Central Administration of Pharmaceutical Product
General Administration of Human pharmaceuticals registration

Guideline

GUIDELINE ON
Reliance Practices During Registration of Medicinal Products

Year 2022

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I. Introduction

Egyptian Drug Authority follows WHO guidelines of GRelP in the context of WHO's approach of regulatory system strengthening and as a cornerstone for effective, efficient and smart regulatory activities of medicinal products.

In view of the extent and complexity of the regulatory challenges, establishing and maintaining a mature regulatory system will require adequate resources, including skilled, capable human resources and a significant financial investment. Thus, EDA promotes considering enhanced, innovative and more effective forms of collaboration to make the best use of the available resources and expertise, avoid duplication and placing greater focus at national level on value-added regulatory activities that cannot be undertaken by other authorities, such as, but not limited to: vigilance, market surveillance, local manufacturing & distribution.

EDA believes that reliance pathways bring benefits to patients, industry and government, by facilitating and accelerating access to quality assured, effective and safe medicinal products while saving resources and decreasing burden on assessors and regulators at EDA.

II. Purpose

The purpose of this document is to promote a more efficient approach to regulation, by providing guidance, definitions, key concepts and illustrative reliance mechanisms & activities that are adopted and implemented by EDA in assessment and evaluation of medicinal products.

III. Scope

This document covers activities and procedures that are conducted in EDA to implement reliance concepts in the field of regulation of medicinal products during registration, renewals & life-cycle maintenance. EDA considers reliance approaches in particular for certain categories of medicinal products, these include, but are not limited to, medicinal products for priority diseases for which there are unmet medical needs, medicinal products to be used in public health emergencies or during shortages and also for innovator medicinal products.

IV. Definitions and Concepts

- **Reliance:**

  The act whereby the NRA in one jurisdiction may consider 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.

- **Recognition:**

  Acceptance of the regulatory decision of another regulatory authority or trusted institution. Recognition should be based on evidence that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of EDA. EDA adopts a unilateral recognition approach.

- **Abridged Registration:**

  Registration procedure that is facilitated by reliance, whereby a regulatory decision is solely or partially based on application of reliance. This allows saving resources and time as compared with standard pathways, while ensuring that the standards of regulatory oversight are maintained.

- **Sameness of Product:**

  Sameness means that two products have identical essential characteristics, i.e. the product being submitted to the relying authority and the product approved by the reference regulatory authority should be essentially the same. (e.g. same qualitative and quantitative composition, same strength, same pharmaceutical form, same intended use, same manufacturing process, same suppliers of active pharmaceutical ingredients, same quality of all excipients).

- **Stringent Regulatory Authority (SRA):**
  A regulatory authority which is:
  (a) a member of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), being the European Commission, the US Food and Drug Administration and the Ministry of Health, Labour and Welfare of Japan;
  (b) or an ICH observer,
  (c) or a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement.

V. EDA's approved list of reference countries

EDA's list of reference countries is approved by the Technical Committee of Drug Control on 31/12/2009 & 16/9/2021 chosen according to the WHO criteria and its definition to the SRAs.
EDA relies on the regulatory decisions and/or regulatory work products of the Regulatory Authorities of those countries while evaluating and assessing applications.
The current list consists of 22 countries that EDA can rely on their regulatory authorities includes:

- Australia (TGA)
- Austria (Bundesamt für Sicherheit im Gesundheitswesen)
- Belgium (afmps)
- Canada (Health Canada)
- Denmark (The Danish Medicines Agency)
- Finland (FIMEA)
- France (ANSM)
- Germany (Pharm Net)
- Iceland (Lyfjastofnun- Icelandic Medicines Agency)
- Ireland (HPRA)
- Italy (AIFA)

- Japan (Ministry of Health, Labour and Welfare (MHLW))
- Luxembourg
- Netherland (CBG)
- New Zealand (medsafe)
- Norway (Legemiddelverket)
- Portugal (infarmed)
- Spain (aemps)
- Sweden (lakemedelsverket)
- Switzerland (Swiss medic)
- United Kingdom (MHRA)
- United States of America (Food & Drug Administration)

VI. Body of Data

Regulatory reliance can take many forms and encompasses a wide range of regulatory practices. It may be limited to certain regulatory process or function or comprise the full scope of regulatory functions throughout the life cycle of medicinal product.
The examples below illustrate the currently used reliance mechanisms in different regulatory functions at EDA.

1 General Reliance Practices

1.1 Abridged Registration

- Products with EMA and FDA approval shall be registered at EDA within 30 days after the verification of the sameness of a medicinal product and taking into consideration the country-specific information submitted for review.
- Products with EMA or FDA approval shall be registered at EDA within 60 days after the verification of the sameness of a medicinal product and taking into consideration the country-specific information.

