Appendix (1)

Request inquiry for registration of innovative product

➢ General notes:

Note I: Font to use" Times New Roman size 12"
Note II: The innovative product is a locally produced medicinal or biological product that has never been registered in local or global market with an added therapeutic value over the registered products.
Note III: The innovative product could be either a new molecule or novel modification of existing drug.

➢ Section 1: "Product description"

1- Name of the Applicant	
2- Company ID	
3- Type of license	**Local ☐ Toll ☐ FToll ☐**
4- Type of the product	**Pharmaceutical ☐ Biological ☐**
5- Active ingredients (or drug substance) with concentrations **** clarify salts of your active ingredients & their equivalence**	
6- Proposed dosage form	
7- Proposed route of administration	
8- Proposed pack in details (Describe the package, package material, package size & if it contains any additional accessories**).**	
9- Manufacturer of the active substance/ drug substance	
10- Manufacturer of the finished product (Clarify primary packager, secondary packager, solvent manufacturer if present)	
11- Proposed indication(s)	

12- Proposed dose, dose regimen & method of administration		
13- Does any active ingredient have a narrow therapeutic index?	Yes ☐	NO ☐
14- Are active ingredient(s) approved for intended indication in treatment guidelines?	Yes ☐	NO ☐
15- Receipt number		

➢ Section 2: "Preliminary evaluation"

- **Which of the following categories can the submitted product be classified?**

1. New molecular entity	
2. New indication	
3. Novel technology in manufacturing	
4. New route of administration of already existing drug	
5. Novel formulation	
6. New Fixed dose combination	
7. New Stereoisomer	
8. Others (kindly mention)	

- **What is the added therapeutic value(s) for the submitted product?**

1. Superior efficacy	
2. Better safety profile	
3. Better pharmacokinetic profile	
4. Improvement of patient compliance	
5. New treatment option	
6. Others (Kindly mention)	

	Yes	No
▪ In case of new molecular entity, did the company apply for a patency at Egyptian patency office?		
▪ Does the manufacturer have the ability to manufacture the submitted product upon approval?		
▪ Is the submitted product new and not registered or under registration in local or global market?		
▪ Was the product previously submitted to any other department in EDA? (If yes please clarify)?		
▪ Is there any supportive evidence from credible literature that support the		

safety and efficacy of the submitted product?		
▪ **Is there any market need for this product?**		
▪ **Is there any safety concern on the active ingredient(s)?**		
▪ **Does the company have the ability to perform clinical trials when needed?**		
▪ **Does the company have a strong PV system?**		

Attachments shall be uploaded to the e-mail:

- A copy of the payment receipt for the services of the inquiry request stamped by the general administration of innovative products. The product's data shall be written on the payment receipt.
- Contracts & licenses of the inquiry request applicant, if they are not present on company profile.
- GMP certificates for active ingredients' factories.
- Contracts between applicant and factory in case of Toll & FToll (if present).
- Authorization letter for company representative who are delegated to deal with the general administration of innovative products.

Notes:

- The payment receipt will not be accepted if there is a scratch or crossing out on the receipt or the absence of the financial management stamp or the purpose of the payment (inquiry request).
- The original payment receipt shall be delivered to the clerk of the General Administration of Innovative Products, and accordingly, the applicant should receive a stamped copy confirming that the original has been delivered.
- The company must attach the stamped copy of the payment receipt to the inquiry request after writing product's data on it. Otherwise, the inquiry request will be rejected and it could be submitted again after fulfilling all conditions.

➢ Contact information:

Name of the pharmacist who prepared the report:

Title:

Company:

Mobile number:

Appendix (2)

Template for scientific evaluation of innovative product

➢ General notes:

Note I: Font to use" Times New Roman size 12"
Note II: If any information isn't available, write NA "Not available"
Note III: After acceptance of your file, sent the soft data to (Innov.scie@edaegypt.gov.eg)
Note IV: The innovative product is a locally produced medicinal or biological product that has never been registered in local or global market with an added value over the registered products.
Note V: The innovative product could be either a new molecule or novel modification of an existing drug.

