ETHIOPIAN FOOD AND DRUG AUTHORITY

Medicine Evaluation and Marketing Authorization Led Executive office

Guidelines on Reliance for Regulatory Decision Making for Marketing Authorization,

Document No.:	**EFDA/GDL/042**	Version No:	002
Date of approval:	30/11/2023	Date of First issue:	2021

Document History

Version No.	Reason for Amendment	Effective Date
001	**Newly issued document**	20/12/2021
002	Amended in line with WHO-GBT audit recommendation to revise the naming of the MA function in line with the new Nomenclature	01/01/2024

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Contents

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
MEMA	Medicine Evaluation and Market Authorization
WHO PQ:	World Health Organization Prequalification

1. Background

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".

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 globally.

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, EFDA 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, including, but not limited to vigilance, market surveillance, local manufacturing & distribution with the special focus of increasing access to quality, safety and efficacy assured medicines for the end users.

Therefore, 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 while saving resources and decreasing burden on assessors and regulators at EFDA.

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 ClinicalTrial has been approved and/or initiated in a recognized regulatory authority (ies). The reliance implies that the recognized regulatory authority (ies) shares the work done through Clinical Trial Assessment reports, Marketing Authorization (MA) assessment reports, GMP inspection reports, and Quality Control (QC) related decisions 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 decisionbut the authority maintains its own regulatory responsibilities for decision-making.

It represents the Authority's current thinking on the safety, efficacy and quality ofmedicines 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. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others.

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 or or essentially the same to support product sameness, 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).

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 atherapeutic products or any subsequent post-authorization changes, evaluation of safety and efficacy data, evaluation as part of an inspection, etc.).

Recognition: The recognition is routine acceptance of the regulatory decision of another regulator or trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B. Recognition should be based on evidence of conformity that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of the relying authority. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement.

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.

Emergency Use Authorization (EUA): **EUA** is a use authorization issued for unregistered drugs and vaccines in a public health emergency.

Reference regulatory Authority: Refers to a national or regional authority, or a trusted institution such as WHO prequalification (WHO PQ), EMA, or USFDA, whose regulatory decisions or work products are relied upon by another regulatory authority to inform its own regulatory decisions.

Regional regulatory system: A system composed of individual regulatory authorities, or a regional body composed of individual regulatory authorities, operating under a common regulatory framework but not necessarily under a common legal framework. The common framework must at least ensure equivalence among the members in terms of regulatory requirements, practices and quality assurance policies. The system or regional body may have enforcement powers to ensure compliance with the common regulatory framework.

Work-sharing: Work sharing is a process by which the regulatory authority of two or more jurisdictions shares activities to accomplish a specific regulatory task. The opportunities for work-sharing include, but are not limited to, jointly assessing applications for authorization of clinical trials, marketing authorizations or good practices inspections, joint work in the post- marketing surveillance of medical product quality and safety, joint development of technical guidelines or regulatory standards, and collaboration on information platforms and technology. Work-sharing also entails the exchange of information consistent with the provisions of existing agreements and compliant with each agency's or institution's legislative framework for sharing such information with other NRAs.

3. Objectives

3.1. General objective

The purpose of the guidelines is to provide a coordinated and consistent mechanism to promote a more efficient approach to regulatory oversight, thereby promoting access to quality-assured, effective, and safe medical products.

3.2. Specific objective

- **a.** Serves as a comprehensive operational plan to address the context of reliance in supporting regulatory practices, procedural documents, and other guidance integration;
- **b.** Defines the reliance operations structure and assigns essential tasks to all functions involved in the regulation of medical products;
- **c.** Provides mechanisms for coordination and cooperation of the Authority with other regulatory authorities within the region or globally;
- **d.** Integrates reliance operations to ensure consistency with nationally recognized regulatory policy and guidance;
- **e.** Develops a common understanding of risk management and establish a system to monitor those risks to ensure early action;
- **f.** Clarifies the roles, principles, and key approaches for regulatory reliance to be used by the EFDA concerning the availability of priority medical products according to the country's needs;
- **g.** Establishes a minimum level of regulatory requirements for selection of reference regulatory Authorities to rely on.

