Ethiopian Food and Drug Authority (EFDA)

Guidelines for WHO Pre-qualified Medicines through Collaborative Registration Procedure

First Edition

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Acronyms & abbreviations

APIs	Active Pharmaceutical Ingredient
CRP	Collaborative Registration Procedure
CPQ	Confirmation of Prequalification
EFDA	Ethiopian Food and Drug Authority
FPP	Finished Pharmaceutical Product
MRAs	Medicines Regulatory Authorities
MRAs	National Medicines Regulatory Authorities
NMRA	National Medicines Regulatory Authorities
PD	Product Dossier
PQ	Pre-qualification
PQP	Prequalification Program
PQT	Prequalification Team
WHO PQP	World Health Organization Prequalified Program
WHO	World Health Organization

1. Introduction

Marketing authorization (MA) of pharmaceutical products is one of the crucial regulatory requirements to ensure safety, quality and efficacy of medicines. The Ethiopian Food and Drug Authority has categorized finished pharmaceutical products (FPP) marketing authorization applications in to various product categories based on their risk level as per provision under the article 19 (1) of Proclamation No. 1112/2019. Various approval pathways are also devised to expedite the MA approval process.The same principle is also substantiated by the 2017 "Expediting Medicine Marketing Authorization Strategy", which has set various initiatives to expedite the evaluation process of medicines registration applications.

This guideline outlines the minimum requirements and procedures to register World Health Organization Prequalified (WHO PQ) medicines by EFDA as one of the reliance-based approval path way. This will avoid duplication of effort which will consume scarce regulatory resources. Application via this approval pathway for registering WHO prequalified medicine would enhance timely access of medicines to patients. Hence, it is in line with the WHO Collaborative Registration Procedure (CRP) for WHO-prequalified Pharmaceutical products and vaccines which aims accelerating registration through improved information sharing between the WHO Prequalification of Medicines Program (PQP) and EFDA.

2. Objective

The objective of this guideline is to describe requirements for market authorization of WHO Pre-qualified Pharmaceutical products and vaccines by EFDA.

3. Scope

This guideline is applicable for all pre-qualified pharmaceutical products and vaccines listed in the WHO PQT website (https://extranet.who.int/prequal/content/prequalified-lists)

4. Submission process

Applicants who request to register WHO prequalified pharmaceutical products and vaccines are encouraged to use this route for accelerated market authorization.

1. Interested manufacturers should inform WHO PQT about the application for national registration and provide written agreement to exchange of information between the Authority and WHO PQT. Thus, manufacturers should submit registration application to the Authority for WHO prequalified pharmaceutical products and vaccines via **www.eris.efda.gov.et** and informs the Authority about the interest to follow the CRP.
2. If the applicant is not the same as the WHO PQ holder, an authorization letter (as per the form annexed 2 of this guideline) should be provided as evidence that the applicant is acting for, or pursuant to rights derived from, the WHO PQ holder and that the PQ holder agrees with the application of the procedure.
3. The dossier submitted to the EFDA should be the same as the one that has been submitted to the WHO-PQP during the initial prequalification procedure
4. The Authority may request additional data or missing parts of the dossier. In such instances, if the applicant takes a long time to complete missing parts of the documentation without any justification or fail to provide additional data or to respond to other queries, the authority may terminate the procedure and switch approval pathway to the normal registration route.The Authority will complete the verification process for applications submitted using this pathway and grant Marketing Authorization (MA) Certificate within **90 days** provided that the required documents are fulfilled.

