**ETHIOPIAN FOOD AND DRUG AUTHORITY**

**Medicine Evaluation and Marketing Authorization Led Executive office**

Guidelines on Reliance for Medicine Marketing Authorization,

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| 003 | Revised the General EFDA Reliance guideline to make it Specific for medicine marketing authorization | 02/12/2024 |

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**Abbreviations and Acronyms**

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| 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 (EFDA) is mandated by Proclamation No. 1112/2019 to ensure that all medicines approved and made available in the market meet the prescribed standards of quality, safety and efficacy. Article 19(1) of the Proclamation No. 1112/2019 states 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 authority has been making continuous efforts to improve access to quality, safety and efficacy assured medicines for end users. In this regard, the EFDA adopts reliance procedures to optimize the use of the available resources and expertise, minimizing duplication of efforts and to place greater focus on value- added regulatory activities at national level.

In its efforts to enhance its performance, the EFDA has been working to optimizing its regulatory processes, proportionating risks of medicines, relying on the decisions made by reference regulatory authorities to ensure timely access to safe, effective and quality assured medicines. This approach helps save resources and reduce the burden on EFDA assessors and regulators.

The Authority may rely on regulatory decisions from other regional and international authorities when necessary. This reliance can be unilateral, bilateral (mutual), or multilateral, but EFDA retains its own regulatory responsibility for decision-making. Legal provisions supporting this process are outlined in Articles 18, 27, and 32 of Regulation No. 531/2023 and Articles 26, 27, and 29 of the Marketing Authorization Directive No. 963/2023.

This Guideline on Reliance for Medicine Marketing Authorization has been developed to promote a more efficient approach to the registration and approval process, ultimately improving access to quality-assured, effective, and safe medicines. It reflects the Authority's current thinking on the safety, efficacy, and quality of medicines and is not an exclusive approach. The Authority reserves the right to use its own procedures to establish the safety, efficacy, and quality of medicines.

## 2. Definitions

**Abridged Review:** A review procedure that is simplified by reliance, whereby partial assessment focusing on critical elements that are specific to local context (including some technical documents such as stability), are carried out while relying on prior evaluations by reference regulatory authorities or trusted institutions.

**Mutual Recognition:** means a process in which the EFDA or the trusted authority accepts and recognizes one another's assessments and legal decisions based on an evidence that ensures the adequacy of the regulatory requirements to meet the requirements of both parties.

**Recognition: It** is acceptance of the regulatory decision of another regulator or trusted institution by EFDA. Recognition indicates that evidence of conformity with the regulatory requirements of the recognized country`s regulatory authority or trusted institution is sufficient to meet the regulatory requirements of Ethiopia. Recognition should be based on evidence of conformity that the regulatory requirements of the reference regulatory authority or institution are sufficient to meet the regulatory requirements of EFDA. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement.

**Reference regulatory Authority:** Refers to a national or regional regulatory body national regulatory authorities whose regulatory decisions or work products are relied upon by another regulatory authority to inform its own regulatory decisions.

**Reliance pathways**: An alternative non-routine approval pathway used by the authority in its regulatory decisions regarding marketing authorization of a product based on assessment outcomes of Reference regulatory authority (ies) or institutions.

**Reliance:** An act whereby the EFDA considers and gives significant weight to assessments performed by Reference regulatory authority, trusted institution, another NRA or to any other authoritative information in reaching its own decision. EFDA remains independent, responsible and accountable for the decisions taken, when it relies on the decisions, assessments and information of others.

**Sameness:** Sameness means that two products have identical essential characteristics or essentially the same to support product sameness, i.e. the product being submitted to the EFDA 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).

**Trusted institutions:** means a regional or international institution that is involved in assessment and approval (prequalification) of medicines for human use such as WHO prequalification (WHO PQ), IGAD, AMA, EMA, etc whose assessment outcomes or regulatory decisions are relied upon by the EFDA.t

**Verification Review**: A streamlined review conducted by the EFDA focusing on administrative process to reach a regulatory decision, based on registration or authorization by a reference regulatory authority or trusted institution

## 3. Objectives

The objective of this guideline is to provide guidance on key concepts and good reliance mechanisms for the authority when utilizing decisions, reports, and information from other National Regulatory Authorities (NRAs) or institutions in the medicines registration and marketing authorization process. It also describes the activities adopted and implemented by the authority in evaluating applications submitted under this approval pathway, with the aim of enhancing the registration and market authorization process and ultimately improving timely access to quality-assured medicines for the public.

