Ethiopian Food and Drug Authority

Guidelines on Reliance for Regulatory Decision Making

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Abbreviations and Acronyms

EFDA:	Ethiopian Food and Drug Authority
EMA:	European Medicine Agency
EU:	European Union
GCP:	Good Clinical Practice
GMP:	Good Manufacturing Practice
IGAD:	Intergovernmental Authority on Development
MA:	Marketing Authorization
NRA:	National Regulatory Authority
REC:	Regional Economic community
QC:	Quality Control
SRA:	Stringent Regulatory Authority
WHO PQ:	World Health Organization Prequalification

1. Background

The advent of globalization and improvements in technology, the development, production, and distribution of medicinal products including vaccines and other biological products, have become more interconnected across countries. Hence, regulatory decision outcomes on safety, efficacy, and quality of medicinal products can be shared among different national regulatory authorities (NRAs). International regulatory cooperation has thus been strategically promoted and adopted by NRAs to improve regulatory processes while ensuring timely access to medicines.

The Food and Drug Authority of Ethiopia is mandated by Proclamation No. 1112/2019 to ensure that all Medical products approved and made available in the market meet the prescribed standards of quality, safety and efficacy. Article 19(1) of this proclamation decrees that “the rigor of regulatory assessment of medicines and medical devices shall be commensurate with the products type, nature and potential risk to human health”. Accordingly, EFDA is continually working to enhance its performance by improving the quality of its regulatory processes, proportionating risk of medicinal products regulated and reliance on the decision made by recognized regulatory authority (ies) to ensure timely access to safe, effective and quality innovative medical products to patients.

The Authority may rely on regulatory decisions from other regional and international regulatory authorities when deemed necessary. Instituting good reliance practices is recognized as one of the impactful initiatives that would facilitate the registration and approval process.

The Authority has developed guidelines on reliance for regulatory decisions to promote a more efficient approach for regulatory oversight, access to quality-assured, effective and safe medical products. The reliance is an alternative /non-routine authorization pathway to the standard approval pathways - especially for applications where the safety and efficacy of the product have already been confirmed or when the Clinical Trial has been approved and/or initiated in a recognized regulatory authority (ies). The reliance implies that the work done through Clinical Trial Assessment reports, Marketing Authorization (MA) assessment reports, GMP inspection reports, and Quality Control

(QC) related decisions is shared by the recognized regulatory authority (ies) while the EFDA uses these works according to its own scientific knowledge and regulatory procedures and retains its own regulatory responsibilities. This will be supported by a post-marketing surveillance system.

The reliance can be unilateral, bilateral (mutual) or multilateral for regulatory decision but the authority maintains its own regulatory responsibilities for decision-making.

It represents the Authority's current thinking on the safety, efficacy and quality of medicines and it should not be considered as an exclusive approach. The authority reserves the right to request any additional information to establish the safety, efficacy and quality of medicines.

2. Definitions

Regulatory Reliance: An act whereby the EFDA takes into account and gives significant weight to assessments performed by another NRA or trusted institution or recognized regulatory authority, or to any other authoritative information in reaching its own decision.

Assessment: Any evaluation of information for conduction of a regulatory function (e.g. evaluation for a clinical trial application, evaluation of an initial authorization for a therapeutic products or any subsequent post-authorization changes, evaluation of safety and efficacy data, evaluation as part of an inspection, etc.).

Mutual Recognition: Mutual recognition is a process which allows conformity assessments (of qualifications, product) carried out in one country to be recognized in another country. Recognition indicates that evidence of conformity with the regulatory requirements is sufficient to meet the national regulatory requirements.

Reliance pathways: An alternative non-routine approval pathways used by the authority in its regulatory decisions regarding marketing authorization, GMP/GCP, Laboratory test results of a product based on assessment outcomes of recognized regulatory authority (ies) or institutions.

Medicinal Products:A substance or combination of substances that is intended to treat, prevent or diagnose a disease, or to restore, correct or modify physiological functions by exerting a pharmacological, immunological or metabolic action.

Authority: Ethiopian Food and Drugs Authority

3. Objectives

To provide guidance and accelerate the regulatory approvals of medicinal products approved by recognized regulatory authority (ies), regional and international bodies.

