



**OVERVIEW OF THE WHO  
PREQUALIFICATION OF  
IN VITRO DIAGNOSTICS ASSESSMENT**

*Prequalification of In Vitro Diagnostics*

Overview of the WHO prequalification of in vitro diagnostics assessment: prequalification of in vitro diagnostics. Version 9  
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## 1. Introduction

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

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

The full prequalification assessment process includes the following components:

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

An abridged prequalification assessment includes the following components:

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

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

- prequalification commitments;
- annual reporting;
- reporting of changes;
- post-market surveillance obligations;
- undergoing routine inspections; and
- ongoing compliance with WHO prequalification technical specifications.

The findings of WHO prequalification<sup>1</sup> are used to assess the safety, quality and performance of commercially available IVDs for the purpose of providing guidance to interested United Nations (UN) agencies and WHO Member States in their procurement decisions.

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

## 2. Intended audience

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

## 3. Definitions

Abridged prequalification assessment	Prequalification assessment by WHO including review of an abridged product dossier, performance evaluation, manufacturing site inspection and labelling review.
Dossier screening	Systematic process to ensure that all requisite sections of the product dossier are submitted.
Dossier review	Review and assessment of documentation including data, protocols, reports, procedures, etc., to support the quality, safety and performance of a product for the purpose of WHO prequalification.
Full prequalification assessment	Prequalification assessment including review of a full product dossier, performance evaluation, inspection of a manufacturing site and labelling review.
Inspection of manufacturing site(s) or manufacturing site(s) inspection	Inspection of the manufacturing site(s), of product undergoing prequalification assessment.
In vitro diagnostic medical device (IVD)	<p>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.</p> <p><i>Note:</i> 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.</p>
Labelling review	Review and assessment of the instructions for use and product labels
Manufacturer	Any natural or legal person with responsibility for design and/or manufacture of an IVD with the intention of making the IVD available for use, under his or her name, whether or not such an IVD is designed and/or manufactured by that person him- or herself or on his or her behalf by (an)other person(s).

Performance evaluation	Performance evaluation including evaluation of operational characteristics of a product for the purpose of the prequalification assessment process.
Post-market surveillance	Systematic process conducted by manufacturers to collect and analyse experience gained from IVD that have been placed on the market.
Rebranded product	A rebranded product is identical in every respect to the product manufactured by the original manufacturer, except that the product is labelled with the "rebranded" product name and product code, and bears the rebrander's name.
Rebrander	A manufacturer of a rebranded IVD.
Regulatory version	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 in question, as well as all documented evidence supporting the safety and performance claims associated with that submission. In the event that (i) regulatory versions of a product have been submitted to different regulatory authorities or assessment 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 <i>different</i> regulatory version.

## 4. Abbreviations

GHTF	Global Harmonization Task Force
IMDRF	International Medical Device Regulators Forum
IFU	Instructions for use
ISO	International Organization for Standardization
IVD	in vitro diagnostic medical device
MDSAP	Medical Device Single Audit Program
SOP	standard operating procedure
UN	United Nations
WHO	World Health Organization

WHOPAR	World Health Organization Public Assessment Report, which summarizes the findings of the prequalification assessment, but excludes confidential and proprietary information.
WHOPIR	World Health Organization Public Inspection Report, which summarizes the findings made during the inspection of the manufacturing site(s) as well as corrective actions taken in respect of the site(s), but excludes confidential and proprietary information.

## 5. About prequalification of IVDs and procurement

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

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

## 6. Eligibility for prequalification of IVDs

### 6.1. Original manufacturer

Applications for WHO prequalification of IVDs are accepted only from the legal manufacturer of the product.<sup>2</sup>

### 6.2. Rebranded products

WHO is aware that several manufacturers purchase finalized products from other companies, and then "rebrand" and place these products on the market under their own name or brand. Such products are also known as original equipment manufacturer (OEM) products.

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

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

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

### 6.3. Commercial availability

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

### 6.4. Eligibility principles and eligibility criteria

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

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

The eligibility principles are applied using a set of eligibility criteria as defined in the document WHO PQDx\_298 *Eligibility criteria for WHO prequalification of in vitro diagnostics*.

## 7. Applying for WHO prequalification

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

The manufacturer must complete a pre-submission form (WHO document PQDx\_015 *Pre-submission form*) and must provide WHO with all requested supporting documentation in accordance with the WHO document PQDx\_017 *Instructions for the completion of the pre-submission form*.

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

The prequalification pre-submission form and supporting documentation will be reviewed by WHO against the established eligibility criteria to determine the product’s eligibility for prequalification assessment. If necessary, the manufacturer may receive a communication from WHO requesting additional information and/or clarifications to assist it in the eligibility decision. The manufacturer must provide WHO with the information and/or clarifications so requested within the deadlines

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<sup>3</sup> <https://extranet.who.int/pqweb/vitro-diagnostics/guidance-documents>  
PQDx\_007 v9 4 January 2021 (This document version supersedes any previous document versions)



prescribed by WHO. WHO will inform the manufacturer in writing of WHO's decision concerning whether or not the product is eligible for prequalification assessment.

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

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

## 8. Prequalification assessment

Two types of prequalification assessment can take place, depending on the regulatory version submitted and evidence from a previous stringent review by a Recognized SRA<sup>5</sup>. WHO will determine the appropriate type of assessment at the time of review of the pre-submission form.

### 8.1. Full prequalification assessment

The full prequalification assessment process consists of the following components (see Figure 1):