➢ Section 1: "Product Description"

1- Name of the Applicant	
2- Type of license	**Local☐ Toll☐ FToll☐**
3- Type of the product	**Pharmaceutical☐ Biological☐**
4- Active ingredients (or drug substance) with concentrations **** clarify salts of your active ingredients & their equivalence**	
5- Proposed dosage form	
6- Proposed route of administration	
7- Proposed pack in details (Describe the package, package material, package size & if it contains any additional accessories**).**	
8- Manufacturer of the active substance/ drug substance	
9- Manufacturer of the finished product (Clarify primary packager, secondary packager, solvent manufacturer if present)	
10- Category of innovation	
11- Proposed added therapeutic value	
12- Proposed indications	

13- Proposed dose, dose regimen & method of administration		
14- Does any active ingredient have narrow therapeutic index?	**Yes** ☐	**NO** ☐
15- Are active ingredient(s) approved for intended indication in treatment guidelines?	**Yes** ☐	**NO** ☐

➢ Section 2: Regulatory status in reference countries:

A- List the nearest registered product(s) to the submitted innovative product that registered in different reference countries.

B- In case of fixed dose combination, add to the previous list the reference products for each active ingredient (if available).
(Please fulfill each item in table 1).

Note I: Links for product search sites in reference countries in the last page.
Note II: The original SmPC for the mentioned reference product(s) should be attached and in case of non-English language, the translated English version should be also attached.

Table (1):

Reference Country	Trade name	Composition & strength	Dosage form	Marketing status	SmPC "Link if available"

➢ Section 3: Clinical safety data & safety Concerns:

A- Mention any available clinical safety data for the submitted innovative product or for the nearest ones.

B- Mention any safety concerns available for active ingredient(s) contained within the submitted innovative product (either single or in combination).

Note: References for the above mentioned data should be attached.

➢ Section 4: For products contain more than one active ingredient:

A-Drug- drug interactions:

If your product contains more than one active ingredient, please clarify if there is a drug-drug interaction between its active ingredients. (Please fulfill each item in table 2).

Note I: Links for Drug-drug interactions search sites in the last page; you can use any of them.

Note II: Using of other drug- drug interaction search sites is also accepted.

Table (2):

Drug-drug interactions	Possible effect	Recommendation/ Management

B-Dosing interval and dose timing:

If your product contains more than one active ingredient, please clarify if they have the same dosing interval and dose timing (Please fulfill each item in table 3).

Table (3):

Active ingredients	Same dosing interval	Same dose timing	Management if different dosing interval or dose timing

➢ Section 5: Proposed composition, incompatibilities & proposed pack:

A- Attach a composition sheet for the submitted product and certificates of analysis for the product ingredients.

B- Clarify if there are any physical or chemical incompatibilities:

Clarify if there are any physical or chemical incompatibilities between ingredients of the submitted products. (Please fulfill each item in table 4).

Table (4):

Ingredients	Physical incompatibility	Chemical incompatibility	Management

C- Clarify the reasons for choosing the proposed pack:

Clarify the reasons for choosing the proposed materials, package size & additional accessories (if present).

➢ Section 6: Guidelines:

Show the guidelines for treatment of targeted disease (please fulfill each item in table 5)

Table (5)

Guidelines title	Guidelines association	Line of treatment (first line or second or third …) & level of evidence	Year

➢ Section 7: Scientific rational for the development of innovative product:

-Attach a summary for innovative product characteristics that explains clearly the need and the impact of the claimed innovation.

-This summary must show the scientific evidence (supported by credible literature as a reference) that explains clearly the added therapeutic value of the submitted innovative product over the registered products either in local or global market (Maximum four pages).

Scientific Evidence Criteria:

I - Credible literature includes guidelines of treatment and other supportive studies (meta-analysis, systematic reviews, clinical efficacy studies, clinical safety studies) that are performed on the submitted product or similar ones (exact active ingredients, composition & dosage form).

