Overview of WHO's prequalification procedure for in vitro diagnostics

Overview of WHO's prequalification procedure for in vitro diagnostics
ISBN 978-92-4-011802-7 (electronic version)
ISBN 978-92-4-011803-4 (print version)

Contents

Abbreviations

DOI	WHO's Declaration of Interest form
FSN	field safety notice
FSCA	field safety corrective actions
GHTF	Global Harmonization Task Force
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IVD	in vitro diagnostic
MDSAP	Medical Device Single Audit Program
PE	WHO's performance evaluation of an IVD
PEL	performance evaluation laboratory
PEPAR	WHO's Performance Evaluation Public Assessment Report
RRA	Recognized Regulatory Authority
SOP	standard operating procedure
UN	United Nations
WHO	World Health Organization
WHOPAR	WHO's Public Assessment Report
WHOPIR	WHO's Public Inspection Report

1. Introduction

This document has been prepared by the World Health Organization (WHO) to provide an overview of WHO's prequalification assessment procedure for in vitro diagnostic medical devices (hereinafter each, an "IVD" or "product"). WHO's prequalification of IVDs is coordinated through WHO's Prequalification Unit.

Effective as of 1 January 2026, WHO's performance evaluation of a product pursuant to and in accordance with WHO's performance evaluation of IVDs[1] is a separate process from (as opposed to a component of), as well as a prerequisite to apply for assessment under, WHO's prequalification procedure for IVDs. This document supersedes *"Overview of the WHO prequalification of in vitro diagnostics assessment: prequalification of in vitro diagnostics. Version 9*".

This procedure excludes medical devices other than IVDs.

WHO's prequalification of IVDs is a comprehensive quality assessment of individual IVDs through a standardized procedure aimed at determining whether a product meets WHO's prequalification requirements. Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings.

[1] Document PQDx_458 *"WHO's performance evaluation procedure for in vitro diagnostics".*

Before an application for WHO's prequalification assessment of an IVD may be considered and/or accepted by WHO, a complete Expression of Interest for WHO's performance evaluation of that IVD must have first been duly completed and submitted by the manufacturer to, and accepted by, WHO. Please refer to document PQDx_458 "*WHO's performance evaluation procedure for in vitro diagnostics*", for more information about the requirements, terms and conditions applicable to WHO's performance evaluation of IVDs. For the avoidance of doubt, WHO's performance evaluation and WHO's prequalification assessment are separate processes, with separate applicable procedures and requirements.

If WHO decides to include a product in WHO's list of prequalified IVDs, then the duration of the validity of the prequalification status of that product is will be subject to and contingent upon the manufacturer's fulfilment, within the applicable deadlines, of its post-qualification obligations and requirements as defined in Section 12 of this procedure. The findings of WHO's prequalification assessment[2] are used to evaluate the safety, quality and performance of IVDs for the purpose of providing guidance to interested United Nations (UN) agencies, relevant intergovernmental or international organizations, and WHO Member States in their procurement decisions.

2. Intended audience

This document has been prepared to provide an overview of the procedure applicable for WHO's prequalification assessment of IVDs. Manufacturers wishing to apply for WHO's prequalification assessment of their product(s) should read this document before doing so, in order to be prepared for all stages of WHO's prequalification assessment process.

3. Definitions

As used in this document, the following terms have the following meanings:

Abridged prequalification assessment	WHO's prequalification assessment of abridged scope, including review of an abridged product dossier, manufacturing site inspection and labelling review.
Design lock-down	A formal milestone in the IVD, medical device, or system development lifecycle at which the design is considered finalized: all design inputs have been addressed, and verification and validation activities are complete. The design is placed under configuration control and formally released for manufacturing, regulatory submission, or subsequent development stages. From this point forward, any modifications are strictly managed through a documented design change control process, including risk management review, necessary validation and verification and—where applicable—regulatory notification or approval, in order to maintain a stable and traceable design baseline.[3]

[2] WHO's prequalification does not constitute or imply any approval, certification or endorsement by WHO of the product, the manufacturer and/or manufacturing site(s). Moreover, WHO's 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] Changes that occur after a design lock-down must be documented and evaluated within the framework of change management.

Dossier screening	Systematic process to assess whether all requisite sections of the product dossier relating to an IVD undergoing WHO's prequalification assessment have been submitted by the manufacturer to WHO.
Dossier review	Review and assessment of documentation including data, protocols, reports, procedures, etc., to support the quality, safety and performance of a product undergoing WHO's prequalification assessment.
Full prequalification assessment	WHO's prequalification assessment of full scope, including review of a full product dossier, inspection of a manufacturing site and labelling review.
Inspection of manufacturing site(s) or manufacturing site(s) inspection	Evaluation of a manufacturing facility of an IVD to determine whether such manufacturing facility is operating in compliance with the requirements and/or commitments applicable to WHO's prequalification assessment of IVDs. The manufacturing site(s) inspections may involve onsite inspection and/or desk assessment, as determined by WHO. Manufacturing site(s) inspections comprise initial, routine, follow-up and for-cause inspections.
In vitro diagnostic medical device or in vitro diagnostic or IVD or product	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 for an IVD undergoing WHO's prequalification assessment.
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). [4]

[4] 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.

Performance evaluation laboratory or PEL	A laboratory that: (i) has been assessed and listed by WHO as a performance evaluation laboratory [5]; and (ii) is commissioned to and responsible for implementing WHO's performance evaluation of an IVD, subject to and in accordance with WHO's performance evaluation procedure and WHO's performance evaluation protocol.
Performance evaluation public assessment report or PEPAR	A report written and published by WHO which summarizes the findings made during WHO's performance evaluation of the IVD, but which excludes confidential and proprietary information.
Post-market surveillance	Systematic process conducted by manufacturer to collect and analyse experience gained from an IVD that has been placed on the market.
Rebranded product	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.
Rebrander	A manufacturer that purchases a finalized product from another company, rebrands that product and places the rebranded product on the market under the manufacturer's own name or brand.
Recognized Regulatory Authority	A National Regulatory Authority or its designated notified body[6] that is recognized by WHO, for purposes of WHO's prequalification assessment, as applying stringent standards for quality, safety and performance in its process of regulatory review of IVDs for marketing authorization.[7]
Regulatory version	Refers to and relates to all the information and documentation associated with a submission for approval of a product by a regulatory authority including, without limitation, all documentation related to development, manufacture, intended use, labelling and post-market surveillance of the product, as well as all documented evidence supporting the safety and

[5] Such assessment and listing are made pursuant to and in accordance with the document PQDx_248 *"WHO's assessment procedure for Performance Evaluation Laboratories for in vitro diagnostics"* or any preceding and/or subsequent versions of the same.

[6] In the European Union or other countries under specific agreement, a notified body is an organization designated by an EU Member State (or other countries under specific agreements) to assess the conformity of certain products before being placed on the market. Notified bodies are entitled to carry out tasks related to conformity assessment procedures set out in the applicable legislation when a third-party intervention is required. The European Commission publishes a list of designated notified bodies in the NANDO information system.

[7] Refer to WHO document PQDx_173 *"WHO's Abridged prequalification assessment for in vitro diagnostics"* for the list of Recognized Regulatory Authorities.

	performance claims associated with that submission. In the event that (i) regulatory versions of a product have been submitted to different regulatory authorities or designated notified bodies (e.g., United States Food and Drug Administration, Health Canada, a Notified Body for CE marking, etc.) and (ii) any aspect of the documentation or information associated with such submitted regulatory versions differs in any way, then the submitted regulatory versions are considered to be a *different* regulatory version.
WHO's performance evaluation	WHO's evaluation, pursuant to and in accordance with the terms and conditions of document *PQDx_458 "WHO's performance evaluation procedure for in vitro diagnostics*", of performance and operational characteristics of a product, as a prerequisite for a manufacturer to separately apply for WHO's prequalification assessment of that product.
WHO's prequalification of IVDs	WHO's assessment of the quality, safety and performance of IVDs pursuant to and in accordance with the terms and conditions of this procedure.
WHO's Public Assessment Report or WHOPAR	A report prepared and published by WHO which summarizes the findings of WHO's prequalification assessment, but excludes confidential and proprietary information.
WHO's Public Inspection Report or WHOPIR	A report prepared and published by WHO which summarizes WHO's report of a manufacturing site inspection (i.e., through an on-site inspection and/or a desk assessment) indicating that the site is compliant with guidelines, standards, norms, and dossier requirements that are applicable to WHO's prequalification assessment, but which excludes confidential and proprietary information.

4. About WHO's prequalification of IVDs and procurement

The purpose and objective of WHO's prequalification of IVDs are to independently assess the safety, quality and performance of IVDs for the purpose of providing guidance to interested WHO Member States, UN agencies, funds and programmes, and relevant intergovernmental or international organizations, in their procurement decisions.

Before an application for WHO's prequalification assessment of an IVD may be considered or accepted by WHO, a complete Expression of Interest for WHO's performance evaluation of that IVD must have first been duly completed by the manufacturer and submitted to, and accepted by, WHO[8]. WHO's performance evaluation is: (a) an evaluation of performance and operational characteristics of an IVD pursuant to and in accordance with the terms and conditions of WHO's performance evaluation procedure for IVDs, and (b) a prerequisite for the manufacturer of an IVD to separately apply for WHO's prequalification assessment of that product. Please refer to document PQDx_458 "*WHO's Performance Evaluation Procedure for In Vitro Diagnostics*", for more information about the requirements, terms and conditions applicable to WHO's

[8] This requirement applies when WHO's performance evaluation of the product is required per document PQDx_459 *"Eligibility criteria for WHO's performance evaluation of in vitro diagnostics".*

performance evaluation of IVDs (which is a separate process and procedure from WHO's prequalification assessment of IVDs).