4. Scope

This Guideline covers reliance procedures for marketing authorization, GMP inspections, GCP inspection and clinical trial authorization, vigilance and laboratory testing for medicinal products.

5. Principles of Reliance

The principles of the reliance in this guideline are in line with the WHO recommendations to optimize innovative and more effective forms of collaboration in order to make the best use of the available resources and expertise, and avoid duplication of efforts to ensure the safety, quality and efficacy of medicinal products.

a. Sovereignty

Reliance is a sovereign decision. The Authority decides when and how to use reliance and in which circumstances. No party imposes to accept or reject any product (s) approval by other parties. Approval by the EFDA recognized Regulatory Authority (ies), regional and international bodies does not oblige the EFDA to approve the applications. The EFDA retains its prerogative to assess applications and apply judgments that consider benefits and risks as it applies to the Ethiopian context.

b. Legal basis

Reliance procedures are coherent with the national legal frameworks and supported by clear mandates that aim at the efficient implementation.

c. Transparency

The reliance approach remains transparent regarding laws, requirements, regulatory systems and processes to be followed as well as the rationale for relying on a specific entity should be disclosed and understood by all parties.

d. Competency

The necessary competencies for critical decision making for proper implementation of the reliance guidelines should be available. The competencies are bench-marked by transparent processes that develop trust on the capacities of recognized regulatory authorities.

e. Consistency

This guideline defines the category of products and practices to ensure consistency of the reliance decisions.

6. Area of Reliance

6.1. Marketing Authorization

The authority may apply reliance procedures for granting Marketing Authorization in the following conditions as applicable:

1. Medicinal products that have been evaluated and listed as a WHO Prequalified Products. Such applications will be verified and approved through the WHO PQ collaborative registration procedure.
2. The medicinal product have been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the EU's Article 58 Procedure or the Swissmedic's Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (launched July, 2014).
3. The medicinal product has been granted marketing authorization by stringent regulatory Authority (ies) as recognized by EFDA. Such applications will be addressed through EFDA SRA Medicine Registration Guideline.
4. The medicinal product has been evaluated and accepted by the intergovernmental agency for development (IGAD) through a joint assessment scheme.
5. Medicinal products that have been approved by different regional economic communities (RECs) as part of African Medicines Regulatory Harmonization (AMRH) initiatives. In addition to the dossier applications submitted by the applicant, assessment outcomes and other relevant documents should be submitted from recognized REC to EFDA for such applications to be evaluated by authority`s guidelines.
6. The medicinal product has been granted marketing authorization by the NRA of the country that has signed unilateral, mutual or multilateral recognition agreement with

EFDA will be considered based on the memorandum of understanding signed by both parties.

6.2. Clinical Trials Authorization

The Authority may apply reliance procedures for GCP Inspection and Clinical Trial Authorization, if:

1. The medicinal product under investigation has already been evaluated and listed as a WHO Prequalified Product.
2. The medicinal product under investigation has already been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the European Union Article 58 Procedure or the Swissmedic Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (launched July, 2014)
3. The trial has been authorized or the investigational product has been granted marketing authorization by EFDA recognized NRAs or regional or international bodies.
4. The trial or the investigational product has been evaluated and judged satisfactory at a joint review meeting of the African Vaccine Regulatory Forum (AVAREF).

6.3. GMP Inspections

The authority may apply reliance procedures for GMP inspection in the following circumstances as applicable:

1. The manufacturing facility GMP compliance has been accepted by WHO pre-qualification team.
2. The manufacturing facility has been inspected by EMA, Swissmedic, or WHO pre-qualification team and the product has been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the EU's Article 58 Procedure or the Swissmedic's Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (launched July, 2014).

3. The manufacturing facility has been inspected by EFDA recognized NRAs and the NRA in the country of origin and the product has been granted marketing authorization by the SRA.
4. The manufacturing facility has been inspected by IGAD joint GMP inspection.
5. The manufacturing facility has been inspected by joint inspection of other regional economic communities (RECs) as part of African medicines regulatory Harmonization (AMRH) and the NRA in the country of origin and the products that have been approved by joint assessments of recognized RECs.
6. The manufacturing facility has been inspected and the producthas been registered or granted marketing authorization by the Regulatory Authority that has signed a mutual recognition agreement with EFDA and the product has been marketed by the country of the NRA.