## 4. Scope

This guideline covers the activities and procedures followed by the authority to implement the principles of good reliance practices in the registration and marketing authorization of medicines approved or listed by reference regulatory authorities or institutions. It is applicable to initial marketing authorization, post-approval changes, and renewals of applications submitted under both routine and non-routine procedures.

## 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 available resources and expertise, and minimize duplication of efforts to ensure the safety, quality and efficacy of medicines.

### *a. Sovereignty*

The Authority decides when and how to use reliance for marketing authorization of medicines and in which circumstances. No party imposes to accept or reject any product (s) approval by the reference regulatory authorities or trusted institutions. The authority retains its right to assess applications and apply judgments that consider benefits and risks as it applies to the Ethiopian context. Whenever deemed necessary, the authority may conduct full assessment of dossiers at any time.

***b. Legal basis***

This reliance guideline is coherent with the national legal frameworks and supported by Regulation No 531/2023 and Marketing Authorization directive 963/2023. This is the legal basis that gives the authority a clear mandate to adopt and implement activity undertaken by the WHO, EFDA recognized reference regulatory authorities, mutual or multi-lateral agreement entered by Ethiopia or other International Organization relevant to its regulatory works.

***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 will be disclosed and understood by all parties.

***d. Competency***

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

***e. Consistency***

This guideline sets criteria for selecting reference regulatory authorities and trusted institutions and defines the practices to ensure consistency of the reliance decisions.

## 6. Reliance pathways for Marketing Authorization

The authority employs reliance as one of its regulatory decision-making pathways to accelerate the approval of medicines marketing authorization. The reliance aims to reduce timelines compared to

standard regulatory practices, so as to ensure timely access to safe, effective and quality assured medicines to end users.

This risk-based approach considers various factors, such as the public health needs and priorities, level of resources and expertise available, and opportunities for reliance. Hence, for marketing authorization, the assessment process for applications submitted via reliance pathway may involve verification of authenticity of documents, verification review and/or abridged review. Hence, EFDA may either verify the assessment outcome of the reference regulatory authority or trusted institution to recognize their decision or conduct abridged review of the applications to make its decision after confirmation of the applicability of the assessment outcomes.

Conformity of the assessment outcome 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, the authority may request additional data or reject the application.

### 6.1. Verification Review

Verification and recognition focus on verifying the authenticity and completeness of documented evidence submitted by the applicant. It is applicable for products approved by reference authorities or institution. The verifications involve confirmation of sameness of submitted data with the applications submitted to the reference authority or institution. Both the medicine and the dossier submitted to EFDA should be the same as the one that has been assessed by the reference regulatory authority or trusted institution with respect to its essential characteristics (e.g. same qualitative and quantitative composition, strength, pharmaceutical form, intended use, manufacturing process, suppliers of active pharmaceutical ingredients, and quality of all excipients and manufactured at the same manufacturing site). This involves procedures in which the EFDA accepts the decision of reference regulatory authority or trusted institution except country specific requirements.

Verification is particularly applicable for products approved under WHO-prequalification programs, those assessed and accepted under AMA and IGAD.

### 6.2. Abridged Review

The reference regulatory authority`s or trusted institution's assessments may not always account for specific circumstances that can significantly affect the benefit-risk of a medicines in other countries or regions. Hence, this review focuses on assessing specific aspects of the dossier that are relevant to the Ethiopian context while relying on prior evaluations conducted by trusted authorities or institutions. It involves either confirmation of the applicability of the assessment outcomes or performing assessment of a specific section of the application dossier regarding the safety, efficacy and quality data, in view of the information provided in the assessment reports of the reference regulatory authority or trusted institution.