If a prequalification application is accepted by WHO, WHO's prequalification assessment can take place through one of two pathways—namely, full or abridged prequalification assessment— as determined by WHO and more fully described in Section 8 below.

The full prequalification assessment process includes the following components:

- review of a full product dossier;
- manufacturing site(s) inspection; and
- labelling review.

The abridged prequalification assessment includes the following components:

- review of an abridged product dossier;
- manufacturing site inspection; and
- labelling review.

WHO's decision (positive or negative) on whether a product may be granted WHO's prequalification listing will be taken based on the outcomes of, and only after completion of, all of the following:

- all components of WHO's prequalification assessment of the IVD; and
- WHO's performance evaluation of the IVD.

Only products that have successfully completed all components of WHO's prequalification assessment and that meet the requirements of WHO's performance evaluation will be considered for possible prequalification listing[9].

If a product is prequalified by WHO, such product will be included in WHO's list of prequalified IVDs. WHO Member States, UN agencies, funds and programmes and/or international or intergovernmental procurement organizations may use WHO's list of prequalified IVDs to inform their respective procurement decisions. Nevertheless, any person or entity using information arising from WHO's prequalification of IVDs should perform additional verification steps prior to purchasing products included in WHO's list of prequalified IVDs. Such steps include, but are not necessarily limited to, verifying the supplier's financing stability and standing, ability to supply the required quantities of the product, security of the supply chain, and other relevant aspects.

5. Eligibility for WHO's prequalification assessment of IVDs

Applications for WHO's prequalification assessment of IVDs are accepted only for products that are found by WHO to meet the eligibility principles and criteria set forth in document PQDx_298 "*Eligibility criteria for WHO's prequalification assessment of in vitro diagnostics*". WHO will review the application against the abovementioned eligibility principles and criteria and will inform the manufacturer, in writing, whether or not the product is accepted for WHO's prequalification assessment according to the provisions of this procedure. See also Section 6.1 below.

[9] Pursuant to and in accordance with Section 9 of this procedure.

6. Applying for WHO's prequalification assessment

6.1. Pre-application readiness; first time applicants

To ensure that WHO can conduct its prequalification assessment of IVDs as efficiently as possible, manufacturers should be fully prepared for WHO's prequalification assessment process when they apply.

Before submitting an application, manufacturers may contact WHO's Prequalification Unit to discuss WHO's prequalification assessment process and its requirements. The relevant contact details are provided in Section 18 below. In addition, manufacturers should consult the relevant documents set forth in Section 17 below as well as WHO's prequalification webpage https://extranet.who.int/pqweb/vitro-diagnostics/guidance-documents, to prepare for WHO's prequalification assessment.

To promote the efficient use of resources by both WHO and the manufacturer, if a manufacturer is applying for WHO's prequalification assessment of an IVD for the first time and/or does not have previous experience with WHO's prequalification assessment, then only one application may be submitted by such manufacturer until the following conditions are met:

- WHO has completed the product dossier review; and
- depending on the outcome of the product dossier review and WHO's assessment of the readiness of the manufacturer, WHO has confirmed to the manufacturer in writing that it may submit additional applications for WHO's prequalification assessment of IVDs.

All of the foregoing is without prejudice to the other provisions in this procedure or to the eligibility principles and criteria set forth in PQDx_298 "*Eligibility criteria for WHO's prequalification assessment of in vitro diagnostics"*.

6.2. WHO's performance evaluation as a pre-requisite to WHO's prequalification assessment

WHO's performance evaluation of an IVD is a prerequisite for certain IVDs (as described in document PQDx_298 "*Eligibility criteria for WHO's prequalification assessment of in vitro diagnostics")* to apply for and undergo WHO's prequalification assessment.

As mentioned above, before a manufacturer may apply for WHO's prequalification assessment of an IVD, an Expression of Interest for WHO's performance evaluation of that IVD must have first been duly completed and submitted by the manufacturer to, and accepted by, WHO. Without prejudice to the other terms, conditions and requirements set forth in this procedure, an application for WHO's prequalification assessment of an IVD will not be accepted by WHO unless and until, among other things, a complete Expression of Interest for WHO's performance evaluation of that IVD has first been received and accepted by WHO[10].

For the avoidance of doubt, WHO's performance evaluation of IVDs and its procedure are separate from WHO's prequalification assessment of IVDs and this procedure. In this respect, WHO's performance evaluation is a prerequisite to, rather than a component of, WHO's prequalification assessment of IVDs. The fact that an IVD has been accepted for, is undergoing and/or has completed WHO's performance evaluation does not mean or imply that such IVD will be accepted for WHO's prequalification assessment and/or be granted WHO's prequalification listing.

[10] This requirement applies when WHO's performance evaluation of the product is required per document PQDx_459 *"Eligibility criteria for WHO's performance evaluation of in vitro diagnostics".*

The data, information, findings, analyses, results and reports arising from or relating to WHO's performance evaluation of an IVD will be used by WHO, among other things, to inform its decision as to whether or not the IVD:

- meets, to WHO's satisfaction, the technical requirements for WHO's performance evaluation in accordance with WHO's performance evaluation protocol; and/or
- if applicable, can be accepted for assessment and/or granted listing under WHO's prequalification procedure for IVDs.

Please refer to document PQDx_458 "*WHO's Performance Evaluation Procedure for In Vitro Diagnostics*" for more information about the terms, conditions and requirements applicable to WHO's performance evaluation of IVDs. See also Section 7 below for other relevant information.

6.3. Pre-submission form

To apply for an IVD to undergo WHO's prequalification assessment, the manufacturer must complete and submit electronically to WHO a pre-submission form (using document PQDx_015 *"Pre-submission form*"), together with the necessary supporting documentation and requisite attachments. The pre-submission form must be completed in accordance with PQDx_017 "*Instructions for completion of the pre-submission form"*.

As part of the pre-submission form, the manufacturer must provide WHO with the names and contact information of two contacts who are duly and fully authorized and designated to act in the name and on behalf of that manufacturer in all respects and for all purposes in connection with WHO's prequalification assessment of the IVD. In the event that, at any time during WHO's prequalification assessment process, there is a change in the name(s) and/or any contact information of for any authorized contact(s), the manufacturer must promptly notify WHO, in writing, thereof and of the updated name(s) and contact information of the authorized contacts. Such notice must be given by official letter as described above, sent to WHO by email to diagnostics@who.int.

The pre-submission form provides summary information about the product, its regulatory version and the manufacturer. The information provided in the pre-submission form and its supporting documentation will inform WHO in its decision on:

a. whether or not the product submitted for WHO's prequalification assessment is the same product as the one in the manufacturer's Expression of Interest form for WHO's performance evaluation; and
b. whether or not the product submitted is eligible for WHO's prequalification assessment; and
c. if the product submitted is eligible for WHO's prequalification assessment, whether or not WHO's prequalification assessment can be abridged; and
d. determining the regulatory version accepted for WHO's prequalification assessment; and
e. the planning of each component of WHO's prequalification assessment process.

It is therefore important for the manufacturer to ensure that the information provided in the pre-submission form and its supporting documentation is accurate and complete.

Once the complete pre-submission form and supporting documentation have been received by WHO, the Organization will review them against the established eligibility principles and criteria (see Section 5 above) to determine whether the product is eligible for WHO's prequalification assessment. If necessary, the manufacturer may receive a communication from WHO requesting

additional information and/or clarifications, including to assist WHO in its eligibility decision. The manufacturer must provide WHO with the information and/or clarifications requested within the deadlines communicated by WHO. The manufacturer will be provided with two opportunities to correctly complete the pre-submission form with all requested information. If the manufacturer fails or delays to provide the necessary information after those two opportunities, the application will be rejected, and the product will not undergo WHO's prequalification assessment.

WHO will inform the manufacturer in writing of WHO's decision on whether the pre-submission form is accepted (i.e., whether or not the product is eligible) for WHO's prequalification assessment.

If the pre-submission form is accepted (i.e., if the product is found by WHO to be eligible for WHO's prequalification assessment), then:

- WHO will request the manufacturer to complete, sign and return to WHO the Letter of Agreement for WHO's prequalification assessment of the product, using the document provided by WHO for this purpose (hereinafter, the "PQ Letter of Agreement"). The PQ Letter of Agreement will serve: (i) as an agreement between WHO and the manufacturer concerning WHO's prequalification assessment of the product; and (ii) as the manufacturer's acceptance of, and commitment to comply with, the terms, conditions and requirements of WHO's prequalification procedure for IVDs and the PQ Letter of Agreement; and
- The manufacturer will be responsible for paying all WHO prequalification fees (as defined in Section 11 below), and no liability or obligation shall attach to WHO in this regard.[11]

If the pre-submission form is not accepted (i.e., if the product is not found by WHO to be eligible for WHO's prequalification assessment), then the application will be rejected, and the product will not be accepted for or undergo WHO's prequalification assessment.

6.4. Conditions before WHO's prequalification assessment may proceed

If a pre-submission form has been accepted, then before WHO's prequalification assessment of the IVD may commence and proceed, the manufacturer must ensure that all of the following conditions have been met:

i. the manufacturer has duly and fully signed, completed and returned to WHO the PQ Letter of Agreement; and

ii. the manufacturer has paid in full, and has submitted to WHO written proof of payment of, all applicable WHO prequalification fees; and

iii. the manufacturer has compiled and submitted to WHO the relevant product dossier (i.e. full or abridged); see Section 8.3 below.

