WHO Prequalification
IVD Assessment

November 2024

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PQ In Vitro Diagnostics Assessment Team

Outline

- Overview of the prequalification (PQ) assessment pathway
- Product dossier assessment
- Performance Evaluation
- Site inspection
- Labelling review
- Post-assessment requirements
- Collaborative Registration Procedure (CRP)
- Q & A

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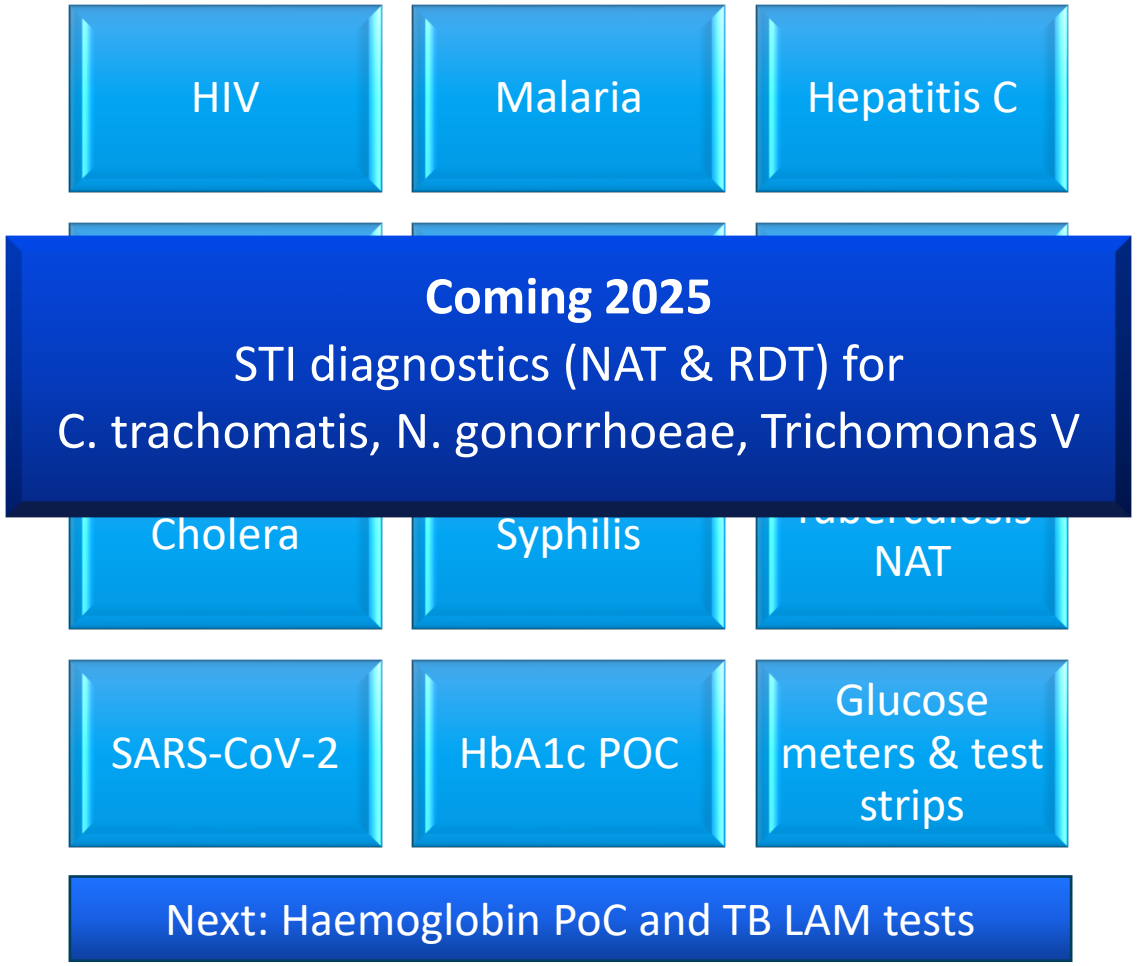
PQ of IVDs: Aim & Scope

- The aim of PQDx is to promote and facilitate **access** to safe, appropriate and affordable IVDs of good quality
- Focus is placed **on IVDs for priority diseases** and their suitability for use in **resource-limited settings**
- The **scope** of IVDs eligible for PQ continues to expand
- Nine IVDs listed in 2024 so far
  - Currently 114 IVDs prequalified
- PQ List available on website: https://extranet.who.int/prequal/vitro-diagnostics/prequalified-vitro-diagnostics



