Instructions for completion of the pre-submission form

WHO's prequalification assessment of in vitro diagnostics

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A. Introduction

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

To apply for WHO's prequalification assessment of an IVD, manufacturers are required to complete and submit to WHO a pre-submission form using the form found in document PQDx_015 *"Pre-submission form*", together with the necessary supporting documentation and attachments.

This document has been prepared to assist manufacturers in correctly completing and submitting the pre-submission form), together with the necessary supporting documentation and attachments. The information provided by the manufacturer in pre-submission form assists WHO to determine:

a. whether or not the product submitted for WHO's prequalification assessment is the same product as the one submitted by the manufacturer in the Expression of Interest form for WHO's performance evaluation (if applicable); 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. the regulatory version that is accepted by WHO for WHO's prequalification assessment; and
e. the planning of each of the components of WHO's prequalification assessment.

Therefore, the manufacturer must fill out the pre-submission form with accuracy and completeness.

Manufacturers applying for WHO prequalification assessment of IVDs should read the instructions in this document and the pre-submission form before completing the pre-submission form. In addition, manufacturers should read the document PQDx_007 *"Overview of WHO's prequalification procedure for in vitro diagnostics"* before applying, so that they can be aware of and prepared for all stages of WHO's prequalification assessment process.

This document supersedes the document PQdx_017 *"Instructions for the completion of the Pre-submission form - Prequalification of In Vitro Diagnostics"* version 6, 1 November 2021.

B. Submitting the pre-submission form

Once the manufacturer has duly and fully completed, signed and dated the pre-submission form, that form and its attachments (e.g. official letter regarding the manufacturer's authorized contacts, photographs, instructions for use of the product in English, abridged assessment eligibility annex, etc.) are required to be submitted electronically to the ePQS portal: https://extranet.who.int/prequal/epqs-portal.

Electronic copy requirements

- The primary file format used for documents submitted to WHO should be Portable Document Format (PDF). The manufacturer must not include any PDF in the electronic submission that requires a password to open it.
- The document must be compatible with optical character recognition programs (OCR). For any scanned document, OCR must be used to allow text to be searchable. This can be verified by: (1) highlighting an area of text and (2) using the software search function to locate a particular word or phrase. If the word or phrase is not returned in the search, then the OCR did not recognize the text and it is, therefore, not searchable.

- The pre-submission form and required attachments must be submitted as separate files named as “Authorization letter”, “Pre-submission [product name]”, “Instruction for Use [IFU code or reference]”, “Photographs of the kits”, and if relevant “Annex 1: Eligibility for abridged prequalification assessment”. Keep the name of the annexes as short and practicable as possible avoiding any special characters like tilde (~), apostrophe (’), colon (:), vertical bar (|), greater than sign (>), various other symbols (e.g., →,*,β,α,∞,±,™) asterisk (*), single quotation mark (‘), forward slash (/), less than sign (<), pound sign (#), elongated dash (–), double quotation marks (“), backward slash (\), question mark (?) and characters not from the Latin alphabet.
- The path length for each document submitted, including any folders and the file name itself, must not exceed 120 characters.
- When completing the pre-submission form, the manufacturer must use font sizes of a style and size large enough to be easily legible. Fonts smaller than 12 points must be avoided except in tables and footnotes where a font size of 10 points is acceptable.
- When creating a PDF from an electronic source document (e.g. Microsoft Word document) the manufacturer must avoid using specialist application plug-ins for capture or display data as not all reviewers of the documentation will necessarily have access to these plug-ins.

Manufacturers who are new to WHO’s prequalification assessment are required to register as new users and complete the registration form available to download on the ePQS login portal.

If necessary, WHO may request the manufacturer to provide 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 determined by WHO. The manufacturer will be provided with two opportunities to correctly complete the pre-submission forms 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.

NOTE: Manufacturers must not submit a product dossier along with the pre-submission form. Product dossiers that are submitted without a formal request from WHO will be destroyed.

The numbering of the following sections corresponds and refers to those sections in the pre-submission form. The manufacturer may not modify the descriptions in the pre-submission form tables.

1. WHO’s performance evaluation

Please refer to WHO document PQDx_298 *“Eligibility criteria for WHO’s prequalification assessment of in vitro diagnostics”* to confirm whether or not a product is required to undergo WHO’s performance evaluation as a pre-requisite to apply for WHO’s prequalification assessment.