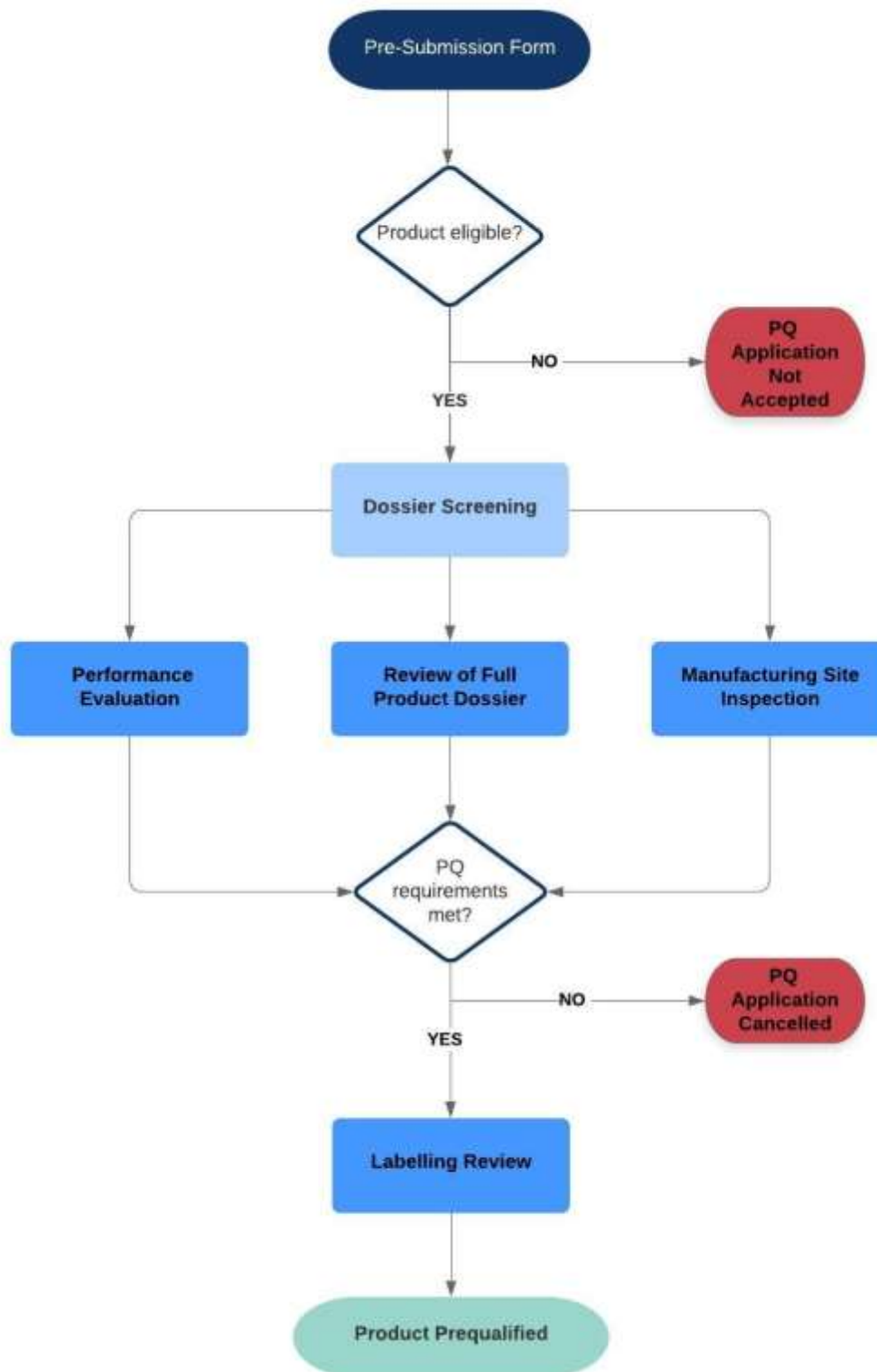
- review of a full product dossier;
- performance evaluation, including operational characteristics;
- inspection of a manufacturing site against all applicable requirements of ISO 13485:2016; and
- labelling review.

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<sup>4</sup> Details on the prequalification fees are provided in WHO document PQDx\_299 Prequalification fees.

<sup>5</sup> For more information about what constitutes a "Recognized SRA", please refer to document PQDx\_173 "Abridged prequalification assessment"

Figure 1 Prequalification of IVDs: full prequalification assessment process



## 8.2. Abridged prequalification assessment

The rationale for abridged prequalification assessment is that a prior regulatory approval 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 jurisdictions, including resource-limited settings.

The aim of abridged prequalification assessment is to avoid duplication of effort and reduce the time taken to prequalify a product by focusing on aspects where WHO prequalification assessment brings added value. WHO will review the pre-submission form and supporting documentation to determine whether the product qualifies for an abridged prequalification assessment. Products that do not qualify for abridged prequalification assessment will require a full prequalification assessment (section 8.1).

WHO will apply the abridged prequalification assessment process, in accordance with WHO document PQDx\_173 – *Abridged prequalification assessment*,<sup>6</sup> in the following instances:

1. if a regulatory version of the product submitted for WHO prequalification has previously been “stringently assessed” and approved by one of the Recognized SRAs; or
2. if a regulatory version of the product submitted for WHO prequalification has not been stringently assessed and approved by a Recognized SRA, but a stringently assessed and approved regulatory version of the product also exists, and there are no substantial differences between the two regulatory versions.

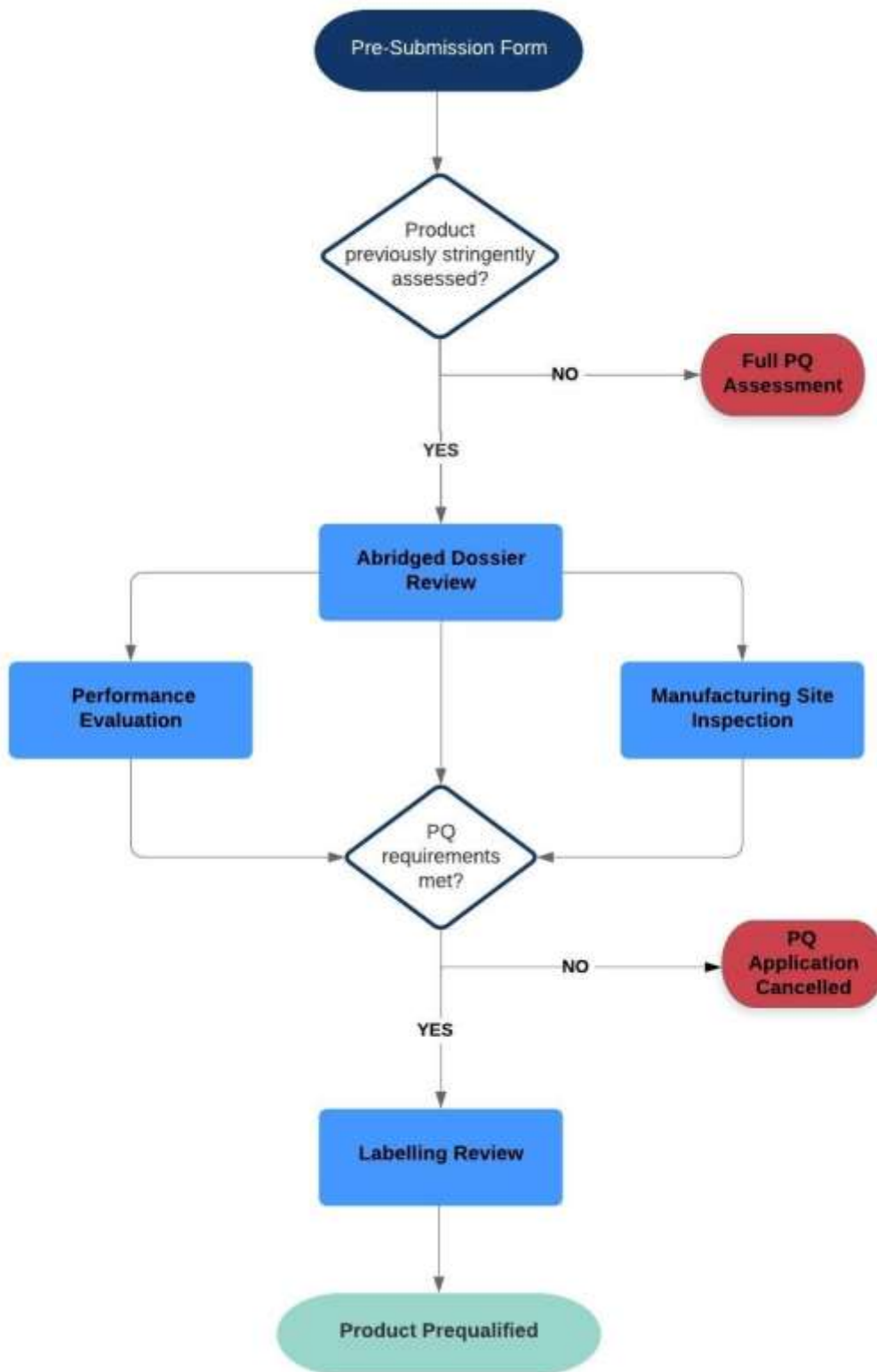
The abridged prequalification assessment consists of the following components, as shown in figure 2:

- review of an abridged product dossier;
- performance evaluation, including operational characteristics;
- inspection of a manufacturing site against all applicable requirements of ISO 13485:2016; and
- labelling review.