WHO's prequalification assessment of a product shall not commence or proceed, unless and until the manufacturer has met all conditions mentioned in clauses (i), (ii) and (iii) above.

For the avoidance of doubt, the issuance, receipt or signature of the PQ Letter of Agreement, the payment of WHO's prequalification fees, and/or the commencement of WHO's prequalification assessment process, do not mean or imply any decision by WHO (either positive or negative) on whether or not the product will be granted WHO prequalification listing.

[11] Details on WHO's prequalification fees are provided in document PQDx_299 "*WHO's prequalification assessment fees*".

7. Parallel or sequential submissions for WHO's performance evaluation and WHO's prequalification assessment

It is the responsibility of the manufacturer to submit an Expression of Interest form for WHO's performance evaluation of a product and, assuming such Expression of Interest is accepted by WHO, decided whether to:

a. submit *in parallel* an application for WHO's prequalification assessment of that product; or

b. wait until WHO's performance evaluation of that product has first been completed, *before* submitting an application for WHO's prequalification assessment of that product.

If option a. is selected, WHO's performance evaluation of the product must be completed and the final performance evaluation report must be available by the time WHO's prequalification assessment components are completed (see Section 9.1 below). If option b. is selected, the manufacturer must apply for WHO's prequalification assessment of the product within 60 days after WHO issues the final performance evaluation report for that product.

Regardless of which of the two options above is chosen, the manufacturer's attention is drawn to the following points:

- WHO's performance evaluation and WHO's prequalification assessment are separate processes, with separate applicable procedures, forms and requirements; and
- subject to WHO's acceptance of the Expression of Interest, the manufacturer commits to applying for WHO's prequalification assessment of the product within 60 days after WHO issues the final performance evaluation report for such product; and
- the product submitted for WHO's performance evaluation must be identical to that which is submitted for WHO's prequalification assessment (and vice-versa), unless any changes made to the product have first been accepted by WHO in writing, pursuant to this procedure; and
- the fact that an Expression of Interest for WHO's performance evaluation of a product has been submitted to, is pending review by and/or has been accepted by WHO does not mean or imply that the application for WHO's prequalification assessment of that product will be accepted by WHO or that, if accepted, the product will be granted WHO's prequalification listing; and
- the fact that WHO's performance evaluation of a product is in the process of being implemented and/or has been completed does not mean or imply that the application for WHO's prequalification assessment of that product will be accepted or that, if accepted, the product will be granted WHO's prequalification listing; and
- WHO's decision (whether positive or negative) regarding WHO's performance evaluation of a product will be taken subject to and in accordance with the terms and conditions of document PQDx_458 "*WHO's performance evaluation procedure for in vitro diagnostics"*; and
- WHO's decision (whether positive or negative) regarding WHO's prequalification assessment of a product—including whether or not to grant WHO's prequalification listing to that product—will be taken subject to and in accordance with the terms and conditions of this procedure.

8. WHO's prequalification assessment process

WHO's prequalification assessment can take place through two pathways—namely, full or abridged prequalification assessment— depending (among other things) on the product's regulatory version and whether the product has been stringently assessed and approved by a Recognized Regulatory Authority (RRA)[12].

WHO will determine the appropriate assessment pathway at the time of review of the pre-submission form and will inform the manufacturer, in writing, if a full or abridged prequalification assessment will be performed.

WHO reserves the right to shift from an abridged to a full prequalification assessment at any stage in WHO's prequalification assessment process, if the manufacturer fails or delays to submit satisfactory evidence that the product was stringently assessed and approved by an RRA and/or if WHO determines that the product or evidence submitted does not meet WHO's requirements for abridged prequalification assessment.

Figure 1 below provides an overview of the prequalification assessment process.

8.1. Full prequalification assessment

The full prequalification assessment consists of the following components:

- review of a full product dossier;
- manufacturing site(s) inspection; and
- labelling review.

8.2. Abridged prequalification assessment

The rationale for abridged prequalification assessment is that a prior regulatory approval by an RRA provides a level of assurance relating to the product's quality, safety and performance in countries where it is approved, but it cannot always provide the same assurance when the product is used in other settings, including resource-limited settings.

The abridged prequalification assessment aims to avoid duplication of effort and promote efficiencies. WHO will review the pre-submission form and supporting documentation to determine whether the product qualifies for an abridged prequalification assessment.

If WHO accepts a prequalification application, WHO's abridged prequalification assessment will apply in accordance with this procedure and document PQDx_173 "*WHO's abridged prequalification assessment for in vitro diagnostics"*, in the following instances:

1. if a regulatory version of the product submitted for WHO's prequalification assessment has previously been "stringently assessed" and approved by one of the RRAs; or
2. if a regulatory version of the product submitted for WHO's prequalification assessment has not been stringently assessed and approved by an RRA, but there exists another regulatory version of the product that has been stringently assessed and approved by an RRA and, in WHO's discretion, there are no substantial differences between the two regulatory versions (including, without limitation, substantial differences as to the product description, intended use, test procedure, labelling, quality management system, design, manufacturing site, key suppliers, verification/validation studies, and/or lot release criteria).

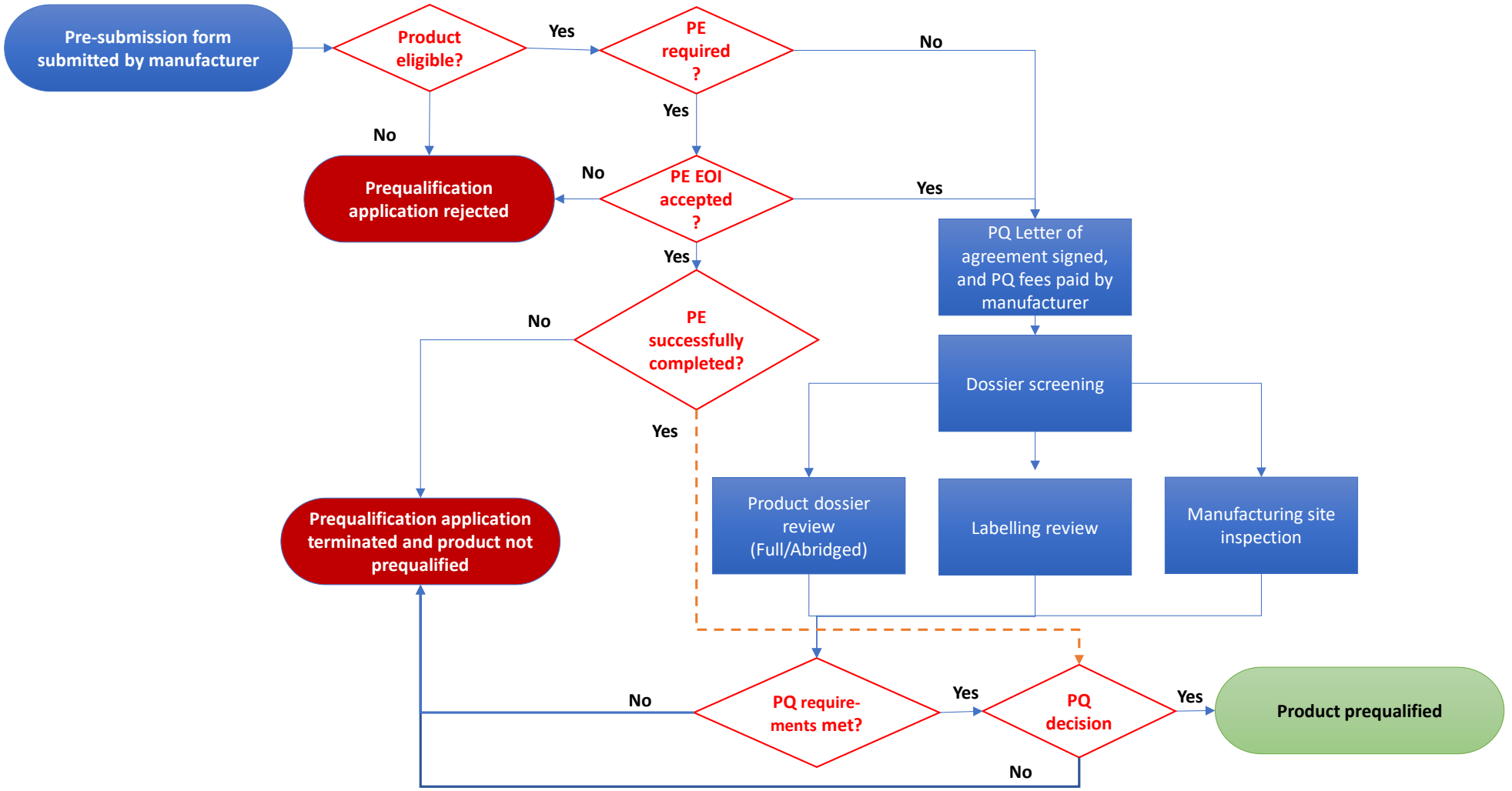
[12] For more information, please refer to document PQDx_173 "*WHO's Abridged prequalification assessment for in vitro diagnostics*"

The abridged prequalification assessment consists of the following components:

- review of an abridged product dossier;
- manufacturing site inspection; and
- labelling review.

If WHO accepts a prequalification application, but the product is not eligible for WHO's abridged prequalification assessment, then the product will be required to undergo WHO's full prequalification assessment pathway.