4. Scope

This guideline covers the different regulatory activities that are conducted in the Ethiopian Food and Drug Authority to implement reliance concepts during Market Authorization of medicinal products, GMP inspections, GCP inspection and clinical trial authorization, vigilance and laboratory testing for medicinal products as well as life cycle management of EFDA regulated products.

This guideline also considers reliance approaches incase of the conditional market Authorization for unmet medical needs and Emergency use authorization of medicinal products during public health emergencies.

5. Principles of good reliance practice

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. Reliance pathways

The authority employs reliance pathways in its regulatory decisions to accelerate the approval of various activities, such as clinical trials, GMP/GCP compliance, quality control procedures, medical product marketing authorization, and vigilance decisions. The reliance aims to reduce timelines

compared to standard regulatory practices, but the authority shall remain responsible and accountable for the decisions taken.

This risk-based approach considers various factors, such as the type of products, public health needs and priorities, level of resources and expertise available, and opportunities for reliance.

For instance, in the case of marketing authorization, the **assessment process may involve** the following five (5) reliance scheme.

i. **Verification of the sameness of the product** is necessary to ensure that the medical product is the same as the one assessed by the reference regulatory authority.

ii. **Confirmation of the applicability of the assessment outcomes of another authority** is essential for regulatory decision-making in the national context. This includes assessing legal and regulatory settings, benefit-risk assessment, comorbidities, unmet medical needs, risk management plans, and quality-related specificities such as climatic zones for product stability. In case of any differences, such as in the target population, epidemiology, and other disease-related features, concomitantly used medicines, and other factors that can substantially affect the benefit-risk profile of the medicine, as well as quality parameters, particularly related to the stability under different climatic conditions, appropriate action needs to be taken.

iii. **An abridged review** of the quality, safety, and efficacy data should be conducted, taking into account the information provided in the assessment reports of the reference regulatory authority.

iv. **Joint assessment or work-sharing** between two or more regulatory authorities is recommended. This can involve a primary review by one authority, followed by a second review by another authority, and a joint assessment session to finalize the assessment report and comments

v. **Recognition procedures** involve a model in which authorities/organizations review medicinal products intended to be marketed in countries or regions other than their own. Examples of such review procedures include, Swissmedic's Marketing Authorization for Global Health products, and medicines reviewed through the WHO collaborative prequalification program. With such review procedures, the authority can directly recognize the outcome of this review.

7. Area of reliance

7.1. Marketing Authorization

- **Conditions for reliance procedures of granting Marketing Authorization**

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 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.
7. Furthermore, products registered by WHO-listed agencies may be considered through the reliance pathways on a case-by-case basis.
8. Where a Certificate of Suitability to the monographs of the European Pharmacopoeia (CEP) or Confirmation of API Prequalification (CPQ) is issued, it may be considered through the reliance pathway by only focusing on specific sections not covered under CEP or CPQ.

A. Eligibility Criteria of the candidate products

Medicine and biological product approval by reference drug regulatory agency and/or by any of EFDA recognized regional or international organization does not oblige the EFDA to approve such

medical product application. on the other hand If any drug at any time, for safety and or quality reasons is withdrawn or banned or certain restrictions are imposed by any of the recognized regulatory body, then the medicine registration and Market authorization office will take similar action and such application are not eligible for review.

- **Reliance under normal or routine procedure**

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 and/ or regional or international organization or essentially the same to support product sameness, and that acceptance of differences is mostly a case-by-case approach based on justification provided by the manufacturer.

- 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
- If incase some potential differences exist between the EFDA submitted dossier and that for recognized body 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.

- **Reliance under emergency situation**

In all applications for reliance-based EUAs, a signed declaration attesting to the sameness that the product, including but not limited to composition/ formulation, strength, manufacturing of finished products and active pharmaceutical ingredients, specifications, packaging, product information, and

others, at the time of the submission and after EUA , are the same in all aspects as the product given the EUA by recognized NRA of the country or regional regulatory body or international organization(WHO) and to notify any updates throughout product life cycle.