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<sup>6</sup> For further information please refer to the abridged prequalification assessment document PQDx\_173. PQDx\_007 v9 4 January 2021 (This document version supersedes any previous document versions)

Figure 2 Prequalification of IVDs: abridged prequalification assessment process



WHO reserves the right to shift from an abridged prequalification assessment to a full prequalification assessment at any stage in the prequalification assessment process, if the manufacturer fails to submit satisfactory evidence supporting a previous stringent review and/or if the submitted evidence does not meet WHO's requirements for abridged 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 Letter of Agreement and proof of payment of the dossier screening fee. For an abridged prequalification assessment, WHO will formally invite the manufacturer to submit an abridged product dossier, together with the duly signed Letter of Agreement and proof of payment of the prequalification assessment fee.

Before any 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), as prescribed by WHO documents PQDx\_018 *Instructions for compilation of a product dossier*, PQDx\_049 *Product dossier checklist and PQDx\_173 Abridged prequalification assessment*; (ii) complete, sign and return to WHO the Letter of Agreement; and (iii) provide WHO with proof of payment of the applicable prequalification fee. Manufacturers should not submit a product dossier or pay the prequalification fee, unless instructed to do so by WHO. Product dossiers that are submitted without a request from WHO will be destroyed without review.

Information that was previously submitted in the pre-submission form will also be considered by WHO during the review of the product dossier.

Manufacturers must ensure that the content of the product dossier is consistent with the information submitted in the pre-submission form and that any changes in the information submitted in or as part of the pre-submission form are promptly notified in writing to WHO.

The product dossier should only include information in support of the product name, product code(s), regulatory version and manufacturing site(s) made eligible by WHO.

Once the product dossier has been received by WHO, it will be screened for completeness by WHO staff before being reviewed. This screening is aimed at ensuring that all requisite sections of the product dossier have been submitted and as such does not take into consideration the technical appropriateness of all the information provided in the product dossier.

If the product dossier is incomplete, the manufacturer will be informed in writing that an incomplete dossier has been received and will be requested to provide supplemental information to complete the product dossier within a specified deadline. The manufacturer will be given two opportunities to submit the required supplemental information within the deadlines set by WHO. In the event of non-compliance, the product dossier will be rejected on grounds of incompleteness and the application will be cancelled pursuant to section 10.3 (Cancellation of the application).

Product dossiers that are considered complete following the screening will be retained by WHO for product dossier review (see Section 8.4.1 below). WHO will inform the manufacturer in writing on the outcome of the dossier screening.

### **8.4. Prequalification assessment components**

#### **8.4.1. Product dossier review**

WHO reviews the product dossier with the purpose of:

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

The information submitted in the product dossier will be assessed by external experts (assessors) appointed by WHO after submission of proof of payment of the applicable prequalification assessment fee. Assessors involved in the product dossier review will have appropriate

qualifications and expertise in the relevant fields and are to comply with the confidentiality and conflict of interest rules of WHO. The assessors will act as temporary advisers to WHO.

The assessment of product dossiers will be conducted in accordance with standard operating procedures (SOPs) established by WHO for that purpose so as to ensure uniformity in evaluation and timeliness of assessment activities. If needed, WHO may provide training to the assessors.

Any deficiencies in the documentation submitted and/or in the data that are identified in the product dossier review will be communicated in writing to the manufacturer by 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 must be provided by the manufacturer to WHO. 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 prequalification assessment procedure is usually suspended (i.e. WHO will not undertake any further action) until a corrective action plan has been submitted by the manufacturer and accepted by WHO. In certain cases, WHO may agree, in its sole discretion, to permit the manufacturer to correct specific nonconformities after prequalification, provided that the manufacturer commits in writing to correct them by an agreed deadline. Such a "commitment to prequalification" will be reflected in the WHOPAR and will be verified during the re-inspection. Failure to comply with prequalification commitments within agreed deadlines will result in the delisting from the WHO list of prequalified IVDs.

The manufacturer may request a hearing or meeting with WHO to clarify issues identified during dossier review. WHO may provide technical guidance and specifications to manufacturers to facilitate compliance with WHO requirements.

If the product successfully meets the WHO prequalification requirements, a summary of the product dossier review will be included in the WHOPAR. If the product dossier does not meet WHO prequalification requirements or if any of the other conditions outlined under section 10.3 (Cancellation of the application) is met, the prequalification application will be cancelled.

#### **8.4.2. Performance evaluation of the product**

The performance evaluation is essential for independent verification of the performance and operational characteristics of IVDs submitted for prequalification. It also allows WHO to verify performance and operational characteristics that are considered essential for use in resource-limited settings. The data obtained complement the verification and validation data submitted by the manufacturer in the product dossier.

The performance evaluation is a component of both a full prequalification assessment and an abridged prequalification assessment. The performance evaluation of the product is carried out by specified WHO collaborating centre(s)<sup>7</sup> or a designated laboratory or laboratories (collectively referred to as "evaluating site(s)"), using the WHO prequalification evaluation protocol. The product will be evaluated against predetermined acceptance criteria established by WHO.

The manufacturer must choose one of the following two performance evaluation options, and must indicate its choice in the pre-submission form:

- Option 1: Performance evaluation commissioned by WHO and carried out at an evaluating site listed by WHO.

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<sup>7</sup> WHO collaborating centres are institutions designated by the WHO Director-General to form part of an international collaborative network carrying out activities in support of WHO's programmes at all levels. In certain instances, additional laboratories may be contracted by WHO to perform laboratory evaluation.

The manufacturer must indicate in the pre-submission form its choice to undergo a performance evaluation coordinated by WHO and performed by an evaluating site selected by WHO.

- Option 2: Performance evaluation commissioned by the manufacturer and carried out at an evaluating site listed by WHO.

The manufacturer must indicate in the pre-submission form its choice to have the performance evaluation performed by an independent laboratory selected by the manufacturer from the list of prequalification evaluating sites.<sup>8</sup> If this option is chosen, the manufacturer will be responsible for paying the full cost of the performance evaluation (in addition to paying the applicable prequalification assessment fee) and for coordinating the performance evaluation directly with the evaluating site.

For option 1 – WHO will commission the performance evaluation at the evaluating site. The evaluating site will conduct the performance evaluation and share the data from the evaluation directly with WHO.

For option 2 – The manufacturer will commission the performance evaluation directly at the selected evaluating site, which will inform the WHO In Vitro Diagnostics Assessment Team when a performance evaluation has been commissioned by a manufacturer. The evaluating site will conduct the performance evaluation and share the data directly with WHO and with the manufacturer. To ensure the independence of the performance evaluation, data analysis will be performed by the evaluating site.

If the product is eligible for prequalification assessment and option 1 is chosen, the manufacturer will receive a letter from WHO outlining the type of assessment that the product will undergo (i.e., either an abridged or a full assessment) and WHO will coordinate the performance evaluation. If the product is eligible for prequalification and option 2 is chosen, the manufacturer will receive a letter from WHO outlining the type of assessment that the product will undergo (i.e., either an abridged or a full assessment) as well as instructions on how the data generated from the performance evaluation will be shared by the evaluating site.

Regardless of the option chosen, the performance evaluation must be carried out in accordance with a publicly available WHO protocol developed in collaboration with international experts.

