OVERVIEW OF THE WHO PREQUALIFICATION OF IN VITRO DIAGNOSTICS ASSESSMENT

WHO PREQUALIFICATION OF IN VITRO DIAGNOSTICS

World Health Organization

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CONTENT

1 INTRODUCTION

World Health Organization (WHO) prequalification of in vitro diagnostics (IVDs) is coordinated through the department of Essential Medicines and Health Products. Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings.

WHO prequalification of IVDs is a comprehensive quality assessment of individual IVDs through a standardized procedure aimed at determining whether the product meets WHO prequalification requirements.

The full prequalification assessment process includes the following components:

- review of a product dossier;
- performance evaluation including operational characteristics;
- inspection of manufacturing site(s); and
- labelling review.

The abridged prequalification assessment includes the following components:

- performance evaluation including operational characteristics;
- manufacturing site inspection of abridged scope; and
- labelling review.

Products submitted for prequalification assessment that meet, as determined by WHO, the WHO prequalification requirements are included in the WHO list of prequalified IVDs. The duration of the validity of the prequalification status of a product is dependent on the manufacturer's fulfilment, within the applicable deadlines, of its post-qualification obligations and requirements, including:

- prequalification commitments;
- annual reporting;
- reporting of changes;
- post-market surveillance obligations;
- receiving re-inspection; and
- ongoing compliance with WHO prequalification technical specifications.

The findings of WHO prequalification1 are used to assess the safety, quality and performance of commercially available IVDs for the purpose of providing guidance to interested United Nations (UN) agencies and WHO Member States in their procurement decisions.

2 INTENDED AUDIENCE

This document has been prepared to provide manufacturers with an overview of the WHO process for prequalification assessment of IVDs (the prequalification assessment process). Manufacturers wishing to apply for WHO prequalification of their product(s) should read this document before applying, so that they can be aware of and prepared for all stages of the prequalification assessment process.

1 Prequalification does not imply any approval by WHO of the product and manufacturing site(s). Moreover, prequalification does not constitute any endorsement or warranty by WHO of the fitness of any product for a particular purpose, including its safety, quality or performance.

3 DEFINITIONS

Abridged WHO prequalification assessment	Prequalification assessment including performance evaluation, manufacturing site inspection of abridged scope and labelling review
Dossier screening	Systematic process to ensure that all requisite sections of the product dossier are submitted
Dossier review	Review and assessment of documentation including data, protocols, reports, procedures, etc., to support the quality, safety and performance of a product for the purpose of WHO prequalification.
Full WHO prequalification assessment	Prequalification assessment including dossier review, performance evaluation, inspection of manufacturing site(s) and labelling review.
Inspection of manufacturing site(s)	Inspection of the manufacturing site(s) of product undergoing prequalification assessment
In vitro diagnostic medical device (IVD)	A medical device, whether used alone or in combination, intended by the manufacturer for the in vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes **Note:** IVDs include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles, and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status.
Labelling review	Review and assessment of the instructions for use and product labels
Manufacturer	Any natural or legal person with responsibility for design and/or manufacture of an IVD with the intention of making the IVD available for use, under his or her name, whether or not such an IVD is designed and/or manufactured by that person him- or herself or on his or her behalf by (an)other person(s).
Performance evaluation	Performance evaluation including evaluation of operational characteristics of a product for the purpose of the prequalification assessment process.
Rebranded product	A rebranded product is identical in every respect to the product manufactured by the original manufacturer, except that the product is labelled with the "rebranded" product name and product code, and bears the rebrander's name.
Rebrander	A manufacturer of a rebranded IVD.
Regulatory version	Relates to the information associated with a submission for approval by a regulatory authority. The submitted version is defined by all of the documentation related to development, manufacture and intended use, labelling and post-market surveillance of the product and all the documented evidence supporting the safety and performance claims associated with that submission. If any aspect of this documentation differs in any way between the submissions to different regulatory authorities or assessment bodies (United States Food and Drug Administration, Health Canada, a Notified Body for CE marking, etc.) it is considered to be a different regulatory version.

4 ABBREVIATIONS

GHTF	Global Harmonization Task Force
IMDRF	International Medical Device Regulators Forum
IFU	instructions for use
ISO	International Organization for Standardization
IVD	in vitro diagnostic medical device
NRA	national regulatory authority
OEM	original equipment manufacturer
SOP	Standard operating procedure
UN	United Nations
WHO	World Health Organization

5 ABOUT PREQUALIFICATION OF IVDS AND PROCUREMENT

The goal of the WHO prequalification of IVDs is to assess the safety, quality and performance of commercially available IVDs for the purpose of providing guidance to interested UN agencies and WHO Member States in their procurement decisions.

Once a product has been prequalified, it is included in the WHO list of prequalified IVDs and becomes eligible to participate in the procurement processes of UN agencies. WHO Member States are encouraged to use the WHO list of prequalified IVDs for their respective procurement decisions. Nevertheless, UN agencies and WHO Member States using information from the WHO prequalification of IVDs process should perform additional steps of qualification prior to purchasing products included in this list including steps such as ensuring the supplier's financing stability and standing, the ability to supply the required quantities of the product, security of the supply chain, quality control testing, and other relevant aspects.