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Prequalification decision

For IVDs that meet PQ requirements

- The product is added to the list of WHO prequalified IVDs
- The public report is prepared & published

→ IVD is eligible for WHO and UN procurement & CRP

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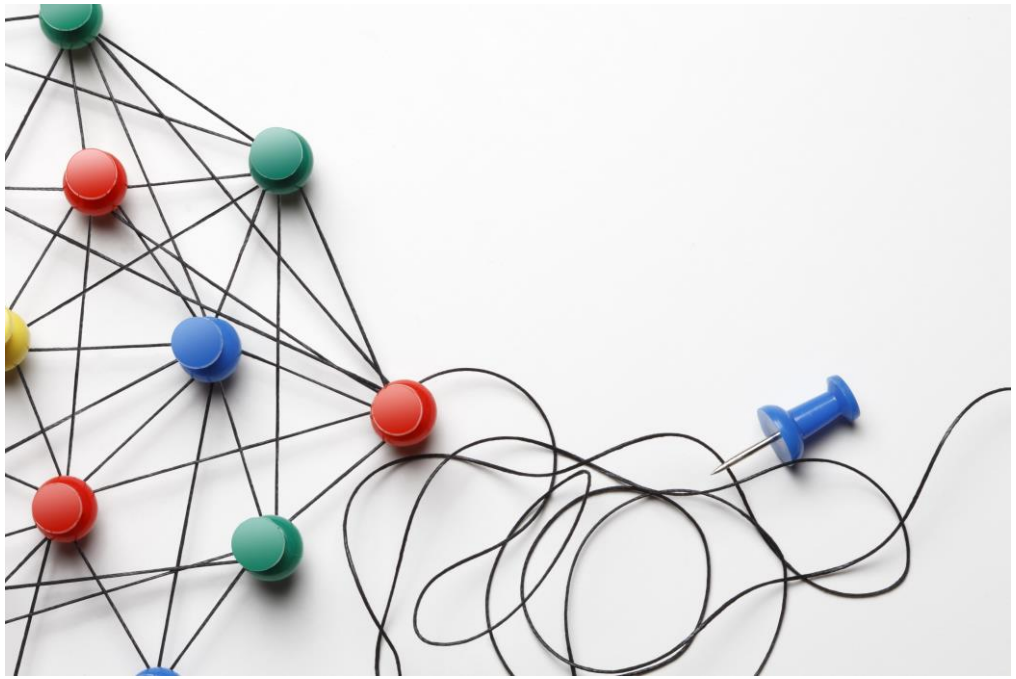
Post-PQ Activities - Ongoing requirements to maintain PQ listing

Manufacturer must comply with:

- Commitments to PQ
- Annual reporting
    - Sales data, complaints, Field Safety Correction Notices (FSCN)
- Change reporting
- Post market surveillance obligations
- Ongoing compliance with TSS
- Routine site inspections