WHO evaluation protocols outlining the procedures used to assess the product performance and operational characteristics are available on the WHO Prequalification of IVDs website.<sup>9</sup> The manufacturer will be requested to send sufficient quantities from at least two different lots<sup>10</sup> of the product. Detailed shipping instructions (e.g. number of test kits and/or instruments, number of lots, etc.) will be communicated in due time to the manufacturer by the evaluating site(s). The manufacturer should not send tests to the evaluating site(s) unless explicitly invited to do so.

The manufacturer must send to the evaluating site(s) the requisite quantities and lots of the product (test kits and/or instruments) “free domicile”, in accordance with the aforementioned detailed shipping instructions, free-of-charge, and delivered with all customs declarations, customs duties,

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<sup>8</sup> The *List of WHO prequalification evaluating laboratories* is available through the following webpage: <https://extranet.who.int/pqweb/vitro-diagnostics/performance-evaluation>

<sup>9</sup> <https://extranet.who.int/pqweb/vitro-diagnostics/performance-evaluation>

<sup>10</sup> For the purposes of WHO performance evaluation, a lot is defined as “The amount of material that is uniform in its properties and has been produced in one process or series of processes. The material can be either starting material, intermediate material or finished product.” Furthermore, the two lots must be sourced from a representative production run and not produced especially for the purpose of the WHO performance evaluation.

and transport and other charges paid for by the manufacturer. If necessary, special equipment needed to perform the assay must be made available by the manufacturer at no charge (i.e. customs declaration and payment of customs duties, transport, installation, training, etc., will be made by the manufacturer) to the evaluating site for the duration of the prequalification assessment process.

WHO will have absolute, exclusive, unfettered control over the manner in which the prequalification assessment process is carried out (including the performance evaluation and/or the publication of results of the prequalification assessment, regardless of the outcome). Without prejudice to the foregoing and in agreement with WHO, the manufacturer may wish to visit the specified evaluating site(s) to observe the operator performing the test procedure on the manufacturer's product(s) before commencing the performance evaluation. There should not, however, be any changes made to the test procedure as outlined in the instructions for use. If so, the manufacturer must notify WHO in writing, and the performance evaluation will be suspended.

If option 1 for the performance evaluation is chosen by the manufacturer, the evaluating site(s) will submit a draft performance evaluation report to WHO. After verification, WHO will send the draft performance evaluation report to the manufacturer, who will have the opportunity to review and comment on the report and results. WHO will reasonably consider any comments by the manufacturer to the draft performance evaluation report, provided that such comments are submitted by the manufacturer in writing to WHO within one month after the manufacturer's receipt of the draft performance evaluation. For the avoidance of doubt, WHO will maintain full and exclusive control over the data analysis, the reporting of the performance evaluation results and the form and content of any publication thereof. After such one-month period, the performance evaluation report will be considered as final.

If option 2 for the performance evaluation is chosen by the manufacturer, the evaluating site(s) will submit a draft performance evaluation report to the manufacturer and to WHO. After verification, WHO will request the manufacturer to review and comment on the report and the results. WHO will reasonably consider any comments by the manufacturer to the draft performance evaluation report, provided that such comments are submitted by the manufacturer in writing to WHO within one month after the manufacturer's receipt of the draft performance evaluation report. For the avoidance of doubt, WHO will maintain full and exclusive control over the data analysis, the reporting of the performance evaluation results and the form and content of any publication thereof. After such one-month period, the performance evaluation report will be considered as final.

A summary of the performance evaluation report will be included in the WHOPAR if the product successfully meets the WHO prequalification requirements. Irrespective of whether or not the product meets WHO prequalification requirements, a summary of the performance evaluation report may be published in a WHO composite report as part of the WHO technical specification series on the performance and operational characteristics of commercially available IVDs or in an article in a scientific journal. If the product fails to meet WHO prequalification acceptance criteria for performance evaluations, the application will be cancelled.

#### **8.4.3. Inspection of manufacturing site(s)**

A WHO inspection of the manufacturing site(s) is a necessary part of a prequalification assessment, is normally product specific, and is based on the principles outlined in ISO 19011:2018 "*Guidelines for auditing management systems*." The aim of the inspection of manufacturing site(s) is to assess compliance of the manufacturer's quality management system and manufacturing practices with applicable international standards, such as ISO 13485:2016 "*Medical devices - Quality management systems - Requirements for regulatory purposes*" and others. The relevant international standards and guidelines produced by ISO, GHTF and IMDRF relating to good practices for the manufacture of IVDs will be utilized as necessary during an inspection of manufacturing site(s).



WHO's inspection of a manufacturing site will focus on the suitability of the implemented processes and procedures for the reliable supply of IVDs to WHO Member States, UN agencies and other relevant intergovernmental organizations.

An inspection of manufacturing site(s) could consist of one or both of the following activities, in WHO's discretion:

- An on-site inspection by inspectors from WHO's Prequalification Inspection Services Team; and/or
- A desk review of information available to WHO's Prequalification Inspection Services Team based on:
  - Information on an inspection of the manufacturing site(s) conducted by a stringent regulatory authority (SRA) or availability of a certified certificate; or
  - Information on an inspection of the manufacturing site(s) conducted in accordance with the terms of the Medical Devices Single Audit Program (MDSAP).

The intention of a desk review is to review available audit reports of the manufacturing site in lieu of a WHO on-site inspection, and to consider whether the scope and inspection activities reflected in the audit reports indicate an adequate assessment of product/process related technologies and the fulfilment of WHO's prequalification requirements. In some instances, the information considered during the desk review is not sufficient to enable WHO to determine if the manufacturing site in question complies with WHO's relevant prequalification requirements, in which case an on-site manufacturing site inspection will be conducted.

When preparing for an on-site manufacturing site inspection, WHO may take into account the previous findings of an SRA's ISO13485:2016 audit for regulatory purposes. Importantly, during the manufacturing site inspection, the inspector will also verify the content of the product dossier or equivalent technical documentation, including through review of reports and raw data on site as well as through interviews with the personnel involved.

The inspection team is composed of a WHO staff inspector and external experts (co-inspectors) appointed by WHO. In addition, the inspection team may include interpreters and observers. The external experts involved in the manufacturing site inspection: are expected to have the competence, appropriate qualifications and expertise in the relevant fields; will comply with the confidentiality and conflict of interest rules of WHO; and will act as temporary advisers to WHO. Representatives of the national regulatory authorities (NRAs) may accompany the inspection team to the manufacturing site(s) as observers or for training purposes.

If serious or critical nonconformities of public health concern are identified in connection with an inspection of manufacturing site(s) (regardless of whether such inspection is for purposes of the prequalification of a product and/or in connection with any post-prequalification activities), WHO reserves the right to use, publish, issue, share with relevant authorities of WHO Member States as well as with UN agencies and other relevant intergovernmental organizations, and/or make publicly available (in each case, pursuant to the provisions of this document, including provisions regarding the protection of any commercially sensitive confidential information of the manufacturer) any outcomes, reports and/or results—whether in draft or final form, and whether positive or negative—arising from or relating to the prequalification assessment process and/or any post-prequalification activities, including without limitation, any WHOPARs, WHOPIRs, WHO Notices of Concern, WHO Notices of Suspension, WHO information notices for users and/or manufacturer-issued field safety notices.

The manufacturer should carefully read the information set out in the WHO document PQDx\_014 – *Information for manufacturers on the inspection of manufacturing site(s)* for more information on the requirements of inspection, reports, nonconformities and Notices of Concern.

