notified by a written letter indicating the reason for the refusal. In the case of approval, the product shall be granted a marketing authorization license valid for five years.

5.5. The requirements for registering imported products:

- The product should be marketed in the country of origin, except for some vaccines enrolled at routine vaccination schedule of the central administration for preventive affairs (ministry of health and populations).
- The product must be WHO prequalified or marketed in one of the reference countries which are approved by the technical committee for drug control.
- For the imported biological products submitted for registration and not WHO prequalified nor marketed in one of the reference countries, the following steps should be followed:-
    1. The inquiry request is submitted through the electronic program designed for this purpose on the EDA website, and the request is forwarded to the scientific file evaluation unit.
    2. The scientific and the vigilance files should be submitted to the scientific evaluation unit within **20 WDs** from submitting the inquiry request.
    3. The initial screening of the scientific and the vigilance files will be performed within **15 WDs**. In the case of any missing documents are required, the company should submit them within **60WDs**, otherwise the application will be considered cancelled.
    4. After receiving of pharmacovigilance report and the evaluation of complete scientific file, the product file is presented to the specialized scientific committee for biological products to make the decision to approve or reject within **60WDs.**

5. In case of approval, the site master file should be submitted to CAO. The manufacturer should be inspected after approving the site master file and submitting the inspection report to the inspection higher committee for the approval and correspondence with the BioInn to inform it of the committee resolution, and then the procedures of the product registration can be proceed. Manufacturers who are accredited (GMP inspected) by one of the reference authorities are excluded from this requirement.

- For plasma derived medicinal products, inspection will be conducted in case the plasma centers are not accredited by a reference country or not accredited by international accreditation bodies such as (Plasma Protein Therapeutics Association /International Quality Plasma Program), in addition to performing the inspection on manufacturing site as previously illustrated.
- In case of biological products which do not have a scientific reference, the product shall be presented to the scientific committee for biological products accompanied by the report of the general administration of pharmacovigilance for a recommendation about approval or refusal of the registration. In case of approval, the product should be presented to the technical committee for drug control for making the final resolution. This procedure shall be carried out before granting the approval of inquiry.

5.6. Procedures for re-registration of biological products:

All biological products shall be re-registered every five years upon a request submitted by the applicant to the administration of biological products registration. That request shall be accompanied with the required documents for re-registration within the last year of the valid product marketing authorization in accordance with the following procedures:

- The product should be exempted of being presented once again to the scientific committee for biological products except in the case of products previously registered without being presented to this committee.
- The product is exempted of stability study re-evaluation in case of assessing stability study through product's initial registration.
- The updated CTD file as well as the list of variations of the product should be reviewed within **40WDs** in accordance with the required documents shown in (**Annex III**) if any missing documents are required, they should be submitted by the applicant within **60WDs**. This period may be renewed only once. In case these requirements are not fulfilled, the file should be submitted to the head of BioInn to take necessary decision concerning the product.

- Inspection file, package leaflets, and outer & inner packs of the product should be assessed.
- Pharmacovigilance documents should be assessed by the General Administration of PV.

5.7. Mandatory rules:

The applicant shall adhere to the following:

1- The applicant should commit to 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. BioInn has the right to stop the track of registration procedures or to withdraw registration upon a recommendation of the technical committee for drug control.

2- The applicant shall commit to write the manufacturer name, the product-owning company, manufacturing date, expiry date, batch number, the barcode, the registration number and the price on the external package and printing the manufacturer name, manufacturing date, expiry date and batch number on the internal package.

3- The applicant shall commit to make no changes to the product without referring to BioInn to submit the variation file 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 administration of biological products registration.

4- In case of using a plasma derived product as an excipient in a biological product, the applicant shall submit a statement proving that the supplier of this substance will inform the applicant of any data pertaining to the safety and efficacy of this substance. This is for the plasma derived product that isn't registered in the Arab Republic of Egypt or the applicant can use a plasma derived product that is registered in the Arab Republic of Egypt.

5- The applicant shall commit to place the product in the market within one and a half year of the date of issuing the marketing authorization.

6- The applicant shall commit that all submitted data in the product registration file are correct and that he is fully responsible for them.

7- The applicant shall commit to acknowledge the full responsibility for the storage of the starting material, the manufacturing phases of the product and the product conformity to the technical specifications up to its complete distribution in accordance with the rules of good distribution (GDP) and storage practice (GSP) in EDA.

8- In case of toll manufacturing, the manufacturing site is required to be licensed by the EDA and to abide by all obligations provided herein and by the good manufacturing practice.