In addition, the application might be accompanied by an undertaking by the manufacturer to complete the development of the drug and biological product applied for an EUA to shift to full registration as applicable.

i. Application Submission

For both types of reliance based application submission (under none emergency and Emergency situation) applicants are recommended to submit their application through designated online eRIS portal.

For specific requirements on the electronic submission using eRIS portal and methods of submission of all documentation (e.g. application submission format, pre-submission check list), refer to the respective registration guidelines (Medicine, Biological, Vaccine, etc) and post-approval changes Authorization guidelines available on EFDA official website at www.efda.gov.et/

ii. Procedure of submission

a. An optional pre-submission technical support step through the pre-screening and pre-import technical support team can be implemented to verify the submitted documents and guide the company to the most suitable review/approval pathways.
b. The applicant should submit their request inquiry remotely through the relevant application pathway of eRIS portal and specify the desired path according to his/her need and upload the required CTD data and annexed documents (cGMP, CPP , payment receipt , all data required to be filled in the online application form of eRIS,) to be reviewed by concerned pre-screening and assessment team members within the specified timeline.

iii. Pre-screening

The pre-screening desk lead at the directorate of medicine registration & Market Authorization shall assign an incoming application (New Medicine, Biological, vaccine, etc) to dossier screener for the determination of the completeness of the application. Thereafter, application with all the mandatory information for initial assessment shall be referred to the medicine quality desk coordinator or none clinical and clinical coordinator and Biological desk coordinators for a simultaneous review of the

application by respective assessment team . On the other hand, any unsatisfactory application may be notified to the applicants or rejected upon screening or unsatisfactory response. An applicant may request for withdrawal of the application after screening, before evaluation, during query response and after unsatisfactory query response. Applicants of rejected applications may appeal to the Authority as per the existing complain handling process.

iv. Evaluation of application data and recommendation

Each desk lead of assessment team shall assign the required section of the CTD section and other relevant documents to the respective level of assessors (primary / lead Quality assessor, Clinical & none clinical assessor, Biological assessors) and each level of assessors shall perform their activities as described below.

a. Evaluation of the submitted dossier and documents shall be performed in compliance with the defined time frames on basis of verification of sameness and/or selective detailed review as deemed necessary by each assessment team.
b. Any questions that may arise during the evaluation process shall be subjected for discussion as deem necessary. The consolidated list of quires will verified and forwarded directly to the applicant and the applicant response reply should be submitted within specified timeframes. as stated in EFDA citizen charter.
c. In case of conditional approval of the product's registration or EUA by the reference agency or Regional body(ies) or international organization, EFDA may take the same decision as that of the reference agency and may also grant the product a conditional approval or EUA. In the event of pandemic, EFDA assessors should fully participate in the joint assessment of medical product intended for public health emergency situation with the recognized NRA or regional or international organization like WHO.
d. The following categories of medicinal products requires the opinion of drug advisory committee on clinical and non-clinical data on case by case bases

   ▪ Innovator medicinal products that are approved by a recognized bodies included and in the approved list of reference countries, but not approved for Ethiopian Market through the registration and Market Authorization system (if the product has been authorized through import permit or EUA at the time of product dossier application , not considered as new drug for Ethiopian market, but an applicant is requested to provide drug safety & efficacy history

in Ethiopia or other African countries)

▪ Multi-source generics having a reference similar product that is approved by the recognized body and included in the approved list of reference countries or a WHO-PQ product, but not approved for Ethiopian Market through the registration and Market Authorization system (if the product has been authorized through import permit or EUA at the time of product dossier application , not considered as new drug for Ethiopian market, but an applicant is requested to provide drug safety & efficacy history in Ethiopia or other African countries)

e. If the applicant fails to provide EFDA with necessary information and cooperation, EFDA is entitled to terminate the procedure and switch to any other pathway including the normal/regular//Routine registration process.

