ETHIOPIAN FOOD AND DRUG AUTHORITY

Medicine Evaluation and Marketing Authorization Led Executive office

Guideline for WHO Collaborative registration procedure

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Document History

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001	Newly issued document	20/12/2020
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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
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 was also substantiated by the 2017 "ExpeditingMedicine Marketing Authorization Strategy", which has set various initiatives to expedite the evaluation process of medicines registration applications.

A legal provision to recognize the medicines prequalified by the World health organization medicine prequalification program was also provided in article 26 of medicine marketing authorization directive No.963/2023.

Recognizing the WHO prequalification decision will avoid duplication of effort which will consume scarce regulatory resources and enhance timely access of quality ensured medicines to patients.

This Guideline succeeds the 2020 Guideline. It is revised to address the provisions in the Medicine Marketing Authorization Directive No. 963/2023, the requirements in the EFDA pharmaceuticals barcoding guidelines and other national and international changes.

This guideline is therefore outlining the minimum requirements and procedures to register World Health Organization Prequalified medicines through collaborative registration procedure (CRP) for 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 for the applications submitted under collaborative registration procedure.

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) for which applicants interested to submit their application through collaborative registration procedure.

4. Submission process

Applicants who request to register WHO prequalified pharmaceutical products and vaccines are encouraged to use collaborative registration procedure 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** through application path way for collaborative registration procedure
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 contain the same information and data as the one that has been accepted by the WHO-PQP
4. The Authority may request additional data or missing parts of the dossier, when found necessary. In such instances, if the applicant takes a long time to complete missing information or 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 (as per the format in annex 2 and 3)
4) Declaration letter of sameness of information in the application dossier as the one accepted by the WHOPQ
5) The latest version of the Confirmation of prequalification (CPQ) or the CEP as applicable with respect to the API information
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 most current Medicine registration guideline.
    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 should be provided.

9) Product information

Product information including the package insert, labelling, and summary of product characteristics (SmPC) should be provided. Any information appearing in the product information [labels, patient information leaflet (PIL), and SmPC] should be in English or Amharic, consistent with the product information accepted by the WHO PQ and any other jurisdiction of Ethiopia and 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 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.

All the pharmaceutical trade items and/or logistic units to be distributed in Ethiopia shall bear a unique barcode and the barcode shall be printed on the label of the product in a visible manner as per the national law and requirements. Applicants are required to consult the EFDA traceability directive and pharmaceutical products barcoding guidelines available on the Authority's website (http://www.efda.gov.et/)

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 application should be accompanied by a relevant service fee for registration. The application fee shall be made per application and the payment receipt shall mention the application number issued by the eRIS. If the payments are made for more than one application and gross payments are made, a tabular listing of the application number and payment for each application shall be prepared and submitted along with the attachment for the total payment.

Applicants are advised to consult the current Rate of Service Fees Regulation of the Authority for the amount to be paid for application and contact the Authority for detailsof mode of payment.

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 accepted by 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 awaiting acceptance 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
   {(Invented) name of product <strength><pharmaceutical form>}
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: Consent of WHO prequalification holder for WHO to share information with the national regulatory authority confidentially under the Procedure

Reference is made to the attached expression of interest in the assessment and accelerated national registration under the Procedure of the following World Health Organization (WHO) prequalified pharmaceutical product or vaccine (hereafter referred to as "the Product") in _____ [country].1

☐ Pharmaceutical product
☐ Vaccine

WHO prequalification details:
WHO prequalification (PQ) reference number:_____
Date of prequalification (dd/mm/yyyy):_____
Date of requalification (if applicable):_____
WHO PQ holder:[2]_____

Application details:

Name of entity_____ ("the Applicant")
Street:_____
City and country:_____
Email:_____
Telephone:_____

The WHO PQ holder hereby consents to the WHO Prequalification Team (WHO/PQT) providing the following information and documentation to the national regulatory authority (NRA) _____ of [country] ("the NRA") for the assessment and accelerated registration of the Product in the country under the Procedure and to freely discuss the same with the aforesaid NRA for this purpose:

- the full WHO/PQT assessment and inspection outcomes (reports),results of laboratory testing and, if relevant, also assessment and inspections reports of other regulatory bodies, provided that these bodies gave their written consent to the use of such reports for the purpose of the Procedure;
- information and documentation on subsequent variations (as defined in WHO guidelines[3]), as well as information and documentation on any actions taken by WHO/PQT post prequalification of the Product;
- all such data, reports, information and documentation being hereinafter referred to as "the Information".

1 Please complete a separate copy of this Annex for each country.
2 If the applicant for national registration is not the same as the WHO PQ holder, the WHO PQ holder must confirm to the NRA and to WHO/PQT by an authorization letter (as per the template annexed to ppendix 3, Part A) 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 in the country concerned.

As regards sharing the outcomes of assessments and inspections, only data owned by the WHO PQ holder and WHO/PQT are shared. Sharing of any other data is subject to additional agreement of the data owners concerned.[4]
Such consent is subject to the NRA having entered into an agreement with WHO/PQT as per Part A of Appendix 1 to the Procedure and having agreed to conduct the assessment and consider the accelerated registration of the Product under the Procedure, by having submitted the form reproduced in Part B of Appendix 3 to the Procedure to WHO/PQT.
The WHO PQ holder/Applicant commits to submit post-prequalification variations to WHO/PQT and any relevant participating authorities respecting national regulatory requirements. Variations should be submitted to participating authorities at the latest 30 calendar days after acceptance of the variation by WHO/PQT. Participating authorities should be informed about the fact that the same application for a variation is being processed by WHO/PQT. If a national variation procedure results in the nationally-registered product being no longer the same[5] as the WHO-prequalified product, or if a variation of the WHO prequalified product is not followed by a variation of the nationally-registered product and, as a consequence, the nationally-registered product is no longer the same, the WHO PQ holder/Applicant will inform WHO/PQT of the differences and their reasons.

For the WHO PQ holder
Signature:_____
Name:_____
Title:_____
Place:_____
Date (dd/mm/yyyy):

3 *For pharmaceutical products*: WHO guidelines on variations to a prequalified product. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-seventh report. Geneva: World Health Organization; 2013: Annex 3 (WHO Technical Report Series, No. 981), (and any updates thereto).
For vaccines: http://www.who.int/immunization_standards/vaccine_quality/variations_pq_vaccine/en/ (and any updates thereto).
4 In the case that certain data submitted to WHO/PQT by the WHO PQ holder in relation to PQ of the Product are not in his/her ownership, the WHO PQ holder specifies such data in an annex to this declaration of consent.
5 Within the context of this Procedure, the same pharmaceutical product/same vaccine is characterized by the same product dossier; the same manufacturing chain, processes and control of materials and finished product, and in the case of vaccines also by the same batch release scheme; the same active ingredient and finished product specifications; as well as the same essential elements of product information for pharmaceutical products, and, in the case of vaccines, by the same product information, packaging presentation and labelling

Appendix 3A

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

Date: _____ *dd/mm/yyyy* _____

To: _____

RE: <SRA> sharing of non-public information concerning <Product> with the <NRA(s)> and the World Health Organization (WHO)[1]

Dear [<NRA>],

On behalf of <manufacturer>, the <MAH> in <SRA country/region> of the above-referenced regulated product, I authorize the <SRA> to share the information described below ("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> harmless 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 <Product> assessment.

Authorization is given to <SRA> 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 <manufacturer> 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:

[1] During the *Collaborative procedure in national registration of pharmaceutical products and vaccines approved by stringent regulatory authorities (WHO Technical Report Series No. 1010, 2018)* WHO plays a facilitating role.