Guideline

Procedures for Registration of Biological products through Reliance pathways

2022

* Article 12 in regulatory guide for mechanisms, procedures and rules of implementing the decree of Egyptian Drug Authority's president No. 343/2021

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1. Introduction

The principle of reliance is central to WHO's approach to regulatory system strengthening and also a cornerstone for effective, efficient and smart regulatory activities of medical products. Accordingly, in the light of Biological Products registration regulations / update of ministerial decree 343/2021, Egyptian Drug Authority is developing this document to provide assistance for the applicants on how to conduct registration through verification or abridged procedures.

Reliance pathways bring benefits to patients and consumers, the industry and national governments, by facilitating and accelerating access to quality-assured, effective and safe medical products, save resources and decrease burden on assessors and regulators at agencies.

2. Scope

This document covers the different regulatory activities that are conducted in the Egyptian Drug Authority to implement reliance concepts during registration of biological products (i.e. vaccines, plasma derived medicinal products, biotechnology derived, advanced therapeutic medicinal products and Extract medicinal products…etc).

3. Definitions

1. **Reliance**: The act whereby the NRA in one jurisdiction may take into account and give significant weight to assessments performed by another NRA or trusted institution. The relying authority remains independent, responsible

and accountable regarding the decisions taken, even when it relies on the decisions and information of others.

2. **Abridged Registration:** Abridged regulatory pathways are regulatory procedures facilitated by the use of reliance, whereby the regulatory decision is solely or widely based on the application of reliance. Normally this would also involve some degree of work by the relying NRA. The expectation is that the use of reliance in these pathways would save resources and shorten the timelines compared to the standard pathways, while ensuring that the standards for regulatory oversight are maintained.

4. Procedures

4.1. Eligibility Criteria of the candidate products:

- The application should be identical to that approved by the reference agency (in terms of dosage form, strength, formulation, manufacturing sites, therapeutic indications…) and the product applied for reliance should be identical to the one applied in reference agency
    - The same qualitative and quantitative formulation;
    - The same manufacturing site(s) for API and FPP including specific block(s)/unit(s), chain, processes, control of materials and final product, and in the case of vaccines also by the same batch release scheme;
    - The same specifications for excipient, API and FPP;
    - The same essential elements of product information

Note: Some potential differences could exist between the EDA submitted dossier and that for EMA/FDA dossier, this changes should be justified for evaluation on case by case basis.

- The submitted product and its intended use (indications, dosage form, and patient groups) have not been rejected, withdrawn, suspended by any drug regulatory agency for safety or efficacy reasons.
- The submitted product should be registered and marketed on the market of the reference country.

4.2. Levels of reliance practice at EDA:

Reliance activities at EDA are applicant driven. Two approaches with different levels of reliance and different time frames are set according to the submitted documents as follows:

4.2.1. Level 1 (Abridged Registration / 30 days)

For products approved by EMA and/or FDA approval, **with** the submission of full assessment report and/or list of questions and answers in addition to CTD.

4.2.2. Level 2 (60 days)

In case of products with EMA and/or FDA approval with the submission of CTD **only**.

4.3. Submission requirements

All needed documents as mentioned in annex I.

4.4. Procedure of submission

Submission of application:

- An optional pre-submission technical support step through the technical support administration, can be implemented to verify the submitted documents and guide the company to the most suitable registration pathway for the product in addition to determining the analysis requirements.
- The applicant should submit the request inquiry through the relevant program and specify the desired pathway according to the attached documents uploaded (CPP , payment receipt , all data required to be filled in the program)
- Request inquiry approval is issued during 5 working days from completion of documents uploaded on the program including the transfer to pricing administration within 30 days of approval issuance.
- The applicant can request directly to submit the complete file to registration administration with proof of payment (after the submission of pricing file).
- Upload all the annexed documents to be reviewed by all concerned administrations within the specified timeline.

4.5. Assessment of information received:

- Evaluation of the submitted dossier and documents will be performed in compliance with the above-mentioned time frames on basis of verification of sameness and/or selective detailed review as deemed necessary by each unit / administration.