2 Detailed Examples of Reliance Practices

2.1 Evaluation of Clinical and Non-clinical Data

The following categories of medicinal products are waived from conduction, or evaluation of clinical and non-clinical data:

- Innovator medicinal products that are approved by an SRA included in the approved list of reference countries.
- Multi-source generics having a reference similar product that is approved by an SRA included in the approved list of reference countries or a WHO-PQ product.

2.2 Evaluation of Stability Data

- Imported medicinal products are waived from Conduction of stability study in Egypt (i.e. EDA only review the resulting data of studies that were formerly conducted at country of origin) provided that study conditions (e.g. Stability Zone) are in accordance with EDA

2.3 Evaluation of Bioavailability and Bioequivalence Data

- Innovator medicinal products that are approved by an SRA included in the approved list of reference countries are waived from conduction and evaluation of BA/BE study.
- Imported medicinal products from reference countries are waived from conducting BA/BE studies in Egypt. (i.e. EDA only review the resulting data of studies that were formerly conducted at country of origin) provided that study conditions are in accordance with EDA.
- Imported medicinal products from reference countries are waived from on-site follow-up of bioequivalence centers by EDA.

2.4 Evaluation of Inserts Data

- Insert from any of SRA included in the approved list of reference countries can be used as a reference (the product must adhere to the reference).
- Warnings/contraindications and any other safety concerns rose by those SRAs, and confirmed by relevant EDA committees are to be generalized in inserts of relevant products.
- Emerging safety issues raised by those SRAs, detected and reviewed by the general administration of Pharmacovigilance and transferred to the general administration of Pharmaceutical references and inserts are presented to the Pharmacology committee to study the Generalization of the safety information in all inserts of relevant products.

2.5 Verification of Sameness

EDA reviews Certificate of Pharmaceutical Product (C.P.P) to verify the sameness of a medicinal product to ensure that it is the same as that assessed by the reference country in order to confirm the applicability of the assessment outcomes that shall be relied upon in making its regulatory decision.

2.6 Quality Evaluation of Active Pharmaceutical Ingredients (APIs)

EDA, under certain conditions, may recognizes Certificate of Suitability (CEP) for monographs in The European Pharmacopoeia for APIs as a validation of the quality of a certain API instead of re-evaluation of the S-Part of the quality module.

2.7 Public health emergency

The EUA is a risk-based procedure for assessing unlicensed medicinal products for use during public health emergency cases in an emergency context when limited data are available and the products are not yet ready for application for licensure through the normal marketing authorization

pathways.

In case of imported products, the product must have been granted an EUA and/or is in market of the country of origin or the product is listed by the WHO for emergency use.

The product should be included in the treatment protocols for such pandemic or epidemic situation which is approved by the WHO or the Egyptian governmental health authorities.

In case of EUA for generic medicinal product, EDA rely on an innovator product which has been at least granted an EUA approval or has a well-established approved indication for treating such epidemic or pandemic situation, for instance by the WHO, EMA, FDA, or Japan.

2.8 *Evaluation of Post-approval Changes*

In accordance with the same reliance principles and mechanisms adopted in the initial marketing authorization, EDA may also broadly apply those mechanisms in assessing post-approval changes that are already approved by another reference countries.

2.9 *Withdrawal and cancellation of medicinal products due to safety and efficacy issues*

- EDA relies on and takes into consideration the information received concerning safety and efficacy issues of medicinal products from the global authorities' especially international organization as World Health Organization 'WHO' and stringent regulatory authorities (SRAs) included in the approved list of reference countries.
- EDA shall review information obtained from communication with international authorities to know the reasons of withdrawal or cancellation understanding other RA's action on the application.
- EDA shall follow evidence-

based and risk-based review approaches based on risk level and reliance approaches, considering national laws, regulations, regional, international guidelines, monograph and standards.

2.10 On-site Factory Inspection

EDA might rely on other's NRAs inspections in some cases as follows:

- Imported medicinal products from reference countries are waived from EDA on-site inspection as a prerequisite for approving the manufacturing site. Whereas EDA shall only review the site valid GMP certificate.
- Imported medicinal products from non-reference countries (That are not marketed in any of the reference countries) may be waived from EDA on-site inspection as a prerequisite for approving the manufacturing site, provided that the site has a valid inspection accreditation report by an SRA included in the approved list of reference countries or certifying international body.

VII. References:

- WHO Annex 10 Good reliance practices in the regulation of medical products: high level principles and considerations
- EDA Chairman Decree 780 for the year 2022
- Ministerial decree 820 for the year 2016
- Ministerial decree 425 for the year 2015, article number 4
- Ministerial decree 146 for the year 2022, article 1 clause b & c
- Guidelines on Emergency Use Approval, version 2 – 2022.
- Technical committee for drug control decision on 28/7/1995.
- Technical committee for drug control decision on 31/12/2009.
- Technical committee for drug control decision on 16/09/2021.