In the case of products approved by the reference regulatory authorities or institutions with which the authority has no mutual recognition agreements, EFDA may accept the decision of the RRAs or trusted institutions based on the partial review of selected sections and/or modules of the application dossier. Such review is applicable for products assessed and accepted by the regional economic communities (RECs) other than AMA and IGAD or agencies evaluating medicines for global health program such as EMA article 58 and through the Swiss medic's Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme could also considered under this scheme

### 6.3. Eligibility for granting Marketing Authorization through reliance procedures

1) Medicines prequalified by WHO collaborative registration.
2) Medicines approved by EFDA recognized reference regulatory authority,
3) Medicines evaluated for Global Health Program: Medicine approved by Swissmedic's, Health Canada, EU-Medicines for all or '**EU-M4all**'
4) For medicines that has been evaluated and accepted via joint assessment (e.g. by IGAD, AMA).
5) For medicines that has been granted marketing authorization by NRA of a country that has signed mutual or multilateral recognition agreement with EFDA,
6) For medicines that have been approved by different regional economic communities (RECs) as part of African Medicines Regulatory Harmonization (AMRH) initiatives, and WHO-listed

agencies may be considered through the reliance pathways in a case by case basis.

## 7. Requirements for application submission

### 7.1. General conditions

**a)** Applications dossier should be only for products assessed and accepted by the reference regulatory authorities or trusted institutions

**b)** The applicant should declare the "sameness" of the reference regulatory authority or trust institution-approved medicine with the one applied for marketing authorization of medicine by the authority. These shall include, but not limited to:

- qualitative and quantitative formulation;
- manufacturing site(s) for API and FPP including specific block(s)/unit(s),
- processes, control of materials and final product,
- in the case of vaccines, batch release scheme;
- specifications for excipient, API and FPP
- essential elements of product information

**c)** If any differences exist between the dossier submitted to EFDA and the dossier submitted to a recognized regulatory authority or institution, all such differences should be clearly indicated and justified.

**d)** The submitted product should be prequalified and/or registered and marketed in the market of one of the reference regulatory authority's countries, except for products prequalified by WHO jointly assessed products and products approved for global health program.

**e)** Submission of the application dossier should be through the electronic Regulatory Information System (eRIS) portal, via appropriate route of application

**f)** For WHO prequalified product, the applicant should provide the "Quality information summary" together with the dossier.

**g)** The applicant should confirm in writing that the review(s) provided is/are complete and unaltered.

**h)** The reference regulatory authority(s) or trusted institutions assessment reports or at least access or link to the portal on the web site of that reference regulatory authority should be provided

**i)** Commitment letter to notify the EFDA when there is pending variation, withdrawal from

the market or banned by reference regulatory or trusted body due to any notice of concern

**j)** GMP waiver certificate/letter issued by EFDA and copy of valid GMP issued by any of the RRA, laboratory testing report (when applicable), and safety report (when applicable)

**k)** Unredacted assessment report from the Reference regulatory authority, if applicable

**l)** Full modules with CTD document as per the Guideline for Registration of Medicines

**m)** A declaration indicating that any post approval changes were reported and accepted by the reference regulatory authority or trusted institution. This declaration should include the list of variations not yet accepted by reference regulatory authority or trusted institution and section of the dossier affected by the accepted variations.

**n)** A copy of the marketing authorization, or the equivalent thereof, issued by the reference NRA or institution to demonstrate that the product is registered or licensed in accordance with the reference NRA or institution requirements. If applicable, a copy of the latest renewal of the marketing authorization should also be provided.

**o)** Public assessment report(s) and/or final acceptance letter issued by the NRA or institution such as the Scientific Discussion of the European Public Assessment Report (EPAR), issued by the reference NRAs or institution. Assessment report(s) issued by the reference SRA that are not publicly available may be requested.

**p)** The latest SRA-approved product information (summary of product characteristics (SmPC), or an equivalent thereof, the patient information leaflet (PIL), or equivalent thereof, and the labelling).

**q)** A copy of the currently approved FPP specifications (release and shelf-life), dated and signed or certified by authorized personnel, with the analytical test procedures in appropriate section of the dossier.