Illustrative guidance on dossier assessment

The reliance of dossier assessment report in combination with the cGMP and GCP inspections reports of the EFDA recognized bodies could form a basis for making decision by the Authority. The evaluation report shall include documented outcome of the evaluation of quality, safety, efficacy/immunogenicity of the product and outcome of the inspections by the assessors and inspectors respectively with review of the additional country specific application dossier section.

The applicant shall be expected to provide tentative timelines for the submission of additional data based on the expected dates of completion or planned interim analyses of studies currently ongoing or being initiated in case of conditional approval and/ or EUA or for application submitted with commitment during the initial submission of the application dossier(dossiers from SRA). The submission of additional data should be clearly numbered as per the respective product specific guidelines.

In instances where external expertise apart from the regulatory reliance is needed, the Authority may use its technical committees or Drug advisory committee that shall also include the internal regulatory experts for accelerated review of data on case-by-case basis.

Based on the depth of the dossier assessment, MRMA's reliance based review practice follows different assessment scheme.

A. Verification of the product.

▪ Products with WHO CRP qualification(s) that were assessed through joint assessment scheme

shall be directly registered at EFDA after the verification of the sameness of a medicinal product.

EFDA assessors should check WHO assessment report, Labeling information's(SmPC,PIL and Labels) to verify the sameness of a medicinal product to ensure that it is the same as that assessed through WHO-CRP joint assessment in order to confirm the applicability of the assessment outcomes that shall be relied upon in making the decision.

Similarly, the Authority may verify the sameness of GMP compliance report, laboratory testing report (when applicable), and safety report shared through world health organization (WHO) to EFDA in making its regulatory decision.

B. Abridged Evaluation /assessment of products

This assessment scheme is refers to the regulatory procedure facilitated by reliance, whereby the regulatory decision is solely or partially based on the reliance.

Two situations are possible under this assessment scheme.

Situation 1. Products with EFDA recognized Agency or regional body (ies) approval or WHO-PQ products shall be registered at EDA after undertaking an abbreviated review focusing on benefit risk assessment of data on Quality, safety, efficacy and by taking into account an information in the assessment report of the reference regulatory Authority and taking into consideration the country-specific information(. Eg. Stability study zonal storage condition)

Situation 2. product that has been approved for use under extraordinary circumstances like public health emergency, by recognized national medicines regulatory authority (NMRA), particularly by a stringent regulatory authority (SRA), like the EMA, USFDA and EAC Member States, AMA or AVAREF and the assessment reports are made available to EFDA will undergo abridged evaluation and regulatory decision through reliance mechanisms. The applicant shall be required to submit quality and abridged clinical data together with evidence of authorization in SRA.

Evaluation under reliance procedure during none emergency situation

The information to be used for reliance shall be evaluated according to the prescribed assessment procedure to ensure that submitted documents fulfill the absolute required information for the purpose of the respective assessment.

For registration, the product characteristics (use, dosage, precautions) should conform to that agreed in the authorization by the recognized regulatory authority and for drugs substance, which are

already approved by the recognized regulatory authorities in a particular strength and dosage form are considered as safe and efficacious, while considering registration applicants of new drugs in local perspective.

During the review process, the MRMA desk leader may request an applicant to submit additional information to be included in the dossier or specific statistical / analytical requirements to ensure the quality, safety and efficacy as the case may be. Similarly, there could be circumstances when local clinical trial data is necessitated.

In addition to the full assessment report from the Recognized regulatory Agency , the applicant shall be required to full CTD document as required by the Authority's guidelines before authorization of the application through the reliance pathway.

The mechanism adopted for relying on information encompasses following and the data review would be limited to:-

I. Review of public assessment reports, summary of product characteristics and labelling information.
II. Recognition of reported safety and efficacy concerns of already registered medicines.
III. Review of Certificate of Pharmaceutical Products (CoPP)
IV. Verification of Market Authorization issued by recognized regulatory body
V. Verification of the cGMP compliance status of the manufacturing facility.
VI. Regulatory status review or any other regulatory information available in the public domain through their website.
VII. In case the information is not available on the official website of the recognized Agency, the reference regulatory authority should be contacted directly via electronic mail for a query or clarification on a particular issue under consideration.
VIII. Review of annual product Quality report
IX. Review of stability study data
X. Review of emerging safety issues raised by recognized regulatory bodies, this should be detected and reviewed by the medicine registration and Market Authorization assessors of all levels as the case may be to impose similar restriction and /or to inform all concerned bodies including the general public.