The inspection of a manufacturing site is normally product-specific; however, WHO may determine, in its discretion, that more than one product may be assessed in a single inspection. The inspection of a manufacturing site will include all organizational units, activities and processes associated with the products that are the subject of such inspection and, to larger or lesser extent, a review of all QMS procedures and processes, as the inspectors take into consideration the findings of the most recent regulatory audit report available from WHO or SRAs.

The manufacturing site inspection will include sampling of some of the general quality management processes and associated records and a follow-up on, or clarification of, individual findings identified during a previous inspection by WHO or as listed in a report that the inspection team had considered. In addition, the manufacturing site inspection will concentrate on those product- and user-specific processes that are a major focus of WHO prequalification inspections (e.g. management of product and process risks, verification of evidence of usability of product in intended conditions and for intended population, in-use stability under poorly controlled conditions, impact on stability of transportation, the effectiveness of the system for collecting feedback from the market of interest, investigation and management of received complaints, and regulatory reporting to WHO, user training and training material).

#### *8.4.3.1 Report on the inspection of the manufacturing site(s)*

If time allows, a preliminary non-conformance report detailing issues of concern (if any) will normally be provided to the manufacturer on the final day of the inspection. A final inspection report, including the graded nonconformities will be issued to the manufacturer after the inspection of the manufacturing site(s).

All nonconformities must be corrected by the manufacturer through suitable corrective actions addressing the root cause of each nonconformity. The manufacturer will have the opportunity to submit up to two corrective action plans. Depending on the nature and number of nonconformities, objective evidence of the effective implementation of proposed corrective actions will be required. WHO will assess the information provided and decide whether the corrective action plan can be accepted. Conformity with prequalification requirements will be established based on assessment of such information. In some instances, the number and criticality of nonconformities may require that the effective implementation of proposed corrective actions needs to be verified in a follow up inspection, before the nonconformities can be closed off.

Following the inspection, the inspection team will publish a summary of the observations and findings made during the inspection as well as corrective actions taken by the manufacturer, but excluding confidential and proprietary information on the WHO website in a WHOPIR. The publication will be done in consultation with the manufacturer. In addition a statement on the compliance of the site inspected will be included in the WHOPIR, if the product successfully meets all the WHO prequalification requirements.

In certain cases, WHO may agree, in its sole discretion, to permit the manufacturer to correct specific nonconformities after prequalification, provided that the manufacturer commits in writing to address them by an agreed deadline. Such a “commitment to prequalification” will be followed-up by the inspection team and verified during a re-inspection of the manufacturing site. Failure to comply with prequalification commitments within agreed deadlines will result in the delisting from the WHO list of prequalified IVDs.

If the manufacturer does not meet WHO prequalification requirements or if any of the other conditions outlined in section 10.3 (Cancellation of the application) are met, the prequalification application will be cancelled.

#### **8.4.4. Labelling review**

Product labelling is considered a critical element of the evidence submitted for prequalification assessment. Only clear and comprehensive labelling will effectively communicate the product information to the intended user and ensure the safe use of the prequalified product.

The version of the instructions for use (IFU) of the product which is submitted with the pre-submission form will be considered during the prequalification assessment. The manufacturer must obtain WHO's written agreement prior to implementing any changes to this version of the instructions for use; otherwise, the application may be cancelled.

The product labelling will be reviewed as part of the pre-submission form, product dossier, performance evaluation and inspection of manufacturing site(s). The IFU is reviewed for clarity, correctness, consistency with the information submitted in the product dossier and in the technical documentation, and with international guidance<sup>11</sup> and requirements, and suitability for the target user group in WHO Member States. The overall feedback on the labelling review will be provided to the manufacturer after all assessment components have been completed. If requested by WHO, the manufacturer must amend the labelling before the product can be prequalified.

The agreed product labelling will be included in the WHOPAR.

## **9. Deadlines for prequalification assessment and requests for extensions**

Prequalification assessments will be carried out in accordance with defined deadlines laid down in the WHO document PQDx\_300 *Prequalification of in vitro diagnostics assessment and change assessment target deadlines*. WHO will perform assessment activities within agreed target timelines.

The manufacturer will be assigned a deadline for the submission of requested information each time such a request is issued by WHO, and the manufacturer will use its best efforts to provide WHO with all requested information by such deadline. In addition, WHO will request that the performance evaluation and inspections of manufacturing site(s) are scheduled within a defined time frame to be communicated by WHO.

The manufacturer is allowed to request an extension of the timeline for submission of the requested information, for scheduling a performance evaluation or for a site inspection.<sup>12</sup>

## **10. Outcome of the prequalification assessment**

### **10.1. Reporting and communication of the results of the prequalification assessment**

As part of the prequalification assessment process, WHO may share the manufacturer's application and related information with interested NRAs, subject to WHO entering into an appropriate confidentiality undertaking with each such NRA. Furthermore, the outcome of any joint review of information by WHO and NRA(s) may be utilized by WHO, at its discretion, as part of the prequalification assessment process.

Each dossier review report, manufacturing site(s) inspection report, performance evaluation report and 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 assessment reports will be communicated in writing to the manufacturer. If any additional information is required, or if corrective action has to be taken by the manufacturer, WHO will postpone its decision on the acceptability of the product and/or manufacturing site(s) concerned

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<sup>11</sup> ISO 18113-2:2009. *In vitro diagnostic medical IVDs – Information supplied by the manufacturer (labelling) – Part 2: In vitro diagnostic reagents for professional use*. Geneva: International Organization for Standardization; 2009.

<sup>12</sup> PQDx\_300 *Prequalification of in vitro diagnostics assessment and change assessment target deadlines*.

until, as applicable: (i) such information has been provided by the manufacturer, assessed and found satisfactory by WHO, and/or (ii) such corrective action has been taken by the manufacturer and found satisfactory by WHO, in light of the specified standards.

As WHO is responsible for the prequalification assessment process, the ownership of the reports arising from or relating to the prequalification assessment process lies with WHO. Thus, WHO shall be entitled to use and publish such reports, subject to the protection of any commercially sensitive confidential information of the manufacturer. Confidential information in this context 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).

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

- the names of products and of manufacturers that have applied for prequalification, the product code(s) submitted for prequalification and the prequalification status of each application;
- a WHOPAR summarizing the findings of the prequalification assessment;
- a WHOPIR summarizing the findings of the manufacturing site(s) inspection; and
- any negative outcomes of the prequalification assessment, including product alerts such as WHO information notices for users, WHO notices of suspension and/or WHO Notices of Concern.

Notwithstanding any of the foregoing, WHO reserves the right to use, publish, issue, share with relevant authorities of WHO Member States as well as with UN agencies and other relevant intergovernmental organizations, and/or make publicly available (in each case, in accordance with the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports, notices and/or results—whether in draft or final form, and whether positive or negative— of the prequalification assessment process including, but not limited to, the dossier review, performance evaluation and/or manufacturing site inspection, and including any confidential information to which WHO may gain access in the course of the prequalification process.

## **10.2. Successful prequalification**

Once WHO is satisfied that the prequalification assessment process is complete for the relevant product, and that the product meets the WHO prequalification requirements, the product bearing a specific product name, product code(s) and regulatory version, as manufactured at the specific manufacturing site(s) inspected, will be included in the WHO list of prequalified IVDs. The WHO list of prequalified IVDs will be compiled in accordance with an SOP established by WHO for final decision-making on inclusion in that list. The list will be published on the WHO website and will specify the prequalified product name, the respective product code(s), regulatory version, the manufacturer's name, the manufacturing site(s), the product packaging and the year in which the product was prequalified.