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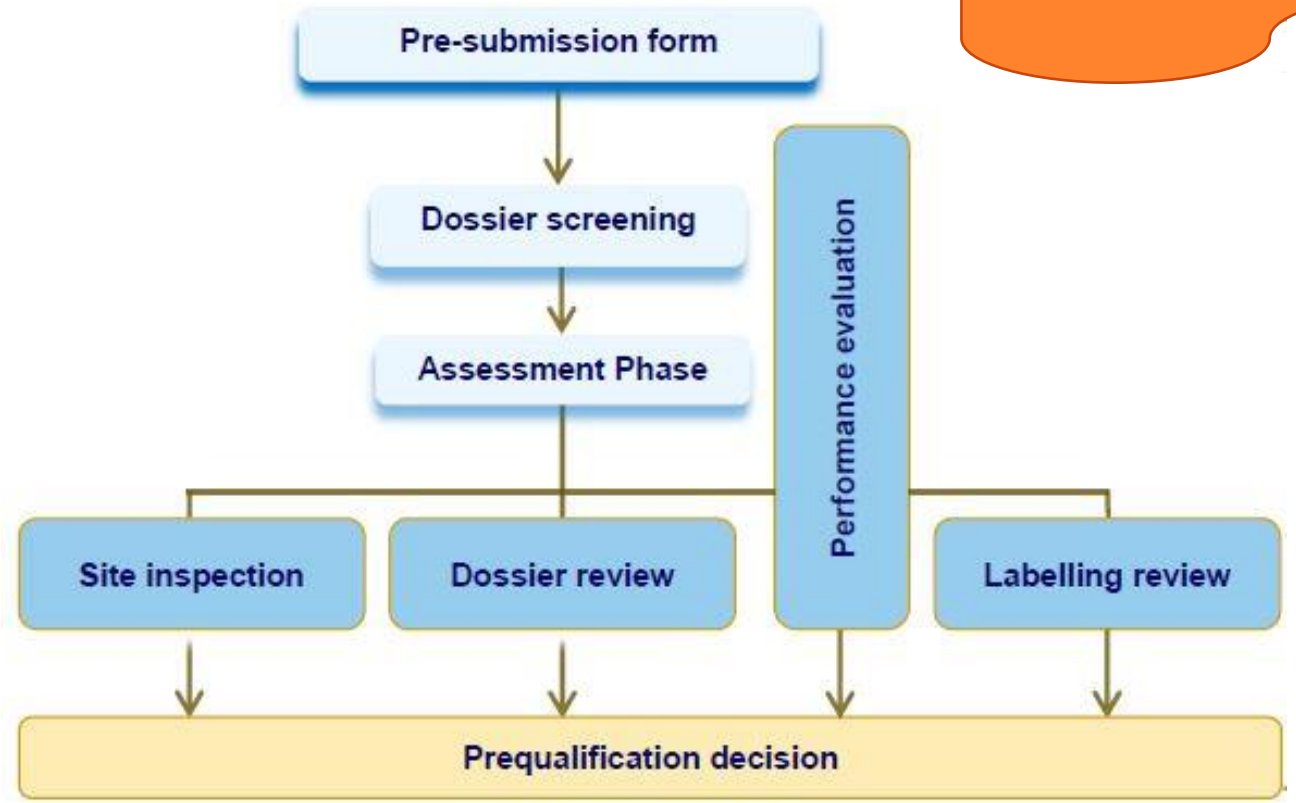
PQ Application Process

UPDATE
Process changes planned with public consultation open to November 30



Pre-submission

- Manufacturer completes the pre-submission form
- WHO schedules a pre-submission meeting
- WHO screens the pre-submission form to determine if product is eligible & type of assessment (full or abridged)

Products accepted for PQ assessment undergo:

- Review of product dossier (full or abridged)
- Performance evaluation
- Site Inspection (reliance on MDSAP)
- Labelling review

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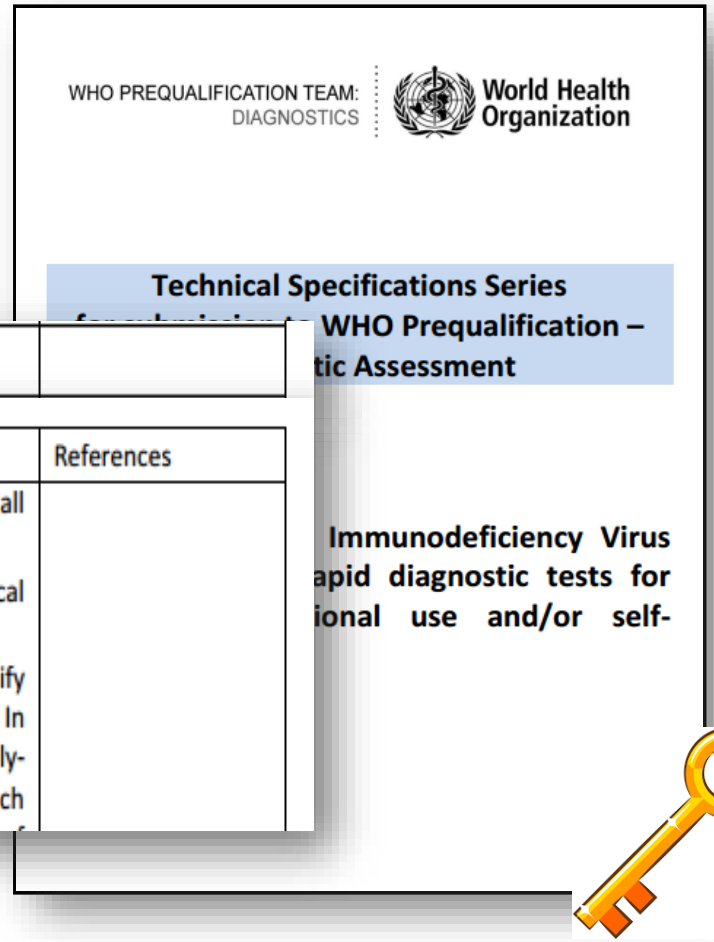
Technical Specifications Series (TSS)