Evaluation under 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 routine and none routine marketing authorization pathways.

In case of imported innovator 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. Moreover, the product should be included in the treatment protocols for such pandemic or epidemic situation which is approved by the WHO or the Ethiopian Ministry of Health.

In case of EUA for generic medicinal product, EFDA 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.

In an event that, EFDA has not fully participated in the joint assessment or no access to the assessment or product dossier, the Authority may use unilateral reliance on the regulatory decision of the trusted competent national medicine regulatory Authorities or organization such as WHO prequalification, EMA,USFDA, Swissmedic, Health Canada, MHRA, Australia TGA and PMDA..

The Authority may employ the following unilateral reliance.

a. **Verification Review:** The Authority shall establish the sameness of the Medical products applied for EUA to ensure that it is the same as that assessed by the reference regulatory Authority. Therefore, the role of the Manufacturer is essential to confirm the sameness of the product and to provide the same documentation to the Authority, except for additional country specific information submitted for review, such as product stability data according to the stability zone and the Local label. As an assurance of the sameness, the applicant is expected to submit at least the following in addition to filling of available supporting documentation which include product-specific characteristics, manufacturing and labelling, nonclinical, clinical and quality information.

   - A formal declaration (as indicated in cover letter in Annex ..) confirming the product offered to the EFDA correspond in all respects (e.g. qualitative/quantitative formula, manufacturing of finished pharmaceutical product (FPP) and active pharmaceutical ingredient (API) facilities, stability, summary product characteristics and labelling, etc.) to the product approved by the reference authority or WHO Prequalification.

- The product EUA/Emergency use listing or marketing authorization certificate issued by the EFDA recognized Authority.
- The corresponding web-link to the registration database
- Lot release certificate issued by the reference regulatory agency. Lot release certificate for imported consignment is based on reliance in the form of summary protocol review along with lot release certificate of recognized regulatory agency of the country.

b. **Abridged assessment:** The Authority shall undertake an abbreviated review focusing benefit risk assessment of data on Quality, safety, efficacy taking into account information in the assessment report of the reference regulatory Authority,

c. **Recognition Review**: The Authority shall confirm the applicability of the assessment outcomes of another Authority or organization for regulatory decision making in the national context, example, in terms of legal and regulatory settings, benefit–risk assessment, co-morbidities, unmet medical needs, risk management plans and any quality-related specificities such as climatic zones for product stability. In case of differences, such as in target population, epidemiology and other features of the disease, medicines used concomitantly and other factors that can substantially affect the benefit–risk profile of a medicine, as well as quality parameters, especially in relation to the stability under different climatic conditions, appropriate evidence should be provided by the manufacturer.

7.2. Clinical Trials Authorization

The authority may apply reliance procedures for clinical trial authorization if:

i. The product under investigation has already been evaluated and listed as a WHO Prequalified Product through the WHO PQ collaborative registration procedure between WHO and the Authority.

ii. The product under investigation has already been evaluated and listed as a product of the WHO collaborative registration pilot for stringently assessed products, including through the Swissmedic Marketing Authorization for Global Health Products or the International Generic Drug Regulatory Programme.

iii. A trial has been authorized or the investigational product has been granted marketing authorization in an ICH founding regulatory member state or region, such as the European Commission (EMA), the United States (FDA), Japan (MHLW/PMDA), or an ICH

standing regulatory members state or region, such as Canada (Health Canada) or Switzerland (Swissmedic).

iv. Products registered by WHO-listed agencies under (SRA) investigation may be considered through the reliance pathways on a case-by-case basis.

v. The trial or investigational product has been evaluated and judged satisfactory at a joint review meeting facilitated by the World Health Organization under the African Vaccine Regulatory Forum (AVAREF).

vi. The clinical trial has been authorized or the investigational product has been evaluated and judged satisfactory by the National Regulatory Authority that has signed a treaty or agreement with EFDA.