The manufacturer will receive a letter of prequalification from WHO informing it of the outcome of the overall prequalification assessment of the product. Once the product is included in the WHO list of prequalified IVDs, the manufacturer will be responsible for:

- fulfilling prequalification commitments;

- annual reporting;
- reporting of changes;
- post-market surveillance obligations;
- continued compliance with WHO prequalification technical specifications; and
- undergoing routine inspections.

The decision to include the product in the WHO list of prequalified IVDs is made based upon information available to WHO at the time of the prequalification assessment, including information obtained as a result of the product dossier review, performance evaluation, the inspection of manufacturing site(s) and/or the labelling review conducted by WHO. This decision is subject to change on the basis of new information that may become available to WHO.

NOTE: If serious or critical non-conformities or concerns (including with respect to quality, safety and/or performance) are identified in connection with the prequalification assessment of a product and/or a prequalified product, WHO reserves the right to use, publish, issue, share with relevant authorities of WHO Member States as well as with UN agencies and other relevant intergovernmental organizations, and/or make publicly available (in each case, pursuant to the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports, notices and/or results—whether in draft or final form, and whether positive or negative—arising from or relating to the prequalification assessment process and/or prequalified product, including without limitation any WHOPARs, WHOPIRs, WHO Notices of Concern, WHO Notices of Suspension, WHO information notice to end users and/or manufacturer-issued field safety notices. Consequently, WHO may delist the product after evaluation of the evidence and risk–benefit assessment, or may suspend the product until results of further investigations become available and are assessed by WHO. WHO may re-list the product only after the aforementioned evidence, risk–benefit and other assessments, and investigation results are considered acceptable by WHO.

Manufacturers must understand and agree that it is not WHO’s mandate to issue any approvals, certificates or licences for IVDs. This responsibility lies with the NRA of each country. Furthermore, WHO does not, as a matter of policy, endorse any specific commercial product over others. As mentioned above, the purpose of the WHO prequalification of IVDs is to provide guidance to interested UN agencies and WHO Member States in their procurement decisions. In this regard, the results of the prequalification assessment, the participation in the WHO prequalification assessment process, the inclusion of any product in the WHO list of prequalified IVDs and/or the WHO name and emblem, may not be used by manufacturers or any other party for commercial and/or promotional purposes. WHO will not accept any liability or responsibility whatsoever for an 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 use of any product as to which WHO has published the assessment results and/or that is included in the WHO list of prequalified IVDs.

#### ***10.2.1 Correcting nonconformities identified during assessment and prequalification commitments***

Nonconformities identified as part of any component of the prequalification assessment must be corrected by the manufacturer within the deadlines agreed with WHO. All critical nonconformities must be corrected before the product is prequalified. In certain cases, WHO may agree, in its sole discretion, to permit the manufacturer to correct specific nonconformities after prequalification occurs, provided that the manufacturer commits in writing to correct them by an agreed upon deadline. Such commitments to prequalification must be fulfilled by the manufacturer within the agreed deadlines in order to keep the prequalification status of the product. Failure to fulfill all

prequalification commitments within the agreed deadlines will lead to delisting of the product from the WHO list of prequalified IVDs.

### **10.3. Cancellation of the application**

WHO reserves the right to cancel the application for a specific product at any time or stage of the prequalification assessment procedure if:

- the relevant product dossier (whether full product dossier or abridged product dossier, as applicable) does not contain all of the required information or does not meet WHO prequalification requirements; and/or
- the manufacturer is not able to, or fails to, provide the required or requested information within a specified deadline; and/or
- the product does not meet the acceptance criteria for the performance evaluation; and/or
- the manufacturer is not able to, or fails to, implement any corrective actions which WHO may require within a specified deadline; and/or
- the manufacturer is unable to meet WHO's technical requirements including, without limitation, as per ISO 13485:2016 and corresponding and applicable MDSAP guidelines and requirements.
- the information supplied is inadequate to complete the prequalification assessment in a timely manner.

In case of cancellation of an application, the manufacturer will not be allowed to re-apply for WHO prequalification assessment for a period of time determined by WHO, usually one year from the date of notification of cancellation, unless otherwise agreed by WHO. Without limiting the foregoing, if the application is cancelled because the product does not meet the acceptance criteria for the performance evaluation, then the manufacturer will not be allowed to re-apply for WHO prequalification assessment unless—based on evidence submitted by the manufacturer to WHO for review—WHO determines that changes to the product design to address performance shortcomings have been successfully implemented by the manufacturer, and such changes are found acceptable by WHO.

### **10.4. Withdrawal from the prequalification assessment**

WHO provides the manufacturer with the right to withdraw its application for prequalification assessment at any time or stage. To exercise this right of withdrawal, the manufacturer must provide WHO with written notice specifying the product(s) to be withdrawn. In this case, the manufacturer will not be allowed to re-apply for WHO prequalification assessment for the products so withdrawn for a period of time determined by WHO, usually one year from date of notification of withdrawal, unless otherwise agreed by WHO. Without limiting the foregoing, if the application for prequalification was withdrawn because the product does not meet the acceptance criteria for the performance evaluation, then the manufacturer will not be allowed to re-apply for WHO prequalification assessment unless—based on evidence submitted by the manufacturer to WHO for review—WHO determined that changes to the product design to address performance shortcomings have been successfully implemented by the manufacturer, and such changes are found acceptable by WHO.

### **10.5. Reporting and communication of outcomes after withdrawal or cancellation of an application**

The cancellation or withdrawal, at any time and for any reason, of an application for prequalification assessment of a specific product will not prejudice or otherwise affect WHO's rights to use, publish,

issue, share with relevant authorities of WHO Member States as well as with UN agencies and other relevant intergovernmental organizations, and/or make publicly available (in each case, in accordance the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports, notices and/or results—whether in draft or final form, and whether positive or negative—arising from or relating to the prequalification assessment process, including without limitation any WHO Notices of Concern, WHO Notices of Suspension, WHO information notices for users and/or manufacturer-issued field safety notices.

#### **10.6. Reporting and communication of outcomes after delisting or suspension of a product**

If the prequalification assessment and/or a prequalified product is suspended or delisted, at any time and for any reason, such suspension or delisting will not prejudice or otherwise affect WHO's rights to use, publish, issue, share with relevant authorities of WHO Member States as well as with UN agencies and other relevant intergovernmental organizations, and/or make publicly available (in each case, in accordance the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports, notices and/or results—whether in draft or final form, and whether positive or negative—arising from or relating to the prequalification assessment process, including without limitation any WHO Notices of Concern, WHO Notices of Suspension, WHO information notices for users and/or manufacturer-issued field safety notices.

### **11. Prequalification fees**

The cost of the activities required to assess IVDs for prequalification will be covered in part by the manufacturer<sup>13</sup>. The non-refundable prequalification fee will contribute to the costs associated with review of the pre-submission form for determining eligibility for prequalification, product dossier screening and review, performance evaluation, inspection of manufacturing site(s), labelling review and dissemination of prequalification information.

Manufacturers should note that WHO reserves the right to decide, based on the prequalification assessment findings, whether a product meets the requirements to become prequalified. Therefore, payment of the prequalification fees does not guarantee that the product will be prequalified and/or that, if prequalified, the product will retain its prequalification status for any minimum duration.