9- The applicant shall commit to notify EDA of the names all of its authorized distributors and of any change that may be made to their data and ensuring that its authorized distributors implement GSP & GDP.

10- The applicant shall update the data regarding the marketing authorization representative as per company profile published on EDA website.

5.8. General rules

- If there is more than one site for manufacturing the raw material, bulk, final product, or solvent, and were evaluated within the registration file (CTD) for the product during registration, one batch of the final product shall be analyzed. The marketing authorization should mention that the analysis of rest of sites is to be carried out in accordance with the EDA Lot release policy.
- In the case of manufacturing pilot batches of a local product from an imported raw material, the CAO " Administration of Inspection for biological sites" monitors the raw materials by monitoring the quantities that are manufactured and ensuring that they are used for their specified purposes. When manufacturing production batches, the required studies are conducted and submitted for evaluation and approval by BioInn before these batches are placed into market.
- A manufacturing site inspection shall be requested in case of non-conformity certificate of the registered product for two times within five years upon a report handed over by BioInn.
- The registered biological products which have registration numbers and shall be published on the EDA electronic website no later than the tenth day of the month following the issuance of approval.
- All concerned stakeholders have the right to object, within two months of publishing date to any of the products whose registration were published.
- If the product registration is rejected, the applicant has the right to request that the product be presented once again to the technical committee and may file a grievance against the final resolution within (60) working days of the date of its issuance, through a reasoned request letter to be submitted to the grievance committee constituted in accordance with EDA law No. 151 for year 2019. The request should be accompanied with the documents and data which he wants to draw upon at considering his grievance.
- The applicant has the right to submit a request for registering a product with fast-track registration in accordance with the applicable and effective rules.
- The applicant may register another biological product for an original product (as a second brand) in accordance with the applicable and effective rules.

- Reliance on data and reports of reference authorities, approved by the technical committee for drug control, may be utilized during the registration procedures of the products approved by these bodies.
- Registration licenses issued in accordance with minister of health decree No. 297 of 2009 are valid until the expiry of their period and applications for re-registration must be submitted in compliance with EDA chairman Decree No. 343 of 2021.

5.9. Scientific references

The registration and re-registration file are received in the form of CTD according to organization of the CTD for the registration of pharmaceuticals for human use (M4)). Review of the files are based on guidelines from WHO and International council for harmonization (ICH) guidelines with its updates as following:

1. Stability ICH Guidelines (Q1A - Q1E).
2. Validation of analytical procedure: text and methodology (Q2).
3. Impurities ICH Guidelines (Q3C - Q3D).
4. Quality of Biotechnological products (Q5A - Q5E).
5. Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products (Q6B).
6. ICH Guidelines (Q7 - Q11).
7. ICH Guidelines (Q13 - Q14).
8. The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life Threatening Conditions (E1).
9. Clinical safety data management: definitions and standards for expedited reporting (E2A).
10. Post-approval safety data management: definitions and standards for expedited reporting (E2D).
11. ICH Guidelines(E3 - E11).
12. ICH Guidelines (E14 - E19).
13. MedDRA-Medical Dictionary for Regulatory Activities (M1).
14. Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals (M3).
15. Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk (M7).
16. Drug Interaction Studies (M12).
17. ICH Guidelines (S1 - S12)

6. References:

Decree of EDA chairman No. (343) of 2021

7. Annexes

Annex I: Documents required for the inquiry request

Annex II: Documents required for a registration file of a biological product

Annex III: Documents required for a re-registration of a biological product

Annex I: Documents required for the inquiry request

The company submits an inquiry request through the program designated for inquiry requests on the EDA website. A request for the name of the drug is also submitted through the electronic program for names, coinciding with the submission of the inquiry request
The applicant for registration must submit a separate inquiry request for each concentration, pharmaceutical form, or product size. It is only permitted to submit a separate inquiry request for packages that differ in the number of units inside them only.
The required documents are attached in accordance with the product submitted for registration
A receipt of payment of inquiry services consideration
A copy of the scientific reference of the product, provided that it is an internationally approved reference, for instance (Official Sites of reference countries defined by Technical Committee Vidal, united states pharmacopeia (USP), Rote Liste, Compendium Suisse, PDR).
For the Pharmacopeial products (British or European, USP), a copy of the most recent monograph followed by the product must be attached
For products imported or manufactured with permission from abroad, the above mentioned documents must be submitted in addition to the following: - The certificate of pharmaceutical product (CPP) in accordance with the WHO's form, attested by the Chamber of Commerce or its equivalent in the country of origin and notarized by the Egyptian Embassy abroad - Products imported by an agent shall submit contracts or letters of delegation provided by product owner working abroad; these documents must be attested by the Chamber of Commerce or its equivalent in the country of origin and notarized by the Egyptian Embassy abroad, clarifying all the data and steps that the applicant has delegate
For products manufactured locally, or the active ingredient or bulk is imported from abroad to manufacture the final product or fill and package it locally, the following documents must be submitted: - Good Manufacturing Practices (GMP) of the active ingredient /bulk shall be submitted. - Local manufacturing site license, and sometimes documents such as risk assessment, cleaning validation & process flow chart are requested for evaluation the condition of the manufacturing site to manufacture the provided product. - The contracts concluded between the company manufacturing the bulk and the registration applicant are authenticated by the Chamber of Commerce or its