5. Requirements

The Applicants should submit the following documents or information:

5.1. Administrative documents

1. A completed and signed application form should be submitted through eRIS and the date of application should correspond to the date of submission of the registration dossier to the Authority.
2. Dated and signed covering letter for submission of the dossier by mentioning the product included in the dossier from the manufacturer and/or local agent or local representative responsible for registration.
3. Copy of signed consent form
4. Declaration letter of sameness
5. Confirmation of prequalification (CPQ)
6. Table of contents of Module 1 through Module 5 (of the PD)
7. Agency Agreement
    i. An agency agreement should be submitted in line with the requirements indicated under the Module 1 (Administrative and product information section) of the Medicine registration guideline, 4th Edition, 2020.
    ii. An agency agreement made between the manufacturer of the product for registration and the agent responsible for the import, distribution, and sale of the product in Ethiopia should be submitted. Where the company manufactures the product at different sites, the agreement should bear the specific site(s) manufacturing WHO Prequalified product deemed for Ethiopian market.
    iii. The agreement should state that if any fraud or unsuspected and unacceptable adverse event occurs to the consumer under normal utilization, all the party's (local agents, manufacturer, and/or license holder) mentioned in the agreement will be responsible for the product recall and for substantiating any related consequences and liable for legal action as per article 38 (1&4) of proclamation 1112/2019 or other relevant laws of the country
8. Good Manufacturing Practice

An officially signed and dated valid cGMP Waiver letter issued by EFDA and valid current good manufacturing practice (cGMP) certificate issued by the local authority in the country of origin.

9. Product information

Product informationincluding the package insert, labelling, and summary of product characteristics (SmPC) should be provided. All product information label statements are required to be in English or Amharic. The information provided should be consistent with the claims made for the same product in the WHO PQ or in any other jurisdiction. Any information appearing in the product information [labels, patient information leaflet (PIL), and SmPC] should be based on scientific justification.

a) Summary of Product Characteristics

Summary of product characteristics should be submitted by the recommended format for the content of the SmPC as provided in **annex 1** of this guideline.

b) Labeling (immediate and outer label)

Only original labels or computer-ready color-printed labels are accepted for final approval. In the case where the text of the labels is printed directly on plastic bottles through a silk screen process, photocopies of these labels will be accepted for approval.

The titles for batch number, manufacturing, and expiry dates should be part of the printing (typewritten materials, stickers, etc., are not acceptable). If the labeling technology of the manufacturer is such that this information is to be printed on the label during production, a written commitment to show all the required information on the label of the finished product must be submitted. The contents of the label should at least contain:

i. The name of the product– brand and generic/International Non-proprietary Name (INN);
ii. Pharmaceutical form and route of administration;
iii. Qualitative and quantitative composition of active ingredient(s) and Special excipients such as lactose, Aspartame, preservative(s), and antioxidant (s);
iv. The volume of the contents, and/or the number of doses, or quantity in container;
v. Directions to consult the package insert or the carton label for complete directions for use;
vi. Handling and storage conditions;
vii. License number of the manufacturer;
viii. Batch number;

ix. Manufacturing date;

x. Expiry date; and,

xi. Country of origin, Name and site (s) address of manufacturer.

When the immediate container label is too small (in size) to contain all the above information, the label needs to contain at least information as indicated on i, ii, iii, iv, vi, viii, ix and x. Additionally, the label needs to contain logo of the manufacturer and/or license holder.

c) Patient Information Leaflet (PIL) or Package Insert

The general content of the PIL should be prepared in line with the content of the SmPC. The information on leaflet of medicine that is included in the national essential medicine list of Ethiopia or widely circulated in Ethiopian market is required to be at least in English and Amharic. The PIL should not be described or presented in a manner that is false, misleading, or deceptive or is likely to create an erroneous impression regarding its use in any respect, either pictorially or in words.

10. Evidence for payment of Service fees

The applicant shall pay all the required application fees for the registration, laboratory testing & GMP inspection as per the rate of service fees for Food, Medicine, health professional and Health institution Registration and licensing regulation 370/2015.

5.2. Technical Section of the Product Dossier

1. Applicant shall submit the product dossier (PD) in CTD format (Module 1 to Module 5) which is the same as what has been submitted for WHO-PQP prequalification to EFDA for verification via www.eris.efda.gov.et.
2. The technical part of the dossier should be updated to reflect the data as accepted by WHO during prequalification, any WHO-accepted variations and requalification (where applicable).
3. Where applicable, the applicant should submit long-term stability studies protocol and report conducted at Zone IVA and/or IVB conditions
4. At the time of submission, the applicant should provide information of any variations awaitingacceptance of WHO prequalification, if any.