If the assessment of a change to a prequalified product or to the quality management system is required<sup>14</sup>, the manufacturer may need to pay an additional fee.

### **12. Duration of the validity of the prequalification status**

WHO will reassess products included in the WHO list of prequalified IVDs and their associated manufacturing sites at intervals determined by WHO using a risk-based approach. If, as a result of this reassessment, it is found that a product and/or specified manufacturing site(s) no longer meets WHO requirements, such products will be removed from the list. Failure of a manufacturer to participate in the reassessment procedure will also lead to delisting of the product from the WHO list of prequalified IVDs.

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<sup>13</sup> PQDx\_299 *Prequalification fees*

<sup>14</sup> PQDx\_121 *Reportable Changes to a WHO Prequalified In Vitro Diagnostic Medical Device*

### **12.1. Fulfilment of prequalification commitments**

Commitments to prequalification must be fulfilled by the manufacturer within the agreed deadlines in order to keep the prequalification status of the product. Failure to meet prequalification commitments within the agreed deadlines will lead to delisting of the product(s) from the list of prequalified IVDs.

### **12.2. Annual reporting**

For all prequalified products, the manufacturer must submit to WHO an annual report that details sales data and all categories of complaints in a summarized form. The annual report, in the format prescribed by WHO, must be submitted by the manufacturer to WHO every year following prequalification. The manufacturer will receive a letter from WHO requesting submission of the annual report together with the prescribed report format. The report for the previous calendar year must be submitted no later than 28 February. The information provided in the annual report will inform WHO's decision on the frequency of re-inspections.

### **12.3. Submission of changes for prequalified IVDs**

WHO prequalifies an IVD as it is submitted to and assessed by WHO at a particular point in time. To meet the WHO 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 and during the inspection of the manufacturing site(s).

The manufacturer of product(s) included in the WHO list of prequalified IVDs must comply with the duties and responsibilities set out in WHO document PQDx\_121 – *Reportable changes to a WHO prequalified in vitro diagnostic* including, without limitation, the obligation to report to WHO:

- changes to the prequalified product or its design, labelling or manufacture;
- changes to the quality management system under which the product was designed and manufactured; and/or
- other reportable administrative changes.

To determine whether a change to the product, including its design, labelling and manufacture, or to the quality management system, requires reporting to WHO, the manufacturer should evaluate the potential effect this change may have on the safety, quality or performance of the product.

For all reportable changes to a prequalified product, the manufacturer must submit to the WHO Prequalification of IVDs team the WHO document PQDx\_119 – *Change report form for a WHO prequalified in vitro diagnostic* and supporting documentation and, in some cases<sup>15</sup>, a new prequalification application.

The manufacturer must communicate to WHO its intent to introduce a reportable change well in advance (i.e. early in the process of designing and validating the change), in order to allow sufficient time for WHO to assess the change before its implementation. WHO will not approve any changes without due assessment. Depending on the type of change, the assessment may also include an inspection of the manufacturing site(s) and/or performance evaluation.

Once the change report form and supporting documentation are received by WHO, they will be screened for completeness and, provided all the required information has been supplied, they will undergo assessment by WHO. If any aspect of the change report form or the supporting

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<sup>15</sup> In some cases, changes affect the safety and performance of the product to such a magnitude that a new application for WHO prequalification assessment is required. This will occur where it is deemed that the changes have resulted in a product or application information of substantial difference to that which was prequalified. In these cases, WHO will notify the manufacturer that a new application to WHO prequalification is required.



documentation is incomplete, the manufacturer will be informed in writing and requested to complete it within a specified timeline set by WHO. If the manufacturer fails to complete the aspect within the specified timeline, the product may be removed from the list of prequalified IVDs.

WHO will inform the manufacturer in writing of the outcome of its assessment of the change. The manufacturer will also be notified if WHO deems (based on the nature of the change and its potential impact on the quality, safety and/or performance of the product), that an inspection of the manufacturing site(s) and/or performance evaluation is also required.

Once WHO is satisfied that the prequalification change assessment of a product is complete and provided that the overall findings demonstrate, as determined by WHO, that the product continues to meet all WHO prequalification requirements, then the WHO list of prequalified IVDs will be updated, as necessary, to reflect the relevant change accepted by WHO.

If the submitted documentation supporting the change does not meet WHO prequalification requirements or if all the requested information is not provided by the manufacturer within the specified timeline, WHO will reject the change. The impact of such a decision on the prequalification status of the prequalified IVD will be communicated to the manufacturer in writing.

#### **12.4. Post-market surveillance of WHO prequalified IVDs**

Post-market surveillance is conducted by manufacturers to collect and analyse experiences with the use of their IVD and to determine any action to be taken. Manufacturers of WHO prequalified products must monitor their products to ensure continued compliance with WHO prequalification requirements. WHO guidance on post-market surveillance includes proactive collection of information on quality, safety and performance of the 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.<sup>16</sup>

As soon as a product is accepted into the prequalification assessment process, 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 the WHO document entitled *Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics*, in particular, comply with the manufacturer's obligations set forth in that document including, for example, the obligation to undertake the following post-market surveillance activities:

- to actively encourage users and their patients/clients to report any feedback related to use of the product to the manufacturer who should evaluate and decide to take any action.
- to notify WHO of any incident relating to the product that have affected (or could have affected) the performance of the product, safety of the person being tested, safety of users of the product or safety of any person associated with the product, including:
  - Serious public health threat<sup>17</sup>, which should be reported to WHO immediately but no later than 48 hours;
  - Death, serious deterioration in state of health of patient, user or other person occurred, which should be reported to WHO as soon as possible but no later than 10 calendar days; and

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<sup>16</sup> WHO guidance on post-market surveillance and market surveillance is without prejudice to national and regional legislation and requirements.

<sup>17</sup> Any event type or device deficiency which could result in imminent risk of death, serious deterioration in the state of health, serious injury, or serious illness of more than one patient, user or other person that requires prompt remedial action.

- Death, serious deterioration in state of health of patient, user or other person might have occurred, which should be reported to WHO as soon as possible but no later than 30 calendar days;
  - All complaints, which must be reported to WHO annually in the periodic summary report.
- to provide to WHO with information relating to any incident notified to WHO, including details regarding the investigation undertaken and any corrections and corrective actions taken, using the WHO manufacturer investigation reporting form as the preferred format. Reporting formats recognised by any member of the International Medical Device Regulators Forum may also be accepted, in English.
  - to notify WHO of all incidents that require field safety corrective actions, such as withdrawal of products from sale or distribution, physical return of the product to the manufacturer or destruction of the product (e.g. recall), product exchange, product modification(s) or provision of additional advice to customers to ensure that the product continues to function as intended; and
  - if required, to supply sufficient quantities of the prequalified product to WHO, or to laboratories designated by WHO, free-of-charge and delivered duty paid, for post-market surveillance lot testing.

WHO will review the investigation of any incident concerning a prequalified product that is communicated to WHO by users or by manufacturers. First, WHO will notify the manufacturer and, depending on the nature of the incident, may also notify relevant NRAs, relevant authorities of any interested WHO Member State and/or interested UN agencies of the incident.