If the product is required to undergo WHO’s performance evaluation, an application for WHO’s prequalification assessment of an IVD will not be considered or 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 submitted by the manufacturer to, and accepted by, WHO.

Please indicate in this section, as applicable:
(1) if the product required to undergo WHO’s performance evaluation as a pre-requisite to WHO’s prequalification assessment; and

(2) if yes, the date on which the product was accepted for WHO's performance evaluation, and the EOI number assigned to the product, or
(3) if no, indicate that WHO's performance evaluation is not applicable to the product.

2. Manufacturer information

2.1. Legal manufacturer

Please provide all information required under this section about the manufacturer of the IVD product in question.

For the purpose of WHO's prequalification, WHO uses the following definition of "manufacturer"[1].

"Manufacturer" means 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).

Applications for WHO's prequalification assessment of IVDs may only be submitted by the original manufacturer of the product.

2.2. Authorized contacts for the manufacturer

Please insert all the information required under this section regarding each of the two authorized contacts for the manufacturer. The "authorized contacts for the manufacturer" are two officers, employees or representatives of the manufacturer who are duly and fully authorized and designated to act in the name and on behalf of the manufacturer in all respects and for all purposes in connection with WHO's prequalification assessment of the IVD in question.

These two authorized contacts will be the primary contact points for WHO in relation to WHO's prequalification assessment for the IVD for which the pre-submission form is submitted. Therefore, the manufacturer must ensure that all contact details provided in the pre-submission form are current, complete and correct.

In connection with this section, the manufacturer must also submit to WHO an official letter, signed by a duly authorized representative of the manufacturer, stating that the persons listed as "authorized contacts" in section 2 of the pre-submission form (which persons must also be named in that letter) are duly and fully authorized/designated to act in the name and on behalf of the manufacturer in all respects and for all purposes in connection with the WHO's prequalification assessment of the product in question (which product must also be identified in that letter).

This letter must be submitted to WHO together with the duly completed pre-submission form.

In the event that, at any time during WHO's prequalification assessment process, there is a change in the name(s) and/or contact information of 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 .

[1]From document PQDx_007 *"Overview of WHO's prequalification procedure for in vitro diagnostics".*

3. Product – Information

3.1. Product name and product code/catalogue number for WHO's prequalification assessment[2]

3.1.1. Only one IVD is permitted per pre-submission form. Provide the name for one product only.

3.1.2. Provide the product code/catalogue number for the product.

3.1.3. For each product code, complete a column in the table with a description of the kit configuration: product kit size, and list the contents, the quantity/volume of all components. Note that if sterile lancets are provided with any configuration of the product, these are required to be regulated by a Recognized Regulatory Authority (refer to the document PQDx_173 "*WHO's abridged prequalification assessment for vitro diagnostics"* for details*).*

- Photographs of all kit components (packaged and individually) must be attached to the pre-submission form.

3.1.4. If reagents are supplied in more than one box, provide the name and product code/catalogue number for each box. For example, if controls are provided separately to the test reagents, provide the catalogue number for the controls here.

- For each different box size of reagent, list the number of tests and product code for each box size
- For blood glucose meter kits, please provide the product code/catalogue number, and number of reagents per box for replacement reagents including test strips, control solutions, and lancets for use with the kit.

3.1.5. Provide all information required under this section regarding any instrument required to run the assay.

In this section, a "**dedicated instrumentation**" defines a situation where the assay must be run on a specific instrument as part of the testing protocol. The instrument and assay reagents are only ever used in combination to perform the assay.

3.1.6. Provide the date of design lock-down for the product.

For purposes of WHO's prequalification assessment, the term **"design lock-down"** relates to 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.

NOTE: Applications are only accepted for products that have final design lock down at the time the pre-submission form for WHO's prequalification assessment is received by WHO.

[2] WHO must be notified of all changes made to the product, as per document PQDx_007 *Overview of WHO's prequalification procedure for in vitro diagnostics.*

3.2. Current instructions for use and user manual

Provide document control details for the instructions for use and the user manual(s) relevant to the product.
Attach a copy of the English language version of the instructions for use (package insert) for the product.

The version of the instructions for use submitted with the pre-submission form will be considered the official version submitted for WHO's prequalification assessment. During the course of WHO's prequalification assessment, the manufacturer cannot make changes to this version of the instructions for use without prior written notice to and agreement from WHO. Any changes to such instructions for use version that was submitted with the pre-submission form must be agreed with WHO prior to their implementation or the prequalification assessment will be terminated.