Figure 1 WHO's prequalification assessment process for IVDs



PE= WHO's performance evaluation; PE EOI= Expression of Interest form for WHO's performance evaluation; PQ= WHO prequalification

8.3. Product dossier submission and screening

For a full prequalification assessment, WHO will formally invite the manufacturer to submit a full product dossier together with the duly signed PQ Letter of Agreement and proof of payment of the prequalification fees. For an abridged prequalification assessment, WHO will formally invite the manufacturer to submit an abridged product dossier, together with the duly signed PQ Letter of Agreement and proof of payment of the prequalification fees.

Before WHO's prequalification assessment (whether full or abridged, as applicable) may commence, the manufacturer must:

(i) compile and submit to WHO the relevant product dossier (i.e., full product dossier or abridged product dossier, as applicable), in accordance with WHO documents PQDx_018 *Instructions for compilation of a product dossier* and PQDx_049 *Product dossier checklist*; and

(ii) duly and fully complete, sign and return to WHO the PQ Letter of Agreement; and

(iii) pay in full, and provide WHO with written proof of payment of the prequalification fees.

The manufacturer should not submit a product dossier or pay the prequalification fees, unless and until instructed to do so in writing by WHO. If a product dossier is submitted or any prequalification fees are paid without a request from WHO, then such dossier will not be reviewed and such fees will be non-refundable.

The manufacturer must ensure that the content of the product dossier is consistent with the information submitted in the pre-submission form for, as well as in the Expression of Interest for WHO's performance evaluation of, the product. The manufacture must also promptly notify WHO, in writing, of any changes in the information submitted in or as part of the pre-submission form and/or Expression of Interest for the product.

The product dossier should only include information in support of the product name, product code(s), regulatory version and manufacturing site(s) that are referred to in the PQ Letter of Agreement.

Once the product dossier has been received by WHO, it will be screened for completeness before being reviewed. Information that was previously submitted in the pre-submission form will also be considered by WHO during the review of the product dossier.

This screening of the product dossier is aimed at verifying that:

- All requisite sections of the product dossier have been completed and submitted; and
- All requisite sections of the product dossier are relevant for the type of product accepted for WHO's prequalification assessment; and
- The information submitted in the product dossier is consistent with the information submitted by the manufacturer in the pre-submission form and the Expression of Interest for WHO's performance evaluation.

As such, the screening of a product dossier does not include a technical review of the information provided therein.

If WHO determines that the product dossier is incomplete following its screening, WHO will inform the manufacturer in writing and will request it to provide supplemental information to complete the product dossier within a specified deadline. The manufacturer will be given two opportunities

to submit the supplemental information within the deadlines set by WHO. In the event the manufacturer fails or unreasonably delays to timely and/or fully provide the requested supplemental information, then the product dossier will be rejected, the prequalification application will be terminated pursuant to Section 9.5 below, and the product will not be prequalified.

If WHO determines that the product dossier is complete following its screening, WHO will proceed to undertake the product dossier review (see Section 8.4.1 below).

WHO will inform the manufacturer in writing about the outcome of the product dossier screening.

8.4. Prequalification assessment components

8.4.1. Product dossier review

The purpose of the product dossier review is to enable WHO to assess:

- evidence in support of safety and performance of the product; and
- the design of the product.

The information submitted in the product dossier will be reviewed and assessed by external experts (assessors) selected and appointed by WHO, but only if and after conditions (i), (ii) and (iii) in Section 6.4 above have been fully met. Assessors involved in the product dossier review will have appropriate qualifications and expertise in the relevant fields, will be required to comply with the confidentiality and conflict of interest rules of WHO, and will act as temporary advisers to WHO.

The review and assessment of the product dossier will be conducted in accordance with standard operating procedures (SOPs) established by WHO for that purpose, including to ensure uniformity in evaluation and timeliness of assessment activities. WHO will review the product dossier against the internationally recognized set of quality, safety and performance principles as described in the IMDRF document "*Essential Principles of safety and performance of medical devices and IVD medical devices*."[13]

Any deficiencies in the product dossier and/or any documentation or data relating thereto that are identified during the product dossier review will be communicated in writing to the manufacturer by WHO. In that case, the manufacturer must submit to WHO a corrective action plan that details the amendments needed to correct the deficiencies (i.e. responses to comments; documentation and/or data that is missing) and deadlines for their submission. The manufacturer will have the opportunity to submit up to two corrective action plans and, provided that the corrective action plan is accepted by WHO, only one amendment to the original product dossier will be permitted. The manufacturer may request a meeting with WHO to clarify issues identified during product dossier review. For the avoidance of doubt, the product dossier review will not proceed (i.e. WHO will not undertake any further action) until a corrective action plan has been submitted by the manufacturer to and accepted by WHO.

In certain cases, WHO may agree, in its discretion, to permit the manufacturer to correct specific deficiencies identified during the dossier review after the product has been granted WHO prequalification listing, provided however that the manufacturer commits in writing to fully correct such deficiencies by a deadline agreed by WHO. If the manufacturer fails to timely and/or

[13] As amended from time to time.

fully comply with the aforementioned commitments within the agreed deadline, WHO reserves the right to delist or suspend the product from WHO's list of prequalified IVDs.

WHO will notify the manufacturer, in writing, about the final outcome of the product dossier review.

If the product successfully meets WHO's prequalification requirements, a summary of the product dossier review will be included in the WHOPAR.

If the product dossier does not meet WHO's prequalification requirements or if any of the other conditions outlined under Section 9.5 below is met, then the prequalification application will be terminated and the product will not be prequalified.

8.4.2. Inspection of manufacturing site(s)

WHO's inspection of the manufacturing site(s) of the product is an essential component of WHO's prequalification assessment, is normally product specific, and is based on the principles outlined in ISO 19011[14] "*Guidelines for auditing management systems."*

The aim of the inspection of manufacturing site(s) is to assess whether the manufacturer's quality management system and manufacturing practices comply with: (i) applicable international standards, such as ISO 13485[15] "*Medical devices - Quality management systems - Requirements for regulatory purposes";* (ii) the manufacturer's own requirements; and (iii) other relevant international standards and guidelines. By way of example, international standards and guidelines relating to good practices for the manufacture of IVDs that are produced by International Organization for Standardization (ISO), Global Harmonization Task Force (GHTF) and International Medical Device Regulators Forum (IMDRF) will be used, as necessary and as determined by WHO, during the inspection of manufacturing site(s).

In addition, WHO's inspection of a manufacturing site will focus on the suitability of the relevant manufacturing processes and procedures for the reliable supply of IVDs of high quality, safety and performance to WHO Member States, UN agencies, funds and programmes, and other relevant international or intergovernmental organizations.

WHO's inspection of manufacturing site(s) consists of one or both of the following activities, as determined by WHO in its discretion:

- An on-site inspection by WHO's inspection team; and/or
- A desk assessment of information available to WHO's inspection team based on:
    - Information on an inspection of the manufacturing site(s) conducted in accordance with the terms of the Medical Device Single Audit Program (MDSAP); or
    - Information on an inspection of the manufacturing site(s) conducted by an RRA .

The decision to perform an on-site inspection and/or desk assessment lies exclusively with WHO, and is determined through risk-based approach considering a number of factors including:

- the results of inspection(s) previously conducted by WHO, of inspections conducted in accordance with the terms of the MDSAP, and/or of inspections conducted by an RRA;
- the comments and outcome of WHO's product dossier review;
- complexity of the site, processes and product;

[14] As amended from time to time.

[15] As amended from time to time.

- number and significance of known quality defects (e.g. complaints, field safety notices [FSN] and field safety corrective actions [FSCA]);
- major changes to, e.g. buildings, equipment, processes, key personnel; and
- site experience with manufacturing and testing of a product.

Each manufacturing site(s) inspection is performed by WHO, acting through an inspection team. WHO's inspection team is generally composed of a WHO staff inspector and external experts (also called "co-inspectors") selected and appointed by WHO. The external experts involved in the manufacturing site inspection are expected to have appropriate competence, qualifications and expertise in the relevant fields; and will be required to comply with WHO's confidentiality requirements and conflict of interest rules. In addition, WHO's inspection team may be accompanied to the manufacturing site inspection(s) by interpreters and/or by representatives of regulatory authorities, as observers or for training purposes.

After a manufacturing site inspection is conducted, a final inspection report (including any graded nonconformities) will be issued by WHO to the manufacturer.

The manufacturer must correct all nonconformities identified in WHO's inspection report through suitable corrective and preventive actions (CAPAs) addressing the root cause of each nonconformity. In this respect, the manufacturer must submit to WHO a CAPA plan for the nonconformities identified in the inspection report. WHO will review and, if necessary, comment on the manufacturer's CAPA plan. The CAPA plan must be agreed to by WHO, in writing, before the manufacturer implements the same.

Depending on the nature and number of nonconformities identified, WHO may also require the manufacturer to submit (within applicable deadline(s) agreed with WHO) objective evidence of the effective implementation of the agreed CAPA actions to such nonconformities.

Subject to WHO's review and acceptance of the CAPA plan and of objective evidence that the manufacturer has implemented the CAPA actions to WHO's satisfaction, the manufacturing site(s) inspection will be concluded, and all of the foregoing will inform WHO's decision on whether to prequalify the IVD.

Following the conclusion of the manufacturing site inspection, WHO will publish a WHOPIR on WHO's website. The publication will be done in consultation with the manufacturer. If the product successfully meets all WHO's prequalification requirements, a statement on the relevant manufacturing site's compliance with the applicable prequalification requirements will also be included in the WHOPIR.