6 ELIGIBILITY FOR PREQUALIFICATION OF IVDS

6.1 ORIGINAL MANUFACTURER

Applications for WHO prequalification of IVDs are accepted only from the legal manufacturer of the product.[2]

6.2 REBRANDED PRODUCTS

WHO is aware that several manufacturers purchase finalized products from other

2 The definition of a manufacturer is based on the definition used by the Global Harmonization Task Force (GHTF), and later adopted by International Medical Device Regulators Forum (IMDRF). This internationally accepted approach has been adopted to ensure that there is a clear understanding of the term "manufacturer" across international markets. For further details see: www.imdrf.org/

companies, and then "rebrand" and place these products on the market under their own name or brand. Such products are also known as original equipment manufacturer (OEM) products.

WHO considers a rebranded product to be one that is manufactured under identical conditions at the same manufacturing site(s) as the original product. In other words, a rebranded product is identical in every respect (including the intended use) to the product manufactured by the original manufacturer, except that the product is labelled with the rebranded product name and product code, and bears the rebrander's name or brand.

Rebranded products are outside the scope of the WHO prequalification of IVDs process, and hence are not accepted for prequalification assessment.

6.3 COMMERCIAL AVAILABILITY

Applications for WHO prequalification of IVDs are only accepted for products that are commercially available at the time of submission for prequalification assessment.

6.4 ELIGIBILITY PRINCIPLES AND ELIGIBILITY CRITERIA

To meet the needs of WHO Member States and UN agencies, the prequalification scope is defined according to the following prequalification eligibility principles:

- need for IVDs for a particular disease or disease state;
- appropriateness of the product for use in resource-limited settings;
- requests from WHO Member States for particular IVDs;
- recommendation in WHO testing guidelines; and/or
- availability of prequalified products that are of a similar assay format and/or assay principle.

The eligibility principles are applied using a set of eligibility criteria as defined in the document WHO PQDx_298 *Eligibility criteria for WHO prequalification of in vitro diagnostics*.

7 APPLYING FOR WHO PREQUALIFICATION

To ensure that WHO can prequalify IVDs as efficiently as possible, manufacturers should be fully prepared for the prequalification assessment process when they apply for WHO prequalification. Manufacturers may wish to contact the WHO Prequalification Team – Diagnostics Assessment (email: diagnostics@who.int) and/or the WHO Prequalification Team – Inspections services (email: prequalinspection@who.int) to commence discussions on the prequalification assessment processes and requirements before applying. In addition, the WHO Prequalification of IVDs webpage provides guidance materials to assist manufacturers in ensuring their readiness for WHO prequalification.[3]

The manufacturer must complete a pre-submission form (WHO document PQDx_015 *Pre-submission form*) and must provide WHO with all requested supporting documentation in accordance with the WHO document PQDx_017 *Instructions for the completion of the pre-submission form*.

3 www.who.int/diagnostics_laboratory/guidance/en/

The pre-submission form and the requisite attachments (authorization letter, instructions for use, photographs and "Abridged assessment" annex) must be submitted, preferably electronically, by the manufacturer to WHO for review. A completed pre-submission form provides summary information about the product, its regulatory version and the manufacturer. The details provided in this form will inform WHO in its decision on whether or not the product submitted is eligible for prequalification assessment and, if so, whether or not the prequalification assessment can be abridged. It is also used to determine the regulatory version intended for prequalification and to plan for each of the components of the prequalification assessment process. It is therefore important for the manufacturer to ensure that the information supplied in the pre-submission form is accurate and complete.

The prequalification pre-submission form and supporting documentation will be reviewed by WHO against the established eligibility criteria to determine the product's eligibility for prequalification assessment. If necessary, the manufacturer may receive a communication from WHO requesting additional information and/or clarifications to assist it in the eligibility decision. The manufacturer must provide WHO with the information and/or clarifications so requested within the deadlines prescribed by WHO. WHO will inform the manufacturer in writing of WHO's decision concernening whether or not the product is eligible for prequalification assessment.

If a product is found to be eligible for prequalification assessment, WHO will request the manufacturer to complete, sign and return to WHO the Letter of Agreement, which will serve: (i) as an agreement between WHO and the manufacturer on the participation of the product in the prequalification assessment process, and (ii) as the manufacturer's acceptance of, and commitment to comply with, the provisions of the prequalification assessment process. A prequalification dossier screening and assessment fee will also be payable by the manufacturer.[4]

Before the prequalification assessment of a product that has been found eligible by WHO may commence, the manufacturer must deliver to WHO: (i) a signed and completed Letter of Agreement, and (ii) proof of payment the the applicable prequalification fee.

8 PREQUALIFICATION ASSESSMENT

Two types of prequalification assessment can take place, depending on the regulatory version submitted and evidence from a previous stringent review by a founding member of GHTF. WHO will determine the appropriate type of assessment at