3.3. Transport, storage and operating temperatures

3.3.1. The transport, storage and operating temperature ranges for all components must be clearly specified by the manufacturer for the product and individually for reagents which are provided in more than one box. The manufacturer shall provide the shelf life of the product as claimed on the packaging (expiry date) and individually for reagents which are provided in more than one box.

"Shelf-life upon manufacture" is the period of time from when the product is released for supply until the expiry date - during which the product performance is assured by the manufacturer while handled and stored under defined conditions.

3.3.2. Provide details of any other specified storage conditions applicable to the product if applicable.

NOTE: If the product is accepted for WHO's prequalification assessment, the manufacturer will be required to provide, as part of its product dossier submission, evidence (such as data generated through stability studies) demonstrating that the product continues to perform within specifications for the claimed shelf life.

4. Product – Disease category, analyte and method

For questions in section 4, tick/check the boxes that are relevant to the product.

5. Product – Operation

5.1. Assay controls

Please provide all information required under this section regarding the assay controls that are part of the product or provided separately.
"**Control specimens**" (also called "test-kit controls") refer to preparations that are specifically designed by the manufacturer for this particular assay. These control specimens are usually a positive and a negative control specimen.

5.2. Product usage

Please provide all information required under this section regarding the product usage and throughput.

"**Single run**" refers to the number of specimens that can be tested consecutively by one operator without interruption (unless the recommended operation requires such interruption).

5.3. Indicative cost

Please provide the indicative cost per test in US Dollars and if applicable, the cost of the dedicated instrumentation required to perform the assay.

6. Product – Performance characteristics

"**Sensitivity**" refers to clinical or diagnostic sensitivity. "Sensitivity" is the ability of a test to give a positive result for individuals that have the disease or disorder for which they are being tested. The disease status of the individual must be predefined by criteria that are independent of the test under consideration.[3]

"**Specificity**" refers to clinical or diagnostic specificity. "Specificity" is the ability of a test to give a negative result for individuals that do not have the disease or disorder for which they are being tested. The negative disease status of the individual must be predefined by criteria that are independent of the test under consideration.[3]

6.1. Performance characteristics for serology or antigen EIAs and RDTs

Please provide all information required under this section regarding the validated performance characteristics of the product. Section 6.1 applies only to serology or antigen EIAs and RDTs and should be left blank for other types of products.

6.2. Specifications for CD4 technologies

Please provide all information required under this section regarding the validated performance characteristics of the product. Section 6.2 applies only to CD4 technologies and should be left blank for other types of products.

6.3. Specifications for nucleic acid tests

Please provide all information required under this section regarding the validated performance characteristics of the product. Section 6.3 applies only to nucleic acid tests and should be left blank for other types of products.

6.4. Specifications for blood glucose monitors, HbA1c point of care analysers, and haemoglobin analysers

Please provide all information required under this section regarding the validated performance characteristics of the product. Information is required for the relevant technologies only and should be left blank for other types of products.

7. Regulatory and commercial status of the product

7.1. Regulatory status of the product

Please provide all information required under this section regarding the regulatory status of the product being submitted for WHO's prequalification assessment.
A **"regulatory version"** 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

[3] This definition is based on terminology used in the publicly available "Harmonized Terminology Database" that is compiled by the Clinical and Laboratory Standards Institute.

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 *different* regulatory version.

7.1.1. Please identify the regulatory version of the product submitted for WHO's prequalification assessment (or planned regulatory version if the product is not yet commercially available).

7.1.2. Please tick/check the boxes that are relevant to your product and provide details of all current regulatory approvals for this product.

"National Regulatory Authority" means a government body or other entity that exercises a legal right to control the use or sale of in vitro diagnostics within its jurisdiction and may take enforcement action to ensure that in vitro diagnostics marketed within its jurisdiction comply with legal requirements.

"**Regulatory Approval**" means that the National Regulatory Authority officially permits supply of this in vitro diagnostic product in the country/region under its authority.

"**Type of Regulatory Approval**" refers to the relevant sections of the legislation that have been applied to the product for regulatory approval. Generally, the details of the legislation applied for regulatory approval should be included on the certificate that demonstrates that the product is approved for supply.

NOTE: Do not include certification information relating to ISO 13485 Medical devices — Quality management systems — Requirements for regulatory purposes here. Questions relating to ISO 13485 are addressed in Section 8 of the pre-submission form.

7.2. Commercial agreements and re-branding

Please provide all information required under this section regarding rebranding of the product, or whether the product or any of the major components thereof sourced from another manufacturer.