WHO reserves the right to take any actions outlined in Section 9.3 (Sharing of information and reports regarding WHO's prequalification assessment) below, in the event that serious or critical nonconformities of public health concern are identified in connection with the manufacturing site inspection(s).

If WHO determines that the manufacturer, the product and/or the manufacturing site(s) inspected do not meet WHO's prequalification requirements, or if any of the other conditions outlined in Section 9.5 below are met, then the prequalification application will be terminated and the product will not be prequalified.

The manufacturer should carefully read the information included and regularly updated on WHO's prequalification inspection services webpage https://extranet.who.int/prequal/inspection-services and https://extranet.who.int/prequal/inspection-services/vitro-diagnostics-and-male-circumcision-devices for more information on the requirements applicable to WHO's

manufacturing site inspection and any reports, nonconformities and Notices of Concern arising therefrom.

8.4.3. Labelling review

For purposes of WHO's prequalification assessment, "product labelling" includes the product's instructions for use, label on the device or packaging, and promotional (marketing) materials if they contain device claims. Product labelling is a critical element of the evidence submitted for WHO's prequalification assessment, as clear and comprehensive labelling is needed to effectively communicate the product information to the intended user and to promote the safe use of the product.

The version of the product labelling that was submitted within the product dossier will be considered for purposes of the labelling review.

The product labelling will be reviewed and assessed by WHO for: (i) clarity and consistency with the information submitted in the product dossier, (ii) compliance with international guidance[16], [17] and requirements, and (iii) suitability for the target user group in WHO Member States.

The findings from the labelling review will be provided to the manufacturer, in writing, by WHO. If requested by WHO, the manufacturer must amend the product labelling as agreed with WHO before the product can be prequalified or as a prequalification commitment.

If WHO determines that the product labelling meets WHO's prequalification requirements, then the product labelling will be included in the WHOPAR.

If WHO determines that the product labelling does not meet WHO's prequalification requirements, or if any of the other conditions outlined in Section 9.5 below are met, then the application will be terminated and the product will not be prequalified.

9. Outcome of WHO's prequalification assessment

9.1. WHO's decision on whether or not to prequalify an IVD

WHO will take the prequalification assessment decision (whether positive or negative) regarding a product only after:

1. all components of WHO's prequalification assessment of the IVD (i.e., product dossier review, manufacturing site(s) inspection and labelling review) have been completed; and
2. if the IVD undergoing WHO's prequalification assessment is also required to undergo WHO's performance evaluation (as per document PQDx_459 *Eligibility criteria for performance evaluation*), WHO's performance evaluation of the IVD has also been completed.

In this respect, the information, results and reports arising from WHO's prequalification components (i.e., product dossier assessment, manufacturing site(s) inspection and labelling review) will be used by WHO to inform its decision on whether or not the IVD may be granted WHO's prequalification listing. A product must have successfully completed all components of WHO's prequalification assessment before it may be considered for possible prequalification listing, subject also to the outcomes of WHO's performance evaluation of the product (see below).

[16] ISO 18113 series as amended from time to time.
[17] IMDRF document "Principles of Labelling for Medical Devices and IVD Medical Devices" as amended from time to time.

In addition the information, results and reports (including the final performance evaluation report) arising from WHO's performance evaluation of the product will also be used by WHO to inform its decision on whether or not the IVD may be granted WHO's prequalification listing. A product must have successfully completed WHO's performance evaluation before it may be considered for possible prequalification listing, subject also to the outcomes of WHO's prequalification assessment components (see above).

If WHO's performance evaluation is not completed or if the final performance evaluation report is not available by the time WHO's prequalification assessment components (i.e., product dossier review, manufacturing site inspection and labelling review) have been completed, a grace period of 60 days will be granted by WHO for the manufacturer to complete WHO's performance evaluation and obtain the final performance evaluation report. If WHO's performance evaluation is not completed and/or the final performance evaluation report is not obtained within the 60 days grace period, the prequalification application will be terminated pursuant to Section 9.5 below, and the product will not be prequalified.

Provided that WHO determines, in its discretion, that:

(i) WHO's performance evaluation of the product has been successfully completed according to document PQDx_458 "*WHO's performance evaluation procedure for in vitro diagnostics*" and the final performance evaluation report has been issued; and

(ii) each component of WHO's prequalification assessment of the product has been successfully completed; and

(iii) the product meets WHO's performance evaluation requirements as well as WHO's prequalification requirements;

then the product bearing a specific product name, product code(s) and regulatory version, as manufactured at the specific manufacturing site(s) inspected, will be prequalified and included in WHO's list of prequalified IVDs.

For the avoidance of doubt, a product will not be considered for or granted WHO's prequalification listing, if:

- the Expression of Interest for WHO's performance evaluation of the product has been terminated by WHO for any reason; or
- the product has not successfully completed WHO's performance evaluation; or
- the application for WHO's prequalification assessment of the product has been rejected or terminated by WHO for any reason; or
- the product has not successfully completed all or any components of WHO's prequalification assessment; or
- the manufacturer's Expression of Interest, application and/or product has been withdrawn from WHO's performance evaluation and/or from WHO's prequalification assessment for any reason.

WHO's list of prequalified IVDs is published on WHO's website. If a product is prequalified, then WHO's list of prequalified IVDs will be updated to specify the following information about the prequalified product: product name, product code(s), regulatory version, manufacturer's name, manufacturing site(s), product packaging, and year in which the product was prequalified.

The manufacturer will receive a letter from WHO informing it: (1) of the outcome (whether positive or negative) for each prequalification assessment component, and (2) of WHO's decision (whether positive or negative, and including in light of the outcomes of WHO's performance

evaluation and of each component of WHO's prequalification assessment) on whether the product will be prequalified.

If the product is included in WHO's list of prequalified IVDs, the manufacturer will be responsible for timely and fully meeting its post-qualification obligations as further described under Section 12 below.

9.2. Ownership of WHO's prequalification assessment reports

WHO will have and maintain full, exclusive, unfettered control over the manner in which the prequalification assessment process is carried out, and over any reports, results, notices, publications and/or other materials (whether in draft or final form, and whether positive or negative) arising from or relating to WHO's prequalification assessment of an IVD and/or any PQ Results (all of the foregoing, collectively "PQ Reports").

As WHO is responsible for the prequalification assessment process, the ownership of and all rights in and to any information, data, findings, analyses, results and/or reports arising from or relating to WHO's prequalification assessment of an IVD (collectively "PQ Results") shall vest exclusively in WHO. Thus, WHO shall have the right to use, reproduce, display, distribute, share and publish any PQ Reports and/or PQ Results in WHO's discretion, subject to the protection of any commercially sensitive confidential information of the manufacturer. As used in this procedure, the term "commercially sensitive confidential information" of the manufacturer means:

- confidential intellectual property, know-how, and trade secrets (including, e.g. formulas, processes or information contained or embodied in a product, unpublished aspects of trademarks, patents, etc.); and
- commercial confidences (e.g. structures and development plans of a company).

9.3. Sharing of information and reports regarding WHO's prequalification assessment

As part of WHO's prequalification assessment process, WHO may share the manufacturer's application (i.e., the pre-submission form) and related information with any interested regulatory authorities, subject to WHO entering into an appropriate confidentiality undertaking with each such regulatory authority. Furthermore, the outcome of any joint review of information by WHO and any regulatory authorities may be used by WHO, in its discretion, as part of WHO's prequalification assessment of the product.

The reports arising from WHO's prequalification assessment (namely, the product dossier review report, manufacturing site(s) inspection report, and/or labelling review report) will be finalized according to the relevant SOPs and format established by WHO, describing the findings and including requests and recommendations to the manufacturer. The manufacturing site(s) inspection report, and a letter summarizing the findings and related requests and recommendations of the dossier and labelling reviews, will be sent by WHO to the manufacturer.

Subject to the protection of commercially sensitive confidential information of the manufacturer, WHO will publish on WHO's website and make publicly available the following information in connection with WHO's prequalification assessment process:

- the names of products and of manufacturers that have applied for WHO's prequalification assessment, the product code(s) submitted for WHO's prequalification assessment, and the prequalification status of each application;
- in the event that the product is granted prequalification listing:
    - a WHOPAR summarizing the findings of WHO's prequalification assessment of each product; and
    - a WHOPIR summarizing the findings of each manufacturing site(s) inspection; and

- a PEPAR arising from WHO's performance evaluation of the prequalified product[18].

Notwithstanding anything to the contrary contained in this procedure or elsewhere, and irrespective of the status (i.e., whether ongoing, completed or otherwise) and/or outcomes (i.e., whether positive or negative) of WHO's prequalification assessment, WHO shall have and hereby reserves the right to use, publish, issue, share with relevant regulatory and/or other authorities, with UN agencies, funds and programmes and/or with other relevant intergovernmental or international organizations, and/or make publicly available (in each case, in accordance with the provisions of this procedure, including provisions regarding the protection of any commercially sensitive confidential information of the manufacturer) any information, results, outcomes, reports (including, but not limited to, any WHOPARs, WHOPIRs and PEPARs), notices (including, without limitation, any WHO Notices of Concern, WHO Notices of Suspension, any WHO information notices and/or any field safety notices), publications and/or other materials—whether in draft or final form, and whether positive or negative— arising from or relating to: (i) WHO's prequalification assessment process including, but not limited to, the product dossier review, manufacturing site inspection and/or labelling review; (ii) WHO's decision whether or not to prequalify a product; (iii) any post-prequalification activities conducted by or on behalf of WHO or the manufacturer; and/or (iv) any confidential information to which WHO may gain access in the course of WHO's prequalification assessment and/or post-prequalification activities. WHO's aforementioned rights shall be exercised in accordance with the provisions of this document including, but not limited to, those relating to the protection of commercially sensitive confidential information of the manufacturer.