- Any questions that may arise during the evaluation process will be addressed directly to the applicant and the reply should be submitted within specified timeframes as stated in annex II.
- In case of conditional approval of the product's registration by the reference agency, EDA may take the same decision as that of the reference agency and may also grant the product a conditional approval.
- If the applicant fails to provide EDA with necessary information and cooperation, EDA is entitled to terminate the procedure and switch to any other pathway including the normal registration process.

4.6. Sample Analysis

4.6.1. Level 1

- In case of providing the full assessment report and/or list of questions and answers between the applicant and the reference agency in addition to complete CTD, the analysis could be postponed to the first shipment before placing into the market.

- A conditional MA approval will be issued to grant analysis before placing first shipment into the market.

4.6.2. Level 2

- In case of providing only the CTD, sample analysis will be conducted in pre-authorization stage.

4.7. Regulatory notes:

- Reliance doesn't mean dependence.
- Approval by reference drug regulatory agency does not oblige the EDA to approve the application.

- During the evaluation and for safety, efficacy or quality concerns; the concerned unit / administrations might request to transfer the application to regular pathway. However, EDA commits to clarify the decisions for any case.
- All the required scientific data should be submitted in English.

5. Glossary:

API: Active Pharmaceutical product

CPP: Certificate of Pharmaceutical Product

CTD: Common Technical Document

DP: Drug Product

DS: Drug Substance

EDA: Egyptian Drug Authority

EMA: European Medicine Agency

FDA: Food & Drug Administration

FPP: Finished Pharmaceutical product

GMP: Good Manufacturing Practice

MA: Marketing Authorization

NRA: National Regulatory Authority

SOP: Standard Operating Procedures

WD: Working Day

WHO: World Health Organization

6. References:

- Good reliance practices in regulatory decision-making for medical products: high-level principles and considerations. Draft working document,WHO, Rev.1, August 2020.
- Saudi Food & Drug Authority: Registration according to verification and abridged, version 2.1.
- Decree of Egyptian Drug Authority's president No. 343/2021

7. Annexes

Annex I: Required documents

Annex II: Time frames

Annex I

Documents required for each track

No.	Required Document	Yes	No	NA
General requirements for all tracts				
1	Complete CTD file, with detailed analytical SOPs, the dossier should be the same as that submitted to the reference drug regulatory agency for modules 2-5.			
2	All annexes and appendices related to safety and efficacy issues of the product with full details.			
3	A declaration letter by the product owner / applicant stating that all aspects of the product's quality, safety and efficacy are identical to the currently approved by the reference agency with the same dose, indication, warnings and precaution.			
For Abridged pathway				
1	Full assessment report along with other relevant supporting documents from the reference regulatory agency such as: reports pertaining to post-approval variations, post marketing commitments, supporting			

	documents on comparative safety and efficacy studies submitted to the reference agency.			
2	Question & Answer documents between the applicant and the reference agency with all annexes.			
3	Any correspondence between the applicant and the reference agency relating to safety and efficacy or queries, the risk management plan, or benefit-risk decisions should be provided.			
Inspection requirements				
1	List of each site where the product (Drug Substance and Drug Product), if authorized, is or would be manufactured			
2	Updated Site Master File including; • Relevant Premises & utilities information about each site. • Current status of the manufacturing site(s) with respect to current good manufacturing practice (cGMP) requirements. • Legible color printouts of water treatment and air-handling systems, including pipeline and instrumentation drawings in A3 or A2 format.			

3	List of all the products and dosage forms manufactured on- the same site especially same production lines.			
4	Process Validations reports for DS & DP manufacturing.			
5	Latest full inspection report(s) for inspection performed by the reference regulatory authority in the past three years and their outcomes.			
6	Last Annual product review.			
7	One complete batch manufacturing and packaging record.			
8	Cold chain Storage & transportation procedures.			
9	List of any recalls in the past three years related to products with quality defects (if found).			
10	Any warning letter or equivalent regulatory action (production-line specific) (if found).			

Annex II

Time frames

No.	Step	Time frame
1	Request inquiry approval	5 WD
2	Submission for pricing	Within 30 WD after Inquiry approval
3	Submission of the registration file	Within 30 WD after pricing submission
4	EDA 1st inquiries	5 WD incase of 30 WD pathway
		10 WD incase of 60 WD pathway
5	Time taken by company to reply for the needed inquiries	Maximum 60 WD (to be renewed once)