equivalent in the country of origin and certified by the Egyptian embassy abroad, clarifying all the steps and powers delegated to the registration applicant and clarifying where the final product will be manufactured and the details of final product.

- For products manufactured locally by third parties : submit contracts concluded between the company and the local manufacturing site, provided that they are authenticated by the legal advisor, clarifying all the details of the product, and submitting a commercial register showing the manufacturing activity of third parties, and the inquiry request is sent via the Toll company's own code.

Annex II: Documents required for a registration file of a biological product

Administrative file (Module 1)	
Required documents	**Notes**
Cover letter	
Copy of Authorization letter for the company representative	
Pricing status	- Pricing certificate - Proof of submission (in case of reliance and fast track)
Copy of all approvals or Exemptions related to the Product (e.g. technical committee, scientific committee, inspection reports …) if any.	
Service consideration	For every evaluation unit
Application form	
CPP	- Authenticated from Embassy. - Valid. - The Arab Republic of Egypt is mentioned as Importing Country. - Number of product license is specified. - Date of issue is specified. - Dosage form (s) and Strength (s) are specified. - License Holder (address, city, country) is specified. - Role of License Holder is specified. - Manufacturer of solvent should be mentioned (if different from manufacturer of the finished product). - Product marketed in the country of origin (COO). - Manufacturing sites involved in the manufacturing of the product should be mentioned with its role (Finished product, Primary Packager, Secondary Packager, Batch releaser, Solvent manufacturer). - GMP of the manufacturer is specified.

	- Pack Presentation and pack size(s) of the Product is (are) specified (could be as an attachment). - Active Ingredient(s) by its salt or hydrate form (if any) with its (their) quantity (ies) per unit dose is (are)specified. - Inactive Ingredient(s) with its (their) quantity (ies) per unit dose is (are) specified (could be as an attachment). - Shelf-life of the Product is specified (could be as an attachment). - Storage Conditions of the Product is specified (could be as an attachment). - SPC or package insert of the product (could be as an attachment). - If the Name of the product may change in Egypt, copy of CPP from any reference country with the name targeted to be in Egypt should be submitted (technical committee decision on 22/5/2014).
GMP for each site (DS, DP, 1ry packager, 2nd packager)	
Manufacturing license (DS, DP, 1ry packager, 2nd packager)	
In case of reliance pathway - List of approved variations after first marketing authorization. - Letter of sameness	
Composition certificate	
Labelling	**Packs:** - Declaration letter stating the type of the submitted pack. - Outer pack & inner label artwork **Summary of Product Characteristic (SmPC) & patient information leaflet (PIL):** - Proposed English Insert marketed in Country of Origin (Numbered). - Proposed translated Arabic Insert, translated from a Certified translation

	office, except (Vaccines- Immunosuppressant- IV infusion products- Hospital use only - Immunological products- Contrast agents except iodinated one). - SmPC and/or company core data sheet. - Comparative table between reference insert & proposed insert (in case of proposed insert is different than reference insert). - Declaration from marketing authorization holder (MAH) that the submitted insert is the most updated & marketed in COO (insert status). - If a biosimilar product: submit Innovator product insert
Contracts	- Official declaration stating the relationship between manufacturer, improper and distributor. - Copy of agency or distribution contract **In case of imported bulk naked container** that manufactured abroad and packed locally, the following is required: 1) Copy of packaging contract between the importing company & local manufacturing 2) Original Authorization letter from the abroad mother company to the importing company for product registration and packaging with a local licensed packaging site - Letter of Acknowledgment of full responsibility for storing the raw materials and for all stages of manufacturing and for the product's conformity with the technical specifications until the completion of distribution. - The manufacturing contract in case of toll manufacturing
Legal documents	- Pledge acknowledging his commitment to the provisions of the Intellectual Property Protection Law No. 82 of 2002.