WHO reserves the right to use, publish, issue, share with relevant authorities of WHO Member States as well as with UN agencies and other relevant intergovernmental organizations, and/or make publicly available (in each case, pursuant to the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports and/or results—whether in draft or final form, and whether positive or negative— of:

- any WHOPARs, WHOPIRs, WHO Notices of Concern, WHO Notices of Suspension or WHO information notices for users;
- any manufacturer-issued field safety notices; and
- any confidential information to which WHO may gain access in the course of any of the foregoing.

WHO will review the investigation conducted by the manufacturer to ensure that it complies with scientific principles and is in accordance with international guidance and standards. WHO reserves the right to request a special inspection to verify that correction and corrective actions have been implemented.

### **12.5. Routine inspection**

Routine inspections of manufacturers will be conducted to ensure continued compliance with prequalification requirements. Routine inspections will typically take place at a manufacturer's manufacturing site(s) following the prequalification of a specific product, and will be planned every three to five years after WHO's initial prequalification of a product or WHO's latest compliance inspection (whichever is later), unless an earlier-inspection is deemed necessary by WHO.

## 12.6. Compliance with WHO Prequalification of In Vitro Diagnostics technical specifications

The purpose of the WHO Prequalification Technical Specifications Series is to provide technical guidance to IVD manufacturers seeking WHO prequalification. Manufacturers must comply with the requirements laid down in the relevant publication in the WHO Prequalification Technical Specifications Series.

For products prequalified before the issuance of the relevant publication in the WHO Prequalification Technical Specifications Series, a transition period will apply. Manufacturers must comply with the relevant technical specifications as outlined in the aforementioned Series within three years from their publication. Compliance with the Technical Specifications will be verified during the re-inspection. Failure to comply with the relevant Technical Specifications will result in the delisting of the product from the WHO list of prequalified IVDs.

## 13. Confidentiality

WHO assessors, inspectors and the designated evaluating sites will treat all information to which they will gain access during the assessments, inspections and evaluations, or otherwise in connection with the discharge of their responsibilities in regard to this prequalification procedure, as confidential and proprietary to WHO or parties collaborating with WHO in accordance with the terms set forth below.

WHO assessors, inspectors and the designated evaluating sites will take all reasonable measures to ensure that confidential information:

- is not used for any purpose other than the assessment, inspection and evaluation activities described in this document; and
- is not disclosed or provided to any person who is not bound by similar obligations of confidentiality and non-use as contained herein.

WHO assessors, inspectors and evaluating sites will not, however, be bound by any obligations of confidentiality and non-use to the extent they are clearly able to demonstrate that any part of the confidential information:

- was known to them prior to any disclosure by or on behalf of WHO (including by the manufacturers); or
- was in the public domain at the time of disclosure by or on behalf of WHO (including by the manufacturers); or
- has become part of the public domain through no fault of theirs; or
- has become available to them from a third party not in breach of any legal obligations of confidentiality; or
- was subsequently and independently developed by or on behalf of WHO, as shown by written records, by persons who had no knowledge of such confidential information; or
- is required to be disclosed by law, provided that WHO shall in such case immediately notify the manufacturer in writing of such obligation and shall provide adequate opportunity to the manufacturer to object to such disclosure or request confidential treatment thereof (provided always, however, that nothing contained herein shall be construed as a waiver of the privileges and immunities enjoyed by WHO and/or to submit WHO to any national court jurisdiction).

## 14. Conflict of interest

Before undertaking the work, each external inspector and assessor will also (in addition to the above-mentioned confidentiality undertaking) be required to complete and sign the WHO declaration of interests form.

If, based on the above-mentioned declaration of interests, it is felt that there is no risk of a real or perceived conflict of interest (or it is felt that there is only an insignificant and/or irrelevant conflict of interest), and it is thus deemed appropriate for the assessor or inspector in question to undertake the work, then he/she will discharge his/her functions exclusively as 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.

All inspectors furthermore agree that, at the manufacturer's request, WHO will advise the manufacturer, in advance, of the identity of each inspector and the composition of the team performing the manufacturing site inspection, and provide *curricula vitae* of the inspectors. The manufacturer then has the opportunity to express possible concerns regarding any of the inspectors to WHO before the inspection visit. If such concerns cannot be resolved in consultation with WHO, the manufacturer may object to a team member's participation in the manufacturing site visit. Such an objection must be made known in writing by the manufacturer to WHO within 10 days of receipt of the proposed team composition. In the event of such an objection, WHO reserves the right to cancel all or part of its agreement with, and the activities to be undertaken by, that inspector.

## 15. Disputes – privileges and immunities of WHO

In the event of any dispute or disagreement between the manufacturer and WHO arising from or relating to the prequalification assessment process, an SOP established by WHO for the handling of such disputes and disagreements will be followed to discuss and resolve the issue.

By virtue of WHO's status as a specialized agency of the UN, WHO, its officials and experts performing missions for WHO (including, e.g. the prequalification assessors and inspectors) enjoy privileges and immunities under national and international laws and conventions, including 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). Nothing contained in or relating to this document or the 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 or otherwise under any national or international law, convention or agreement, and/or as submitting WHO, its officials and/or experts aforesaid to any national court jurisdiction.

## 16. Relevant documents

The following documents provide information to guide the manufacturer through the requirements of the prequalification assessment<sup>18</sup>.

- Eligibility criteria for WHO prequalification of in vitro diagnostics. Geneva: World Health Organization; (PQDx\_298).
- Pre-submission form. Geneva: World Health Organization; (PQDx\_015).

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<sup>18</sup> Documents are available at the following website: <https://extranet.who.int/pqweb/in-vitro-diagnostics>  
PQDx\_007 v9 4 January 2021 (This document version supersedes any previous document versions)

- Instructions for the completion the pre-submission form. Geneva: World Health Organization; (PQDx\_017).
- Instructions for compilation of a product dossier. Geneva: World Health Organization; (PQDx\_018).
- Product dossier checklist. Geneva: World Health Organization; (PQDx\_049).
- Abridged prequalification assessment. Geneva: World Health Organization; (PQDx\_173).
- Information for manufacturers on the manufacturing site(s) inspection (assessment of the quality management system) Geneva: World Health Organization; (PQDx\_014).
- Reportable changes to a WHO prequalified in vitro diagnostic medical device. Geneva: World Health Organization; 2016 (PQDx\_121).
- Change report form for a WHO prequalified in vitro diagnostic. Geneva: World Health Organization; (PQDx\_119 ).
- Guidance for post-market surveillance and market surveillance of medical devices, including in vitro diagnostics. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO..<sup>19</sup>
- WHO performance evaluation protocols: In vitro diagnostics and laboratory technology. Geneva: World Health Organization.<sup>20</sup>
- Prequalification assessment and change assessment target deadlines. Geneva: World Health Organization; (PQDx\_300).
- Prequalification fees. Geneva: World Health Organization; (PQDx\_299).
- Prequalification of in vitro diagnostics Technical Specification Series.<sup>21</sup>
- Labelling review for prequalification assessment. Geneva: World Health Organization; (PQDx\_361).

## 17. Contact information

Any enquiries regarding the WHO Prequalification of IVDs Programme should be addressed to: [diagnostics@who.int](mailto:diagnostics@who.int)

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<https://www.who.int/publications/i/item/guidance-for-post-market-surveillance-and-market-surveillance-of-medical-devices-including-in-vitro-diagnostics>

<sup>20</sup> <https://extranet.who.int/pqweb/vitro-diagnostics/performance-evaluation>

<sup>21</sup> <https://extranet.who.int/pqweb/vitro-diagnostics/technical-specifications-series>

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