الإدارة المركزية إدارة المركزية للمستحضرات الحيوية والمبتكرة والدراسات اإلكلينيكية
الإدارة العامة للمستحضرات المبتكرة

(ملحق)١

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 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?		

مرفقات يتم رفعها على الإيميل:

- صورة من إيصال سداد مقابل خدمة طلب الاستعلام مختوم من الإدارة العامة للمستحضرات المبتكرة ومدون عليه بيانات المستحضر.
- نسخة من العقود و التراخيص الخاصة بطالب الاستعلام فى حالة عدم توافرهم على Company profile.
- شهادات التصنيع الجيد (GMP) الخاصة بمصانع المواد الفعالة.
- في حالة Toll وFToll، العقود والاتفاقات المبرمة بين ال Applicant والمصنع (إن وجد).
- التفويض الخاص بالمندوب المنوط بالتعامل مع الإدارة العامة للمستحضرات المبتكرة.

ملاحظات:

- لن يتم الإعتداد بإيصال السداد فى حالة وجود كشط أو شطب على الإيصال أو عدم وجود ختم الإدارة المالية أو والغرض من السداد (طلب استعلام).

- يتم تسليم أصل ايصال السداد للإدارى الخاص بالإدارة العامة للمستحضرات المبتكرة و بموجب ذلك يتسلم صورة مختومه منه تفيد تسليم الأصل.

- يجب على الشركة إرفاق الصورة المختومة لإيصال السداد مع طلب الإستعلام و ذلك بعد كتابة البيانات الخاصة بالمستحضر على صورة الإيصال ، و إلا سيتم رفض طلب الإستعلام ويتم تقديمه من جديد مستوفياً جميع الشروط.

➢ Contact information:

Name of the pharmacist who prepared the report:

Title:

Company:

Mobile number:

ملحق (٢)

Template for scientific evaluation of innovative product

➢ General notes:

Note I: Use font" Times New Roman size 12"
Note II: If any information isn't available, write NA "Not available"
Note III: Send 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- 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 <u>nearest</u> registered product(s) to the submitted innovative product that registered in different reference countries.

B- In case of <u>fixed dose combination</u>, 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	Reference of dose interval and dose timing	Management if different dosing interval or dose timing

C-Incompatibility test:

If your product contains more than one active ingredient, please conduct incompatibility study choosing one of the following:

1- **Differential Scanning Calorimetry (DSC) & X-ray diffraction.**

2- **Fourier transform infrared spectroscopy (FTIR).**

3- **Proton nuclear magnetic resonance (1H NMR).**

➢ Section 5: Proposed composition, Certificates of analysis & proposed pack:

A- Attach a composition sheet for the submitted product.

B- Attach certificates of analysis for the product ingredients.

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 taking inconsideration the epidemiological evidence for the magnitude of the problem that will be addressed by the submitted innovative product.

-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 (systematic reviews & 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"

-Mention the used search strategy, the searched data bases as (PubMed, Google scholar, Cochrane library, Embase, Web of Science, etc…) & the results from each data base.

- <u>Mention the main findings, the relevance of the study to the whole submitted product & its reflection on the proposed added therapeutic value.</u>

-Provide a <u>full text article</u> for studies demonstrating the scientific evidence mentioned in section 7. (Please fulfill each item in table 6)

Table (6)

no.	Literature Type	Title	Publication year	ain findings, the relevance of the study to the whole submitted product & its reflection on the proposed added therapeutic value	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

ملحق (٣)

المستندات المطلوبة لملف تسجيل مستحضر مبتكر:

**يتم تقديم ملف تسجيل CTD كاملا طبقا لـ ICH guidelines (نسخة ورقية ونسخة الكترونية محفوظة علي CD)

اولا- (Module 1) Hard file :

- نسخة من موافقة الإدارة فيما يخص طلب الإستعلام
- نسخة من اخطار التسعير
- تعهد بصحة البيانات مختوم بختم الشركة
- اسطوانة مدمجة تحتوي علي جميع المستندات الورقية المقدمة
- نسخة من خطاب التفويض لمندوب الشركة طالبة التسجيل لدي الادارة
- إيصال سداد الرسوم مقابل خدمات تقديم ومراجعة ملف التسجيل
- بيان تركيب المستحضر موقع ومختوم بختم الشركة
- صورة من رخصة المصنع موضحا بها خطوط الانتاج التي تلائم شكل المستحضر الصيدلي
- في حال التصنيع لدي الغير، يتم تقديم عقد التصنيع الخاص بالمستحضر موثق بصحة توقيع .
- شهادة تثبت خلو المواد الداخلة في تركيب المستحضر من TSE/BSE مع تقديم Certificate of Suitability للمواد المستخدمة في تصنيع المستحضر في حال طلبها
- نموذج العبوة الداخلية والخارجية والبطاقة الداخلية للمستحضرمحتويه علي البيانات الواجب توافرها
- المادة الفعالة:

  - مواصفات المواد الفعالة والاختبارات الخاصة بها
  - شهادة تحليل المادة الفعالة
  - اسماء الموردين
  - إذا كانت المواد الداخله فى تركيب المستحضر من مشتقات الدم، تقدم المستندات السابق ذكرها بالإضافة إلى مايلى:
    - الملف الخاص بالبلازما plasma master file ويشمل معلومات توضح مصدر البلازما بدءا من عملية التجميع مرورا
      بجميع مراحل التصنيع و in process control وال Viral Safety

- شهادات رسمية توضح مصدر البلازما
- شهادة تثبت خلو البلازما من HCV , HIV-1, HIV-2, HBsAg

- المواد الغير فعالة:

- مواصفات المواد الغير فعالة والاختبارات الخاصة بها
- شهادة تحليل المواد الغير فعالة
- اسماء الموردين
- في حال استخدام مشتقات الدم كمواد غير فعالة، تقدم المستندات السابق ذكرها بالإضافة إلى مايلى:
  - شهادات رسمية توضح مصدر البلازما
  - شهادة تثبت خلو البلازما من HCV , HIV-1,HIV-2,HBsAg

- المستحضر النهائي:

- مواصفات المستحضر النهائي
- شهادة تحليل المستحضر النهائي صادرة من المصنع

ثانيا- ملف التفتيش (فى حالة المستحضرات المبتكرة الحيوية):

- الملف الخاص بمكان التصنيع Site Master File وذلك لمصانع المادة الفعالة, المستحضر النهائي،مصنع التعبئة ومصنع المذيب (إن وجد)
- نسخة من شهادة التصنيع الجيد لمصنع المادة الفعالة (في حال استيراد المادة الفعالة)
- نسخة من ترخيص المصنع موضحا بها خطوط الانتاج
- وصف الخطوات المتبعة لضمان الحفاظ علي سلسلة التبريد (cold chain)
- طريقة التصنيع مع توضيح In process control & validationالمستخدمين في عملية التصنيع

ثالثا- ملف الثبات: (طبقا لمتطلبات وحدة الثبات)

رابعا - الملف الخاص بالتقييم المعملى والجودة:

- 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)

خامس ا ـ ملف الدراسات الإكلينيكية:

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