- Each TSS document is tailored to a pathogen/type of test
  - Requirements address needs of Member States in LMIC
  - Requirements related to general performance characteristics
- Summarize minimum performance requirements for WHO prequalification, to establish:


WHO PREQUALIFICATION TEAM: DIAGNOSTICS

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Technical Specifications Series

WHO Prequalification –

tic Assessment

Immunodeficiency Virus

apid diagnostic tests for

ional use and/or self-

1.3 Precision of measurement

Aspect	Testing requirements	Comments	References
	The effect of operator-to-operator variation on IVD performance is to be included as part of the precision studies (see also Comment 8). Testing should be done: • by personnel representative of intended users; • unassisted; and • using *only* those materials provided with the IVD (e.g. instructions for use, labels and other instructional materials).	5. Where possible, the testing panel should be the same for all operators, lots and sites. 6. Lots should be composed of different batches of critical components. 7. Results must be statistically analyzed by ANOVA to identify and isolate the sources and extent of any variance. In addition, the percentage of correctly-identified, incorrectly-identified and invalid results should be tabulated for each	

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Technical guidance series documents (TGS)

- Stability
- Principles of performance studies
- Test method validation
- IFU
- Quality assurance and quality control panels
- Risk management
- Quality control

- Each TGS provides detailed guidance on a specific aspect related to IVD performance
- Covers broad principles related to validation and verification of an IVD
- TGS provides detailed guidance with examples relevant for PQ assessment
- Reflect our current thinking and not a requirement

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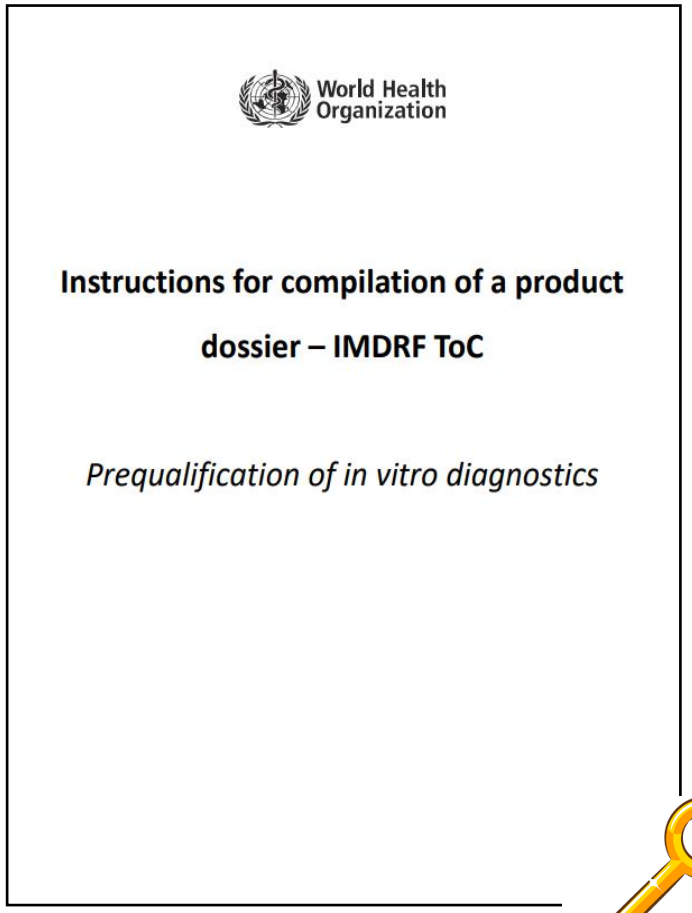
Compiling a product dossier for PQ assessment