9.4. Correcting nonconformities/deficiencies and fulfilling prequalification commitments

Nonconformities and deficiencies identified as part WHO's prequalification assessment must be corrected by the manufacturer within the deadlines agreed with WHO. If any additional information or corrective actions are required from the manufacturer, WHO will postpone its decision on whether or not the IVD may be granted WHO's prequalification listing until such information and corrective actions have been provided/completed by the manufacturer and have been assessed and found satisfactory by WHO, in light of the applicable technical requirements and standards.

All critical nonconformities and deficiencies must be corrected before the product may be prequalified by WHO. In certain cases, WHO may agree, in its discretion, to permit the manufacturer to correct specific nonconformities and/or deficiencies after the product is prequalified, provided that the manufacturer commits in writing to correct those nonconformities and/or deficiencies by the deadline(s) agreed by WHO. The manufacturer is responsible for fully implementing its prequalification commitments (including, but not limited to, the correction of any relevant non-conformities and/or deficiencies) within the deadlines agreed with WHO. WHO reserves the right to verify the manufacturer's compliance with its prequalification commitments at any time. If the manufacturer fails or delays to implement its prequalification commitments, then WHO may (in its discretion) suspend or delist the product from WHO's list of prequalified IVDs.

If any additional information or corrective actions are required from the manufacturer as an outcome of WHO's performance evaluation, the manufacturer must address, to WHO's satisfaction, any requests and recommendations included in the final performance evaluation

[18] This applies when WHO's performance evaluation of the product is required as per document PQDx_459 *"Eligibility criteria for WHO's performance evaluation of in vitro diagnostics"*

report as a pre-condition for WHO's prequalification listing unless WHO expressly consents in writing to defer such requests and recommendations to prequalification commitments.

If serious or critical non-conformities or concerns (including with respect to quality, safety and/or performance) are identified in connection with WHO's prequalification assessment of a product and/or with a product that has been prequalified, then:

1. WHO reserves the possibility to exercise any of its rights under Section 9.3 above; and
2. WHO may delist or suspend the product from WHO's list of prequalified IVDs following WHO's assessment of: (i) the outcomes/results of any inspections or investigations regarding those serious or critical non-conformities or concerns; and (ii) the manufacturer's implementation of any corrective actions regarding those non-conformities/concerns.

9.5. Termination of the prequalification application

WHO reserves the right to terminate the prequalification application for a product at any time or stage of WHO's prequalification assessment, if WHO determines that:

1. conditions (i), (ii) and (iii) under Section 6.4 of this procedure have not been fully met/completed within 60 days after the date on which WHO informs the manufacturer of WHO's acceptance of the pre-submission form;
2. WHO's performance evaluation is not completed and/or the final performance evaluation report is not obtained within the 60 days grace period described in Section 9.1 above; and/or
3. the manufacturer has not applied for WHO's prequalification assessment of the product within 60 days after WHO issues the final performance evaluation report for that product; and/or
4. the product dossier (whether full or abridged, as applicable) does not contain all of the required information; and/or
5. based on the outcomes/results of any components of WHO's prequalification assessment (i.e., product dossier assessment, manufacturing site inspection and/or labelling review), the product does not meet, to WHO's satisfaction, WHO's prequalification requirements; and/or
6. the manufacturer is not able to, or fails or unreasonably delays to, provide the required or requested information within the applicable deadline(s); and/or
7. during the course of WHO's prequalification assessment, the manufacturer makes changes to the product and/or the product labelling without WHO's prior written agreement; and/or
8. WHO's performance evaluation of the product is not accepted or is terminated early by WHO, or is withdrawn by the manufacturer, for any reason; and/or
9. the product does not meet to WHO's satisfaction, the technical requirements for WHO's performance evaluation; and/or
10. based on an analysis of the overall outcomes and results of WHO's prequalification assessment, WHO has concerns regarding the use of the IVD and its potential impact on public health; and/or
11. the manufacturer is not able, or fails or unreasonably delays: (a) to allow WHO to conduct any manufacturing site(s) inspections, or (b) to implement, to WHO's satisfaction, any

corrective and preventive actions which WHO may require within the applicable deadline(s); and/or

12. the information supplied to WHO is inadequate or insufficient to complete WHO's prequalification assessment in a timely manner.

If a prequalification application is terminated, WHO will inform the manufacturer in writing, and the manufacturer will not be allowed to re-apply for WHO's prequalification assessment of the product for one year from the date of the notification of termination, unless otherwise agreed by WHO.

Without limiting the foregoing, if the prequalification application is terminated because the product does not meet, to WHO's satisfaction, the applicable technical requirements for WHO's prequalification and/or for WHO's performance evaluation, then the manufacturer may not re-apply for WHO's prequalification assessment for the product, unless and until all of the technical requests communicated by WHO in writing have been addressed (to WHO's satisfaction) by the manufacturer, and WHO has confirmed the same in writing.

9.6. Withdrawal from WHO's prequalification assessment and/or from WHO's list of prequalified IVDs

At any time or stage, the manufacturer may: (1) withdraw its application for WHO's prequalification assessment, or (2) withdraw a product or manufacturing site from WHO's prequalification listing; provided, however, that the manufacturer must provide WHO with prior written notice specifying the product(s)/manufacturing site(s) to be withdrawn. The effective date of the withdrawal will be the date on which WHO receives the aforementioned written notice, unless another effective date is mutually agreed in writing by WHO and the manufacturer.

If a product is withdrawn from WHO's prequalification assessment (i.e. scenario (1) above), then:

1. If applicable, WHO's performance evaluation of the product(s) withdrawn will be terminated; and
2. WHO's prequalification assessment of the product withdrawn will be terminated and the product will not be prequalified; and
3. The manufacturer will not be allowed to resubmit an Expression of Interest for WHO's performance evaluation and/or to re-apply for WHO's prequalification assessment of the product withdrawn for a period of time determined by WHO, usually one year from the effective date of withdrawal, unless otherwise agreed in writing by WHO.

Without limiting the foregoing, if the application for WHO's prequalification was withdrawn because the product does not meet or is unlikely to meet the technical requirements for WHO's performance evaluation in accordance with WHO's performance evaluation protocol, then the manufacturer will not be allowed to re-apply for WHO's prequalification assessment of the product, unless and until all of the following conditions have been met:

- A design change in respect of the product and its performance is implemented by the manufacturer (the "Design Change"); and
- The manufacturer submits to WHO, for its review, the Design Change and any supporting documentation requested by WHO; and
- WHO reviews and, in its discretion, finds acceptable the submitted Design Change and supporting documentation; and
- WHO informs the manufacturer in writing that the product may be re-submitted for WHO's prequalification assessment.

If a product or manufacturing site is withdrawn from WHO's prequalification listing (i.e., scenario (2) above), then the product or manufacturing site, as applicable, will be delisted from WHO's list of prequalified IVDs; provided, however, that the manufacturer shall nevertheless continue to comply with the provisions of Section 12.4 (Post-market surveillance) for as long as the product is on the market.

9.7. Sharing of information or outcomes after withdrawal or termination

If at any time and for any reason an application for WHO's prequalification assessment is terminated or withdrawn, or a product is withdrawn from WHO's prequalification assessment or from WHO's list of prequalified IVDs, then notwithstanding such termination or withdrawal, WHO will continue to have (and such termination or withdrawal will not prejudice or affect any of) WHO's rights set forth under Section 9.2 and/or Section 9.3 above.

9.8. Sharing of information or outcomes after delisting or suspension of a prequalified product

If a prequalified product is suspended or delisted by WHO at any time and for any reason, then notwithstanding such suspension or delisting, WHO will continue to have (and such suspension or delisting will not prejudice or affect any of) WHO's rights set forth under Section 9.2 and/or Section 9.3 above. See also Section 12.8 below.

10. Deadlines and requests for extensions

WHO's prequalification assessment will be carried out in accordance with deadlines set forth on WHO's Prequalification of IVDs Timelines webpage https://extranet.who.int/prequal/vitro-diagnostics/timelines.

Whenever WHO requires any information from the manufacturer in connection with WHO's prequalification assessment, the manufacturer will be provided a deadline for the submission of the requested information. The manufacturer must use its best efforts to provide WHO with all requested information by such deadline.

WHO may grant to the manufacturer additional time for the submission of the requested information in accordance with the timeline extensions indicated on the WHO's webpage referred to above.

11. Prequalification fees

The fees and costs arising from or relating to any activities carried out by or behalf of WHO that are necessary for WHO's prequalification assessment of a product (collectively, "WHO's prequalification fees" or the "prequalification fees") must be paid for and covered by the manufacturer[19], and no liability or obligation in connection therewith shall attach to WHO. For the avoidance of doubt, prequalification fees are separate from and in addition to any fees, costs or expenses arising from or in connection with WHO's performance evaluation of the product.

Without limiting the other conditions set forth in Section 6.4 above, there shall be no obligation for WHO or any third party to commence or continue WHO's prequalification assessment and/or any activities relating thereto, unless and until the prequalification fees have been fully and timely paid by the manufacturer.