**r)** Stability study report conduct as per the conditions prescribed in the Medicine Registration Guideline of the Authority.

**s)** A copy of the recent Annual Product quality review Report as described in Appendix 1 of Medicine Registration Guideline of the Authority.

### 7.2. Specific Requirements

**A. For the WHO-prequalified products,**

a) the medicines for which application is submitted to EFDA should be in the list of WHO

prequalified products on the WHO PQT website (https://extranet.who.int/prequal/content/prequalified-lists)

b) Consent/agreement letter sent by the applicant to WHO PQ for the exchange of information between the EFDA and WHO PQT. This also holds true for the WHO collaborative registration through SRA CRP.

c) For detail procedure the applicants should refer EFDA guideline for registration of WHO PQ medicines.

**B. For products assessed and accepted by reference regulatory authority with which EFDA has agreement**

Written agreement for the exchange of information between the EFDA and the Reference Authority should be provided.

**C. For products accepted by the reference authority(s) or institution(s) unilaterally recognized by EFDA**

a) A bridge(redacted) assessment report of the reference regulatory authority (optional)

b) The bridge report should be dated and signed by authorized personnel and should indicate:

i. comparability of the studied population to the target population (e.g. ethnicity, gender representation, age groups) as regards demonstration of efficacy and safety;

ii. relevance of reference regulatory authority/ institution-approved conditions of use as regards epidemiology and disease pattern in Ethiopia as well as other implications for efficacy and safety

iii. interactions with food and with other medications relevant in Ethiopia that are not discussed in the reference regulatory Authority`s or institution`s assessment report;

iv. therapeutic role of a product and its recommended use according to relevant national and international treatment guidelines;

v. quality issues, including but not limited to, storage conditions and conditions of administration and use;

vi. risk management plan for a new molecule

*Note: Provision of a bridging report may substantially facilitate conduct of the regulatory assessment, reduce the number of potential regulatory questions and shorten the duration of the regulatory approval process.*

**D. For products accepted by IGAD joint assessment**

A letter for the expression of interest including the reference number of the application submitted to IGAD

## 8. Requirement for selection of Reference regulatory Authority or trusted Institutions

Regulatory authorities or institutions shall fulfil at least the following criteria to be included in the list of EFDA recognized reference regulatory authorities/trusted institutions.

1) NRA or institution that 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
2) Member of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), and an ICH observer, being the European Free Trade Association,
3) A regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement,
4) National regulatory authority or institution that has signed memorandum of understanding or legally binding agreement with authority
5) WHO PQP
6) Global health program such as EMA article 58 and through the Swiss medic's Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (Swissmedic, Health Canada and EU Medicine for all)
7) Compliance history of the reference country
8) Regional Economic communities should be considered

## 9. List of Reference Regulatory Authorities/ trusted Institutions

The EFDA lists the National Regulatory Authorities, and regional and international institutions as Reference Regulatory Authorities or trusted institutions based on the above criteria lusted in section 9. The list is dynamic and is subject to change by the EFDA as needed. The authority relies on decisions, reports or information of the Reference Regulatory Authorities or trusted institution to ensure the safety, efficacy, and quality of medicines for decision for registration and marketing authorization. To qualify for a market authorization through reliance pathway, an application must have been approved by one or more of the RRAs or trusted institutions. The authority relies on the following reference regulatory authorities or trusted institutions:

a. Category A: Reference Regulatory Authorities or trusted institutions

Applications submitted for products evaluated and approved by WHO PQP, IGAD or AMA and Agencies for global health program are registered after the verification of documented evidences and the sameness of the medicine.

b. Category B Reference Regulatory Authorities or trusted institutions-

Applications submitted for products assessed and approved by NRAs/institutions listed in annex 1 of this guideline and products approved by the NRAs that have mutual agreement with EFDA.
shall undergo abbreviated review.

## 10. Application submission and assessment

### 10.1. Application Submission

**a)** For both types of reliance-based application submission (under routine and non-routine situation) applicants are recommended to submit their application through eRIS portal.

**b)** For specific requirements on the electronic submission using eRIS portal and methods of submission of all documentation (e.g. application submission format, screening check list), refer to the respective registration guidelines (Medicine, Biological, Vaccine, etc.) and post-approvalchanges authorization guidelines.