WHO requires that this commercial agreement information be made available to WHO in order to determine whether or not a product is eligible for WHO's prequalification assessment. Applications for WHO's prequalification assessment of IVDs are accepted only from the original manufacturer of the product.

7.3. History of product assessment by WHO

Provide information required under this section on any previous WHO assessments of the product.

8. Manufacturer – Quality management system

An effective quality management system is a key consideration for all manufacturers of IVDs. Therefore, products submitted for WHO's prequalification assessment must be manufactured under an appropriate quality management system.
The quality management standard "*ISO 13485 Medical devices — Quality management systems — Requirements for regulatory purposes"* is considered to be a benchmark in quality management for the manufacturers of diagnostic products by regulatory agencies throughout the world. WHO's prequalification assessment (including its manufacturing site inspections) are based on the requirements of this internationally recognized quality management standard.

Provide all information required under this section about the manufacturer's quality management system and conformity to the referenced standards.

9. Manufacturer – Quality management system certification

If the manufacturer holds any certifications (including, but not limited to, ISO 13485:2016) regarding the quality management system used for the manufacture of the product, then provide the requested information of such certification(s) in this section. The certification(s) must list all sites involved in the manufacture of the product.

NOTE: The manufacturer will be required to provide evidence of all quality management system claims as part of the product dossier submission.

10. Manufacturer – Sites of product manufacture

10.1. Sites of manufacture

Please provide all information required under this section about all sites that are involved in each and every stage of the manufacture of the product as per the table provided under this section. Please do not modify the description of the table.

10.2. Contact person(s) for inspection

Please provide the details of the manufacturer's authorized contact(s) for the planning and conduct of manufacturing site(s) inspection, in the event that WHO determines that such inspection if required. If there are multiple manufacturing sites, you may provide one contact per site.

10.3. Production

Provide information on the number of lots manufactured per year, their average size and the total number of products manufactured per year (including instruments).

10.4. Key suppliers

Please provide all information required under this section about all key suppliers which supply products/components and/or services for the manufacture of the product (e.g. raw materials, enzymes, key components, bulk chemicals and reagents, instruments, sterile lancets etc.). If a sterile lancet is provided in the kit, provide the type and validity dates of regulatory approval[4] in the "Other information" section.

11. Manufacturer declaration

The manufacturer declaration appearing under Section 11 of the pre-submission form must be completed, signed and dated on behalf of the manufacturer before the pre-submission form is considered for WHO's prequalification assessment. The declaration must be completed, signed and dated by a duly authorized representative of the manufacturer designated under section 2.2 of the pre-submission form.

[4] Sterile lancets must be assessed and approved by a Recognized Regulatory Authority as described in PQDx_173 *"WHO's abridged prequalification assessment for vitro diagnostics"*

Annex 1: Information to determine the product's eligibility for WHO's abridged prequalification assessment

If a regulatory version of the product submitted for WHO's prequalification assessment has not been stringently assessed and approved by any of the Recognized Regulatory Authorities listed in the WHO document PQDx_173 *"WHO's abridged prequalification assessment for vitro diagnostics"*, but a stringently assessed and approved regulatory version of the product also exists (see information requested in section 7.1.2 of the pre-submission form), then please complete the table in Annex 1 with the requested information so that WHO may review and determine whether the product qualifies for an abridged prequalification assessment[5].

12.Relevant documents

The following websites and guidance documents provide information to guide the manufacturer through the process for WHO's prequalification assessment of IVDs:

- https://extranet.who.int/prequal/vitro-diagnostics/what-we-do
- https://extranet.who.int/prequal/vitro-diagnostics/prequalification-guidance
- Overview of WHO's prequalification procedure for in vitro diagnostics. Geneva: World Health Organization; (PQDx_007)
- Pre-submission form. Geneva: World Health Organization; (PQDx_15)
- WHO's abridged prequalification assessment for 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
- https://extranet.who.int/prequal/ivd-performance-evaluation
- WHO's performance evaluation procedure for in vitro diagnostics. Geneva: World Health Organization; (PQDx_458)
- ISO 13485 Medical devices - Quality management systems - Requirements for regulatory purposes. Geneva: International Organization for Standardization (ISO). https://www.iso.org/iso-13485-medical-devices.html

[5] Refer to PQDx_173 "*WHO's abridged prequalification assessment for vitro diagnostics"* for an overview of WHO's abridged prequalification assessment.