[19] PQDx_299 "*WHO's prequalification fees*"

Payment of any prequalification fees does not mean or imply any decision by WHO (either positive or negative) on whether or not the product:

- will be accepted for WHO's prequalification assessment; or
- will be found to meet, to WHO's satisfaction, the technical requirements applicable to WHO's prequalification assessment; or
- will be granted WHO's prequalification listing; or
- will retain its prequalification status for any minimum duration.

The manufacturer must pay an additional fee[20] in the event that an assessment of a reportable change to a prequalified product is required[21].

In addition, for each product that is listed on WHO's list of prequalified in vitro diagnostics, an annual fee will be payable by the manufacturer.

WHO's prequalification fees are non-refundable. The terms and conditions of document PQDx_299 "*WHO's prequalification assessment fees*" apply to the prequalification fees and their payment.

12. Duration of prequalification status; post-qualification obligations; suspension and delisting of prequalified IVDs

If a product has been prequalified, the duration of the validity of the product's prequalification status is subject to and dependent upon the manufacturer's fulfilment, within the applicable deadlines and to WHO's satisfaction, of all post-qualification obligations and requirements described below. Failure or delay to comply with any of the post-qualification obligations and requirements may result in the suspension or delisting of the product from WHO's list of prequalified IVDs, as determined by WHO in its discretion (see Section 12.8 below).

For the avoidance of doubt, WHO may exercise any of its rights under Sections 9.2 and/or 9.3 above in connection with any information, results, outcomes, reports, notices, publications and/or other materials (whether in draft or final form, and whether positive or negative) arising from or relating to any post-prequalification activities by or on behalf WHO and/or the manufacturer.

12.1. Fulfilment of prequalification commitments

It is the manufacturer's responsibility to fully address WHO's prequalification commitments arising from WHO's prequalification assessment of the product (e.g., the product dossier review and/or labelling review) within the deadlines agreed with WHO. Compliance with WHO's prequalification commitments may be verified by WHO at any time after prequalification listing of the product.

12.2. Annual reporting

For each prequalified product, the manufacturer must submit to WHO an annual report that details the production and sales data, and all categories of complaints, regarding the product in a summarized form. The annual report, in the format determined by WHO, must be submitted by the manufacturer to WHO every year following the product's prequalification listing. The manufacturer will receive a request from WHO for submission of the annual report and providing the requisite report format. The annual report for the previous calendar year must be submitted

[20] Pursuant to and in accordance with document PQDx_299 "*WHO's prequalification fees".*

[21] PQDx_121 "*Reportable changes to WHO prequalified and emergency use listed in vitro diagnostics: Application guidance".*

no later than 28 February of each year. The information provided in the annual report will inform WHO's decision on the frequency of re-inspections.

12.3. Submission of changes

WHO prequalifies an IVD as it is submitted to and assessed by WHO at a particular point in time. Post-prequalification changes, such as modifications to components, manufacturing processes, or quality management systems, must be reported by the manufacturer to and approved by WHO prior to their implementation.

To meet WHO's prequalification requirements, the manufacturer must establish, maintain and implement a procedure for categorizing and documenting any changes to the product and/or the quality management system. This procedure must be available as part of the product dossier assessment and during the inspection of the manufacturing site(s).

For each prequalified product, the manufacturer must comply with the provisions of document PQDx_121 "*Reportable changes to WHO prequalified and emergency use listed in vitro diagnostics: application guidance"*.

12.4. Post-market surveillance

For each prequalified IVD, the manufacturer must conduct post-market surveillance to collect and analyse experiences with the use of the IVD and to determine any action to be taken. The manufacturer must monitor the prequalified product to ensure continued compliance with WHO's prequalification requirements.

Starting when a product is accepted for WHO's prequalification assessment, and as long as that product is included in WHO's list of prequalified IVDs, the manufacturer must, as a condition of prequalification, follow the guidance contained in WHO's document entitled "*Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics"*. WHO guidance for post-market surveillance includes proactive collection of information on quality, safety and performance of a product after it has been placed on the market and/or prequalified, through scientific, regulatory and other sources, as well as reactive notification and evaluation of user feedback (including complaints), enabling appropriate action to be taken.[22]

WHO will review the investigation of any incident concerning a prequalified product that is communicated to WHO. First, WHO will notify the manufacturer and, depending on the nature of the incident, may also notify relevant regulatory and/or other authorities, interested UN agencies, funds and programmes and/or relevant intergovernmental or international organisations, of the incident.

WHO will review the investigation conducted by the manufacturer to confirm whether it complies with scientific principles and is in accordance with international guidance and standards. WHO will have the right to perform a special inspection of any manufacturing site(s) of the prequalified product to verify that corrective and preventive actions have been implemented.

12.5. Routine and non-routine inspections

In addition to the initial manufacturing site(s) inspection which constitutes an integral part of WHO's prequalification assessment, following the prequalification of a product, WHO will perform

[22] For the avoidance of doubt, WHO's guidance on post-market surveillance and market surveillance of medical devices, including IVDs, is without prejudice to national and/or regional legislation and requirements.

routine and/or non-routine inspections of manufacturing site(s) of prequalified IVDs to verify continued compliance with prequalification requirements.

Routine manufacturing site(s) inspections are conducted at intervals determined by WHO using a risk-based approach and are typically scheduled every three to five years from the date of the last WHO manufacturing site(s) inspection, unless an earlier inspection is deemed necessary by WHO.

Non-routine manufacturing site(s) inspections (also called follow-up or for-cause inspections) are triggered by specific events, concerns or findings (e.g., complaints, regulatory actions initiated by a regulatory authority) and are usually event-driven and focused in scope. The timing and scope of non-routine inspections will be determined by WHO on a case-by-case basis.

If as a result of a routine or non-routine manufacturing site(s) inspection, WHO determines that a manufacturer, a product and/or specified manufacturing site(s) no longer meets WHO's applicable requirements, then the product(s) manufactured at that site (even partly) will be suspended or delisted from WHO's list of prequalified IVDs.

Failure or delay by the manufacturer to participate in, or to allow WHO to conduct, a routine or non-routine manufacturing site(s) inspection may also lead to suspension or delisting of the product from WHO's list of prequalified IVDs.

WHO reserves the right to issue WHO Notices of Suspension and/or WHO Notices of Concern as may be necessary to inform the relevant stakeholders, users and the general public.

12.6. Compliance with WHO's prequalification technical specifications

The purpose of WHO's prequalification Technical Specifications Series is to provide technical guidance to IVD manufacturers seeking WHO's prequalification. Where WHO's prequalification Technical Specifications Series documents for a specific product type eligible for WHO's prequalification exist, manufacturers must comply with the requirements laid down in the relevant publication in WHO's prequalification Technical Specifications Series.

For products prequalified before the issuance of the relevant publication in WHO's prequalification Technical Specifications Series, a transition period to ensure compliance will apply. Manufacturers must comply with the relevant technical specifications as outlined in the aforementioned Series within three years from their publication by WHO.

12.7. Payment of the annual fee

For each product listed on WHO's list of prequalified in vitro diagnostics, a non-refundable annual fee will be payable by the manufacturer to WHO pursuant to and in accordance with document PQDx_299 "*WHO's Prequalification assessment fees"*.

The annual fee is applicable to all IVDs that, by 1 September of each year, have been listed on WHO's list of prequalified in vitro diagnostics for 12 months or more.

An invoice for the annual fee will be issued by WHO to, and must be paid by, the manufacturer in accordance with the provisions set forth in document PQDx_299.

12.8. Suspension or delisting of a prequalified IVD

WHO reserves the right to suspend or delist (as determined by WHO) a prequalified product from WHO's list of prequalified IVDs, in the following cases:

1. Failure or delay by the manufacturer to comply with any post-qualification obligations and requirements as described in this Section 12. The foregoing includes, but is not limited to, the failure or delay by the manufacturer to participate in or to allow WHO to conduct any routine or non-routine inspections; and/or

2. If serious or critical non-conformities or concerns (including with respect to quality, safety and/or performance of the prequalified product or any of its manufacturing sites) are identified as described in Section 9.4; and/or
3. If WHO determines (including based on the outcomes/results of any routine or non-routine manufacturing site(s) inspection) that the prequalified product or any of its manufacturing sites no longer meet(s) WHO's applicable requirements.

The provisions of Section 9.8. above will also apply in the event of suspension of delisting of a prequalified product.

13. Confidentiality

In preparation or otherwise in connection with the conduct of WHO's prequalification assessment, the manufacturer or WHO (acting as a "Disclosing Party") may disclose to other persons or entities including, without limitation, to assessors, inspectors and/or co-inspectors (each, a "Receiving Party") certain information, data, documents and/or materials (including, without limitation, relating to a product and/or WHO's prequalification assessment) which the Disclosing Party considers to be confidential, non-public and/or proprietary to the Disclosing Party and/or third parties collaborating with it (hereinafter, "confidential information").

Whenever a Disclosing Party provides or otherwise makes available any confidential information to a Receiving Party in connection with WHO's prequalification assessment of a product, the Disclosing Party shall ensure that:

- Any confidential information that is disclosed in written or other tangible form shall be clearly marked by the Disclosing Party as "confidential" at the time of its disclosure; and
- Any confidential information that is disclosed in oral form shall be clearly stated by the Disclosing Party to be "confidential" at the time of its oral disclosure.