**** If the available credible literature is insufficient for the submitted product or similar products, other credible literature for the nearest product(s) could be submitted.**

**** Comparative studies are preferred.**

II – Pharmacokinetics data such as: absorption, distribution, metabolism, excretion could be submitted (if available) especially for products with new dosage form or new route of administration or novel formulation or new fixed dose combination.

III- Animal pharmacological data could be submitted for new molecules (if available).

IV- Animal toxicology data (systemic toxicity studies, reproductive studies, local toxicity, genotoxicity, carcinotoxicity) could be submitted for new molecules (if available).

****Local Toxicity data as dermal toxicity, topical ocular toxicity, inhalation toxicity, vaginal toxicity, photo allergy, rectal tolerance test; could be submitted for innovative local products (if available).**

➢ Section 8: "Supportive studies"

Provide a full text article for studies demonstrating the scientific evidence mentioned in section 8.

(Please, fulfill each item in table 6 and then attach the full study)

Table (6)

no.	Literature Type	Title	Publication year	Main findings	Link
1	Systematic reviews & meta-analysis				
2	Systematic Reviews				
3	Clinical efficacy studies				
4	Clinical safety studies				
5	Pharmacokinetics studies				
6	Animal pharmacological data				
7	Animal toxicology data				
8	Others				

➢ Contact information:

Name & title of the pharmacist who prepared the scientific file:
Mobile number:
Email:
Submission date:

➢Links for product search sites in reference countries:

Name of regulatory authority	Home page	Online product database
EMEA	http://www.ema.europa.eu	https://www.ema.europa.eu/en/medicines
FDA	www.fda.gov	https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
TGA (Australia)	www.tga.gov.au	https://www.ebs.tga.gov.au/ebs/ANZTPAR/PublicWeb.nsf/cuMedicines?OpenView
MHRA (UK)	www.mhra.gov.uk	https://products.mhra.gov.uk/

EMC(Electronic Medicines Compendium)	http://www.medicines.org.uk/emc/	https://www.medicines.org.uk/emc#gref
France	https://ansm.sante.fr/documents/reference/repertoire-des-medicaments	http://agence-prd.ansm.sante.fr/php/ecodex/index.php
Health Canada	https://www.canada.ca/en.html	https://health-products.canada.ca/dpd-bdpp/index-eng.jsp
Japan	http://www.pmda.go.jp/english/index.html	http://www.info.pmda.go.jp/psearch/html/menu_tenpu_base.html
IMB (Ireland)	https://www.hpra.ie/homepage/about-us	https://www.hpra.ie/
Italy	http://www.agenziafarmaco.it/en	https://farmaci.agenziafarmaco.gov.it/bancadatifarmaci/
Germany	http://www.pharmnet-bund.de/dynamic/en/am-info-system/index.html	http://www.pharmnet-bund.de/dynamic/en/am-info-system/index.html
Swiss medic (Switzerland)	http://www.swissmedic.ch/index.html?lang=en	https://www.swissmedicinfo.ch/?Lang=EN
Spain	http://www.aemps.es/	https://www.aemps.gob.es/cima/fichasTecnicas.do?metodo=detalleForm
Sweden	http://www.lakemedelsverket.se/english/	http://www.lakemedelsverket.se/Sok-efter-lakemedel-och-mediciner-i-Lakemedelsfakta/
Belgium	http://www.fagg-afmps.be/en/human_use/medicines/herbal_medicinal_products/pharmacovigilance/	http://bijsluiters.fagg-afmps.be/?localeValue=nl
Austria	http://www.ages.at/	https://aspregister.basg.gv.at/aspregister/faces/aspregister.jspx?_afrLoop=50195861171580298&_afrWindowMode=0&_adf.ctrl-state=16yka9pwvp_4
Denmark	https://laegemiddelstyrelsen.dk/en/	http://produktresume.dk/AppBuilder/search
Finland	http://www.fimea.fi/	http://www.fimea.fi/web/en/databases_and_registeries/fimeaweb
Iceland	http://www.lyfjastofnun.is/	http://serlyfjaskra.is/