7.3. GMP Inspections

The authority may apply reliance procedures for GMP inspection in the followingcircumstances 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 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 theNRA 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 thathave been approved by joint assessments of recognized RECs.
6. The manufacturing facility has been inspected and the producthas been registeredor

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.

7. Imported medicinal products approved by recognized regulatory Agencies are waived from on-site follow-up of bioequivalence centers by EFDA

7.4. 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 onother laboratory test results.

7.5. Reliance in Vigilance Related Decisions

The Authority shall continue to ensure the safety of marketed products through its established vigilance systems. To ensure that safety issues are promptly identified and the necessary interventions implemented, the Authority considers decisions from competent

authorities on the safety of medical products that impact negatively on the health of patients.

i. Regulatory decisions of the Authority by leveraging safety decisions from reference regulatory authority (ies), regional or international bodies are geared towards ensuring appropriate and safe use of registered medical products of reporting and sameness of the product is assured

ii. The medical product of concern should have been registered and/or granted marketing authorization in either an ICH founding regulatory member state or region such as European Commission (EMA), United States (United States Food and Drug Administration), Japan (MHLW/PMDA) or an ICH standing regulatory member state or region such as Canada (Health Canada), Switzerland (Swissmedic).

iii. Further, Vigilance decisions on products registered by WHO-listed agencies may be considered through the reliance pathways on a case-by-case basis.

v. Vigilance regulatory decisions taken, reports, or safety information published on medical product reports by the National Regulatory Authority, regional, and international bodies that have signed treaties with EFDA

8. Evaluation of Post-approval Changes

Following the same reliance principles and mechanisms adopted in the initial marketing authorization, EFDA may also broadly apply those mechanisms in managing post-approval changes that are already approved by reference authorities

9. Withdrawal and cancellation of medicinal products due to safety and efficacy issues

EFDA shall conduct periodic safety, efficacy and quality review of the registered products. For this purpose EFDA may rely on and takes into consideration the information received concerning safety and efficacy issues of any registered medicinal products, in particular those accepted under its reliance procedure reference countries as per this guideline.

Received information shall be reviewed based on the based on the available supporting evidence and risk-based approaches shall be followed by considering national laws and regulations, regional and international guidelines, monograph and standards.

10. Requirement for selection of Reference regulatory Authority

The following selection criteria shall be considered as a minimum requirement to include regulatory bodies or organization in the list of EFDA's reference regulatory authority

10.1. Publishes detailed information on the approved medicines (like public assessment report, labeling information and regulatory action, deferred or rejected product information) on its website or include in the approved or qualified list of medicines throughout the product life cycle as applicable

10.2. Has to be a founding members of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH),

10.3. Has Robust Pharmacovigilance system: a strong pharmacovigilance system has to be in place to monitor and report adverse events associated with drugs, ensuring timely safety updates

10.4. International Compliance: That regulatory authority should be in compliance with international agreements, treaties, and conventions related to pharmaceuticals and medical products.

11. EFDA's Reference regulatory Authority*

The following regulatory authorities are recognized by EFDA as stringent regulatory Authorities:

1. 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.

2. EFDA may list different regional economic communities (RECs) as part of its reliance approach.

*This list of Reference regulatory Authority will be updated on regular basis.

References

1. WHO. (2021). Good reliance practices in regulatory decision-making: High-level principles and recommendations. TRS No. 1033, Annex 10.
2. FDA. (2019). FDA GHANA Reliable Policy. January 1–13. Version1, DocumentNo. FDA/GEN/POL-02
3. Rwanda FDA (2021). Guidelines on Reliance for Regulatory Decision Making in Rwanda, Doc. No.: DIS/GDL/033.
4. South Africa Health Products Regulatory Authority (2021). Reliance Guideline.Version 2.0.