In addition to the foregoing, before the Disclosing Party provides or otherwise makes available any confidential information to a Receiving Party in connection with WHO's prequalification assessment, the Disclosing Party shall first require the Receiving Party to be legally bound and abide by the following terms:

1. The Receiving Party will treat all confidential information as confidential and proprietary to Disclosing Party or third parties collaborating with it;
2. The Receiving Party shall use the confidential information solely for the following purposes (hereinafter, collectively, the "Purpose"): (a) enabling the Receiving Party to conduct any of its activities and/or obligations arising from or in connection with WHO's prequalification assessment of the product, subject to and in accordance with the terms and conditions of this procedure and the other documents applicable hereto.
3. The Receiving Party shall take all reasonable measures to ensure that confidential information shall not be used for any purpose(s) whatsoever other than the Purpose (as defined above), unless and until a further written agreement permitting such other use/purpose has first been executed by a duly authorized representative of the Disclosing Party.
4. The Receiving Party shall ensure that confidential information is not disclosed to any other person or entity, unless such other person or entity: (a) has a need to know the confidential information for the Purpose, and (b) is bound by similar obligations of confidentiality and restrictions on use as contained herein.

Notwithstanding the foregoing, the obligations of confidentiality and non-use stated above will not apply to any part of the confidential information that the Receiving Party is clearly able to demonstrate (as evidenced by written records or other competent proof):

A. was lawfully known to or in the possession of the Receiving Party prior to any disclosure by or on behalf of Disclosing Party; or

B. was in the public domain or the subject of public knowledge at the time of disclosure by or on behalf of the Disclosing Party; or

C. becomes part of the public domain or the subject of public knowledge through no fault of the Receiving Party; or

D. has become available to the Receiving Party from a third party not in breach of any legal obligations of confidentiality or restrictions on use; or

E. was subsequently and independently developed by or on behalf of the Receiving Party without access or reference to any confidential information; or

F. is required to be disclosed by the Receiving Party pursuant to law applicable thereto, provided that the Receiving Party shall in such case immediately notify the Disclosing Party in writing of such obligation and shall provide adequate opportunity to the Disclosing Party to object to or restrict such disclosure or request confidential treatment thereof; provided always, however, that nothing contained herein shall be construed as a waiver of any privileges and immunities enjoyed by WHO or any of its officials or experts and/or as submitting WHO or any of its officials or experts to the jurisdiction of any regional, national or subnational court or tribunal; see Section 16 below.

For the avoidance of doubt, nothing contained in this Section 13 shall: (i) prevent a Disclosing Party from disclosing any confidential information that is owned by the Disclosing Party to any third party for any purpose; or (ii) limit, modify or prejudice any of WHO's other rights under this procedure (including, but not limited to, Sections 9.2 and 9.3 above) or otherwise.

14. Conflict of interest

Before they undertake any activities relating to WHO's prequalification assessment, WHO will require each non-staff, external inspector and assessor to complete and sign WHO's declaration of interest (DOI) form as well as a confidentiality undertaking.

WHO will review and assess the DOI Form(s) submitted by the external inspectors and assessors.

If, based on the DOI forms, WHO considers that a declared interest is insignificant or minimal and is unlikely to affect or be reasonably perceived to affect the judgment of the assessor or inspector, then he/she will discharge his/her functions exclusively as a temporary adviser to WHO. In this connection, each assessor and inspector is required to confirm that the information disclosed by him/her in the declaration of interest is correct and complete, and that he/she will immediately notify WHO of any change in this information.

If based on the DOI Form(s), WHO considers that a declared interest is potentially significant and/or may give rise to a real or perceived conflict of interest, then the following will apply:

- Another assessor or inspector will be selected by WHO; and
- The newly selected inspector or assessor will be required to complete, sign and return to WHO a DOI Form and a confidentiality undertaking, and the process set forth under this section will apply and recommence.

At the manufacturer's request, WHO will inform the manufacturer, in advance, of the proposed composition of WHO's inspection team that will perform the manufacturing site inspection and will provide the names and *curricula vitae* of the inspectors comprising such team. The manufacturer may object to an inspector's participation in the manufacturing site inspection; provided, however, that such objection (together with full details on the grounds therefor) must be communicated in writing by the manufacturer to WHO within 10 days after WHO first provides the proposed team composition. In the event of such an objection is timely received by WHO, then WHO will have the right to appoint a replacement inspector and/or to reschedule the manufacturing site(s) inspection.

15. Disclaimers

By submitting a product for WHO's prequalification assessment, the manufacturer understands and agrees that: (a) it is not WHO's mandate to, and WHO does not, issue any approvals, certificates, certifications, authorizations or licences for IVDs (such prerogative and responsibility lies with the national regulatory authority of each country); and (b) WHO does not, as a matter of policy, endorse, recommend or certify any specific product, manufacturer and/or entities over any others.

The purpose of WHO's prequalification assessment is to provide information to interested WHO Member States, UN agencies, funds and programmes, and/or international or intergovernmental organizations to guide their procurement decisions. In this regard, the outcome of WHO's prequalification assessment, the participation of the manufacturer and/or any product in WHO's prequalification assessment process, WHO's decision (whether positive or negative) regarding WHO's prequalification assessment and/or listing of any product, as well as WHO's acronym, name and emblem may not be used by manufacturers or any other party for any commercial, marketing, advertising and/or promotional purposes.

WHO will not accept any liability or responsibility whatsoever for any injury, death, loss, damage or other prejudice of any kind that may arise as a result of or in connection with the procurement, distribution and/or use of any product that has undergone WHO's prequalification assessment and/or as to which WHO has published any reports, notices or other materials.

16. Disputes; privileges and immunities of WHO

In the event of any claims or disputes arising from or in connection with WHO's prequalification assessment and/or this procedure (including, but not limited to, their implementation, findings, outcomes or decisions) (hereinafter, collectively, "Disputes"), such Dispute must be submitted in writing by the relevant manufacturer or other person or entity (hereinafter, the "Claimant") to WHO's Director of the Department of Regulation and Prequalification (RPQ), with a copy to the relevant Team Lead responsible for Prequalification of in vitro diagnostics. Upon receipt of any Dispute, WHO's Director of RPQ, or one of his/her authorized representatives, will acknowledge receipt in writing and will conduct an investigation into the Dispute within 30 days. Following the investigation, WHO's Director of RPQ, or one of his/her authorized representatives, will provide a written response to the Claimant that submitted the Dispute. If the Claimant is dissatisfied with the written response, then the Claimant must object in writing to WHO within 30 days of the date of WHO's aforementioned written response. In the event that the Claimant does not object to WHO in writing within such 30-day period, then the content of WHO's written response (including, without limitation, any findings or decisions contained therein) will be final and can no longer be challenged by the Claimant in any way. However, if the Claimant does object to WHO in writing

within such 30-day period, then the Dispute will be referred to WHO's Director-General for his or her decision which will be final and binding on the parties.

By virtue of WHO's status as a Specialized Agency of the United Nations, WHO, its officials and experts performing missions for WHO (including, but not limited to, assessors and inspectors) enjoy privileges and immunities under national and international laws and conventions, including without limitation: (i) the Convention on the Privileges and Immunities of the Specialized Agencies, adopted by the General Assembly of the United Nations on 21 November 1947 (the "1947 Convention"); and (ii) the United States' International Organizations Immunities Act of 1945 and Executive Order 10025 relating thereto (collectively, the "IOIA"). Nothing contained in or relating to this procedure, or any documents relating hereto and/or any aspect of WHO's prequalification assessment will constitute or be deemed as a waiver of any of the privileges or immunities which WHO, its officials and/or experts performing missions for WHO enjoy pursuant to the 1947 Convention, the IOIA or otherwise under any national or international law, convention or agreement, and/or as submitting WHO, its officials and/or experts aforesaid to the jurisdiction of any regional, national or subnational court or tribunal.

17. Relevant documents

The following documents and webpages provide information to guide the manufacturer through WHO's prequalification assessment, and are an integral part of this procedure.

- https://extranet.who.int/prequal/vitro-diagnostics
- Pre-submission form. Geneva: World Health Organization; (PQDx_015).
- Instructions for completion of the pre-submission form. Geneva: World Health Organization; (PQDx_017).
- Instructions for compilation of a product dossier. Geneva: World Health Organization; (PQDx_018 – IMDRF ToC).
- Product dossier checklist. Geneva: World Health Organization; (PQDx_049).
- Application form: Change request form for WHO prequalified and emergency use listed in vitro diagnostics. Geneva: World Health Organization; (PQDx_119).
- Reportable changes to WHO prequalified and emergency use listed in vitro diagnostics: application guidance. Geneva: World Health Organization; (PQDx_121).
- WHO's abridged prequalification assessment for in vitro diagnostics. Geneva: World Health Organization; (PQDx_173).
- Eligibility criteria for WHO's prequalification assessment of in vitro diagnostics. Geneva: World Health Organization; (PQDx_298).
- WHO's Prequalification assessment fees. Geneva: World Health Organization; (PQDx_299).
- WHO's performance evaluation procedure for in vitro diagnostics. Geneva: World Health Organization; (PQDx_458) available on the webpage https://extranet.who.int/prequal/ivd-performance-evaluation
- Information for manufacturers on manufacturing site inspections, available on WHO's website at https://extranet.who.int/prequal/inspection-services/vitro-diagnostics-and-male-circumcision-devices.
- Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics. Geneva: World Health Organization;

- Prequalification of in vitro diagnostics Technical Specification Series available on WHO's website https://extranet.who.int/pqweb/vitro-diagnostics/technical-specifications-series.

18. Contact information

For inquiries on manufacturing site inspections, please contact WHO's Prequalification Unit – Inspections services at prequalinspections@who.int. Any other inquiries regarding WHO's prequalification of IVDs should be addressed to: diagnostics@who.int.