	- The updated Tax card. - Updated scientific office license. - Importer register for all importers. - Updated Storage License for all Storage sites. - Commercial register
Adventitious agent's documents	- Transmissible Spongiform Encephalopathies (TSE) free certificate from license holder. - Certificate of suitability
Specific documents for plasma derived medicinal products	- Plasma Master File - Official certificates declaring plasma source (legalized in case of API of Plasma derived medicinal products) - HIV-1, HIV-2, HBsAG, HCV freedom legalized certificate for the plasma - Copy of Certificate of release from Health authority (Drug substance only) - Plasma master file (PMF) approval from health authority (if present).
Detailed Standard Operating Procedures (SOP) for finished product	Contain information related to: equipment used, proper quantities used in each step in procedure and mention the dilution of the sample and standard, the detailed description of calculation mentioning any used equation or software.
Summary protocol (for vaccines & plasma derived medicinal products)	
Documents regarding manufacturing sites	- Site master file (SMF) for all manufacturing sites. - Latest full inspection report(s) for inspection performed by a stringent regulatory authority in the past three years and their outcomes. - Last Annual product review. - One completed batch manufacturing and packaging record. - List of any recalls in the past three years related to products with quality defects (if found).

	- Any warning letter or equivalent regulatory action (production- line specific) (if found).
Documents for pharmacovigilance	- Confirmation e-mail by plasma site master file (PSMF) reception portal. - Updated version of Summary of PSMF(s)/ Pharmacovigilance Sub-System Master File (PSSF). - PV agreement between the MAH & the service provider covering all the PV activities including the concerned product(s). - The latest Periodic Safety Update Report (PSUR) in PSUR format “as per good pharmacovigilance practice (GVP) for Arab Countries V.2.0” covering at least the last 3 years OR separate PSURs covering at least the last 3 years. - The most updated “European union (EU) / Global/ Core-Risk Management Plan (RMP)"of the product. - The Egyptian display of EU-RMP. - Egyptian-RMP of the product (for locally manufactured products)

N.B: For more information, please refer to guideline for content file of biological products for registration & re-registration file Code: EDREX.GL. BioInn.004.

Annex III: Documents required for a re-registration of a biological product

Administrative Data (Module 1)	
Required documents	**Notes**
Service consideration	For every evaluation unit
Composition certificate	
List of variations	
A declaration from the license holder mentioning the product name declare that the submitted Module 3 (version number & date) at the renewal process is the updated and complete one	
-A declaration letter from the applicant mentioning that there are no updates in the scientific & stability files at the renewal submission date and all updates are submitted and approved previously (or there are no updates undertaken from the product license issuance till renewal submission	
-List of the countries where the product is registered & marketed including trade name in each country & marketing status	
Adventitious agent's documents	- TSE free certificate from license holder - Certificate of suitability
Specific documents for plasma derived medicinal products	- Plasma Master File. - Official certificates declaring plasma source (legalized in case of API of Plasma derived medicinal products). - HIV-1, HIV-2, HBsAG, HCV freedom legalized certificate for the plasma. - Copy of Certificate of release from Health authority (Drug substance only). - PMF approval from health authority (if present).
Detailed SOP for finished product	Contain information related to: equipment used, proper quantities used in each step in procedure and mention the dilution of the sample and standard, the detailed description of calculation mentioning any used equation or software.

Summary protocol (for vaccines & plasma derived medicinal products)	
Documents regarding manufacturing sites	- SMF for all manufacturing sites. - Latest full inspection report(s) for inspection performed by a stringent regulatory authority in the past three years and their outcomes. - Last Annual product review. - One completed batch manufacturing and packaging record. - List of any recalls in the past three years related to products with quality defects (if found). - Any warning letter or equivalent regulatory action (production- line specific) (if found).
Documents for pharmacovigilance	- Confirmation e-mail by PSMF reception portal. - Updated version of Summary of PSMF(s)/PSSF. - PV agreement between the MAH & the service provider covering all the PV activities including the concerned product(s). - The latest PSUR in PSUR format “as per GVP for Arab Countries V.2.0” covering at least the last 3 years OR separate PSURs covering at least the last 3 years. - The most updated “EU / Global/ Core-Risk Management Plan (RMP)"of the product. - The Egyptian display of EU-RMP. - Egyptian-Risk Management Plan (RMP)"of the product (for locally manufactured products).

N.B: For more information, please refer to guideline for content file of biological products for registration & re-registration file Code: EDREX.GL.Bioinn.004.