Netherlands	http://www.cbg-meb.nl/cbg/nl	https://www.geneesmiddeleninformatiebank.nl/nl
Luxembourg	https://sante.public.lu/fr.html	https://cns.public.lu/en/legislations/textes-coordonnes/liste-med-comm.html
New Zealand	http://www.medsafe.govt.nz/	http://www.medsafe.govt.nz/regulatory/DbSearch.asp
Norway	http://www.legemiddelverket.no/	https://www.legemiddelsok.no/
Portugal	http://www.infarmed.pt/portal/page/portal/INFARMED/ENGLISH	https://extranet.infarmed.pt/INFOMED-fo/

➢Drug- drug interactions sites:

https://www.drugs.com/drug_interactions.html
https://reference.medscape.com/drug-interactionchecker
https://www.webmd.com/interaction-checker/default.htm

Appendix (3)

Documents required for an innovative product registration file

** Complete registration file (Common Technical Document) shall be submitted according to ICH guidelines (hard copy and soft copy on CD).

First - Hard file (Module 1):

- A copy of the administration's approval for the inquiry request.
- A copy of the pricing notification.
- An undertaking of data validity stamped with the seal of the company.
- A CD containing copies of all paper documents submitted.
- A copy of the Delegation Letter for the representative of the company requesting registration from the Authority.
- A receipt of payment of charges and registration service fees. (A receipt of payment of charges and registration service consideration.)
- A statement of the product composition signed and stamped with the seal of the company.
- A copy of the factory (manufacturing) license, showing the production lines that fit the shape of the pharmaceutical product.
- In the case of manufacturing at a third party, the product manufacturing contract notarized as having an authentic signature shall be submitted.
- A certificate proving that the substances used in the product composition are free from TSE/BSE and submitting a Certificate of Suitability for the substances used in the product composition, in the case of request for such certificate.
- The inner and outer packaging form and the product inner label containing the required data.
- Active ingredient:
    - Specifications and tests of active ingredients.
    - A certificate of analysis for the active substances.
    - Names of suppliers.

- If substances used in the product composition belong to blood products, the aforementioned documents shall be submitted in addition to the following:
  - The plasma master file that includes information showing the source of plasma, starting with assembly process (**collection process**) and passing through all manufacturing phases, in process control and viral safety.
  - Official certificates stating the source of plasma.
  - Certificates proving that the plasma is free of HCV, HIV-1, HIV-2 & HBsAg.

- Inactive ingredients:
  - Specifications of inactive materials and their tests.
  - Certificate of analysis of inactive substances.
  - Names of suppliers.
  - In the event that blood derivatives are used as inactive substances, the aforementioned documents must be submitted in addition to the following:
  - Official certificates showing the source of the plasma.
  - A certificate proving that the plasma is free of HCV, HIV-1, HIV-2 & HBsAg
  - Final product:
  - Final (Finished) product specifications.
  - An analysis certificate of the final product (finished product) issued by the factory (manufacturer).

Second - The inspection file (in the case of bio-innovative products):

- Site Master File of the factories (manufacturers) of active ingredients and final product, the packaging factory (manufacturing site) and the solvent factory (manufacturer) (if any).
- A copy of Good Manufacturing Practice Certificate of the active ingredients' manufacturer (in case of importing the active substance).
- A copy of the factory (manufacturing) license showing the production lines.
- A description of the steps taken to guarantee the preservation of the cold chain.
- Manufacturing method that shows in process control and validation used in manufacturing.
-

Third - the stability file: (according to the requirements of the stability unit)

Fourth - the laboratory and quality evaluation file:

- Module 3 quality
- Summary protocol for vaccines & plasma derived medicinal products (if required)
- Detailed SOPs for all methods of analysis for finished product (if required)

Fifth - Clinical Studies File:

- Module 4 pre-clinical (if required)
- Module 5 clinical (if required)