Annexes

Annex 1: Summary of product Characteristics

Summary of the product characteristics should contain the following

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT
2. QUALITATIVE AND QUANTITATIVE COMPOSITION
3. PHARMACEUTICAL FORM
4. CLINICAL PARTICULARS
    - 4.1. Therapeutic indications
    - 4.2. Posology and method of administration
    - 4.3. Contraindications
    - 4.4. Special warnings and special precautions for use

        Drug interactions

        Acute hemolytic

        Hyperglycemia

        Patients with coexisting conditions
    - 4.5. Interaction with other FPPs and other forms of interaction
    - 4.6. Pregnancy and lactation
    - 4.7. Effects on ability to drive and use machines

        < {Invented name} has <no or negligible influence><minor or moderate influence><major influence> on the ability to drive and use machines.> [describe effects where applicable]

        <No studies on the effects on the ability to drive and use machines have been performed.><Not relevant.>
    - 4.8. Undesirable effects
    - 4.9. Overdose
5. PHARMACOLOGICAL PROPERTIES
    - 5.1. Pharmacodynamic properties

        Pharmacotherapeutic group: {group}

        ATC code: {code}

        Mechanism of action

Microbiology (when applicable)

Drug resistance (when applicable)

Cross resistance (when applicable)

Pharmacodynamic effects

Adults

Pediatric patients

5.2. Pharmacokinetic properties

Absorption

Distribution

Biotransformation

Elimination

Characteristics in patients

5.3. Preclinical safety data

<Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.><Preclinical effects were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.>

<Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows.>

Mutagenicity

Carcinogenicity

Developmental Toxicity

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

6.2. Incompatibilities

6.3. Shelf life

6.4. Special precautions for storage

6.5. Nature and contents of container

6.6. Instructions for use and handling <and disposal>

7. MARKETING AUTHORISATION HOLDER
8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS
9. DATE OF FIRST AUTHORISATION/RENEWALOF THE AUTHORISATION
10. DATE OF REVISION OF THE TEXT

Annex 2: Manufacturer's consent for information sharing with participating national regulatory authority (ies) and the World Health Organization.s

Date:_____*dd/mm/yyyy* _____

To: _____

RE: <SRA> sharing of non public information concerning <Product> with the <NRA(s)> and the World Health Organization (WHO)

Dear [<SRA>],

On behalf of <manufacturer>, the <MAH> in <SRA country/region>of the above-referenced regulated product, Iauthorize the<SRA>to share the information described be low ("Information") only with <NRA focal point–contact person/function>and WHO<contact person/function>solely for the purpose of the *Collaborative procedure in assessment and accelerated national registration of pharmaceutical products and vaccines approved by stringent regulatory authorities* <date; version>. Confidentiality agreements are in place between <manufacturer> and WHO.

I understand that the Information may contain confidential commercial or financial information or trade secrets that are exempt from public disclosure. I agree to hold <SRA> harm less for any injury caused by <SRA>'s sharing of the Information with the <NRA>and WHO under the terms set out herein.

Information authorized to be shared with the <NRA> and/or WHO:

- all available quality data on<Product>;
- all available nonclinical data on<Product>;
- all available clinical data on<Product>;
- any other document reasonably requested by the<NRA or WHO>during the evaluation procedure;
- all other information regarding GxP inspections and assessment.

Authorization is given to to provide the Information without deleting confidential, commercial or financial, or trade secret information. As indicated by my signature, I am authorized to provide this consent on behalf of and my full name, title, address, telephone number and email address are set out below for verification.

Yours sincerely,

Name: _____

Title: _____

Address: _____

Manufacturer: _____

Email: _____

Telephone number: _____

Fax number: _____

CC.