**c)** The Pre-evaluation and Pre-import Approval Desk may be contacted for pre-submission

technical support for verifying the required documents and get guidance to the most suitable review and approval pathways.

**d)** The applicant should submit the application 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).

### 10.2. Assessment

**a)** Assessment of applications will be conducted in accordance with the relevant marketing authorization guidelines and assessment SOPs

**b)** The assessment time line shall be in line with the MA directive no 963/2023

## 11. Evaluation of Post-Approval Changes

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

## 12. Evaluation of Renewal

EFDA apply same reliance principles and mechanisms adopted in the new marketing authorization managing renewal application submitted by already approved by reference authorities or institutions

## 13. Withdrawal and cancellation of medicines due to safety and efficacy issues

EFDA shall conduct periodic reviews of safety, efficacy and quality of registered medicines. For this purpose, the EFDA may rely on and takes into consideration information concerning safety, quality and efficacy of any registered medicines, particularly those accepted under its reliance procedure as per this guideline.

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

**Annex I: List of Reference NRAs or institutions**

The list of NRA and Institutions considered as reference regulatory authority or trusted institution for reliance for marketing authorization

| **NMRA/Institution** | **Country** |
|---|---|
| 1. US FDA | United States of America |
| 2. Therapeutic Goods Administration (TGA ) | Australia |
| 3. The Austrian Medicines and Medical Devices Agency (AGES MEA) | Austria |
| 4. Federal Agency for Medicines and Health Products (FAMHP) | Belgium |
| 5. Health Canada | Canada |
| 6. Danish Medicine Agency | Denmark |
| 7. Finnish Medicine Agency | Finland |
| 8. National Agency for the Safety of Medicines and Health Products (ANSM) | France |
| 9. The Federal Institute for Drugs and Medical Devices (BfArM ) | Germany |
| 10. Health Products Regulatory Authority (HPRA) | Ireland |
| 11. Italian Medicine Agency (AIFA) | Italy |
| 12. the Pharmaceuticals and Medical Devices Agency (PMDA) | Japan |
| 13. Medicine Evaluation Board | Netherlands, |
| 14. Norwegian Medical Products Agency (NOMA) | Norway |
| 15. Swiss Agency for Therapeutic Products (Swissmedic) , | Switzerland |
| 16. Medicines and Health Products Regulatory Agency (MHRA) | United Kingdom |
| 17. Regional economic communities (RECs) operating under the umbrella of | |

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|---|---|
| African Medicine Agency where joint assessment conducted (such as IGAD) and AMA joint assessment | |
| 18. Bulgarian Drug Agency | Bulgaria |
| 19. Agency for Medicinal Products and Medical Devices of Croatia (HALMED) | Croatia |
| 20. Ministry of Health — Pharmaceutical Services | Cyprus |
| 21. State Institute for Drug Control (SUKL) | Czech Republic |
| 22. State Agency of Medicines (Ravimiamet) | Estonia |
| 23. National Organization for Medicines | Greece |
| 24. National Institute of Pharmacy and Nutrition (OGYEI) | Hungary |
| 25. Icelandic Medicines Agency | Iceland |
| 26. State Agency of Medicines | Latvia |
| 27. Office of Health / Department of Pharmaceuticals | Liechtenstein |
| 28. State Medicines Control Agency (VVKT) | Lithuania |
| 29. Ministry of Health | Luxemburg |
| 30. Medicines Authority | Malta |
| 31. Chief Pharmaceutical Inspectorate | Poland |
| 32. National Authority of Medicines and Health Products (Infarmed) | Portugal |
| 33. National Agency for Medicines and Medical Devices | Romania |
| 34. State Institute for Drug Control (SIDC) | Slovakia |
| 35. Agency for Medicinal Products and Medical Devices (JAZMP) | Slovenia |
| 36. Spanish Agency of Medicines and Medical Devices (AEMPS) | Spain |
| 37. Medical Products Agency | Sweden |

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|---|---|
| 38. WHO PQ | |
| 39. EMA | |