6.4. Laboratory Services

According to article 19 (1) of the Food and Medicine Administration Proclamation No. 1112/2019, the rigorousness of regulatory assessment of medicine shall depend on the product's type, nature, and potential risk to human health. Considering this, to ensure timely access to safe, quality and effective medicines to the patients, EFDA may rely on laboratory test results/ certificates of analysis from WHO Pre-qualified or ISO/IEC 17025accredited laboratories for regulatory decisions.

1) The authority will retain list of accredited/WHO prequalified medicine testing laboratories with their scope of accreditation and update the list on regular basis by verifying validity of their certificate of accreditation.

2) The authority may use the laboratory test results, with verification as necessary, of other accredited or WHO prequalified subcontracted laboratory for products collected from Ethiopian market (consignment, suspected or PMS samples).

3) The authority may use information regarding PMS data from such accredited laboratories as an alarm to conduct post market surveillance on the same

product but shall not take any measures on products on the market based on other laboratory test results.

6.5. Reliance in Vigilance Related Decisions

The Authority is mandated by article 4(10) to “ensure that evidence of existing and new adverse events and information about pharmaco-vigilance of globally monitored products are followed upon and, as appropriate, take the necessary legal measure”. In order to ensure that safety issues are promptly identified and the necessary interventions implemented, the Authority considers decisions from EFDA recognized regulatory authority (ies), WHO safety monitoring, and regional collaboration schemes on the safety of medical products.

The regulatory decisions of the Authority leveraging safety decisions from such recognized regulatory Authority (ies) are geared towards ensuring appropriate and safe use of registered medical products.

The authority may apply reliance procedures for using pharmacovigilance reports from reliable sources in the following circumstances:

1. If the product is available in the market (in use) at the time of reporting and sameness of the product is assured
2. if the information sources is WHO Member States and its shared data on the safety of medical products in the WHO database of individual case reports of safety, VigiBase, the shared information may be used as a single source of pharmacovigilance information to confirm and validate any signals of adverse events associated with medicines and vaccines that they have observed.
3. If the information shared is from other reliable NRA, the information may be used as a signal for initiating safety monitoring on the same product in the Ethiopian market
4. If the source of the information is WHO alert system, the authority may take appropriate measures by verifying sameness of the product.

7. Reliance Procedures

The authority may fully rely on EFDA recognized NRAs, regional or international bodies, or may undertake verification or partial assessment as necessary.

7.1. Verification of Documentation

The Authority may verify the sameness of GMP compliance report, dossier assessment report, laboratory testing report (when applicable), and safety report shared through WHO to EFDA.

7.2. Abbreviated review

The Authority may conduct abbreviated review of dossiers, and verify clinical trial authorization report, cGMP report or certificate, laboratory testing report (when applicable), and safety report shared through recognized NRA and other recognized RECs.

7.3. Joint assessment

The Authority accepts all regulatory outcomes of all joint dossier assessment, GMP inspections, GCP inspection and clinical trial authorization undertaken by IGAD.

8. EFDA Recognized Regulatory Authorities

1. The following regulatory authorities are recognized by EFDA as stringent regulatory Authorities:
2. Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Ireland, Italy, Japan, Netherlands, Norway, Switzerland, United Kingdom, United States of America, European Medicine Agency (EMA) and WHO Prequalification.
3. EFDA may list different regional economic communities (RECs) as part of its reliance approach.
4. These list of recognized SRA and/or regional RECs will be updated on regular basis.

References

- WHO. (2021). Good reliance practices in regulatory decision-making: High-level principles and recommendations. TRS No. 1033, Annex 10.
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- Rwanda FDA (2021). Guidelines on Reliance for Regulatory Decision Making in Rwanda, Doc. No.: DIS/GDL/033.
- South Africa Health Products Regulatory Authority (2021). Reliance Guideline. Version 2.0.