Product dossier

Selection of manufacturer's records and documents for a product

- Dossier submitted to PQ must be in IMDRF "Table of Contents" format
  - Chapters and subheadings
  - Files need to be searchable
  - Page number format: page x of y
  - Clear cross-referencing to annexes
  - Legible font size



Dossier screening

WHO check that dossier is complete

- WHO prepares a screening letter
  - Confirmation that a complete dossier has been received

  OR
  - Requests to provide missing information and/or address formatting issues
- No analysis of data at the screening stage
  - Ensures that a complete dossier is available for technical review

Product dossier assessment

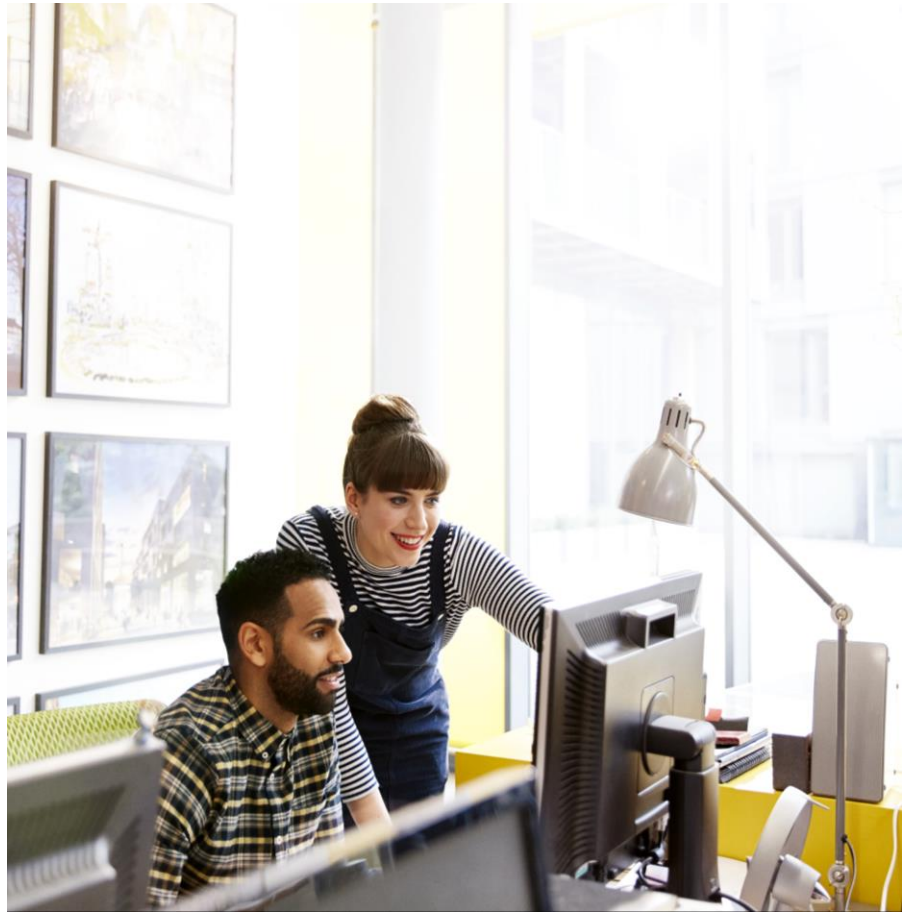
Technical review of manufacturer's evidence of quality, safety & performance

- Performed by subject matter experts

- Analyzing the relevance of the data in the dossier
  - Reliable data that supports the manufacturers claims of quality, safety and performance
  - Appropriate & well-designed validation studies
- Review of completeness, accuracy and consistency of data
  - From initial product design, through validation, manufacture, quality control and release onto the market

➢ Are the specifications in the TSS met?

➢ Has the manufacturer considered IVD use in RLS?



Dossier assessment Update

Subject matter experts work in teams to review product dossiers and corrective action plans

Assessment sessions were piloted by PQT-IVD in 2023 and implemented in 2024 with 6 sessions held

- Increase pool of technical experts
- Ensure standardization of technical reviews conducted
- Capacity building

6 sessions scheduled for 2025

1. 10 - 14 February	**4.** 25 - 29 August
2. 7 - 11 April	**5.** 13 - 17 October
3. 16 - 20 June	**6.** 8 - 12 December

- Materials for review received 15 days prior to an assessment session will be available for assessment
- Participants from NRAs invited to each session

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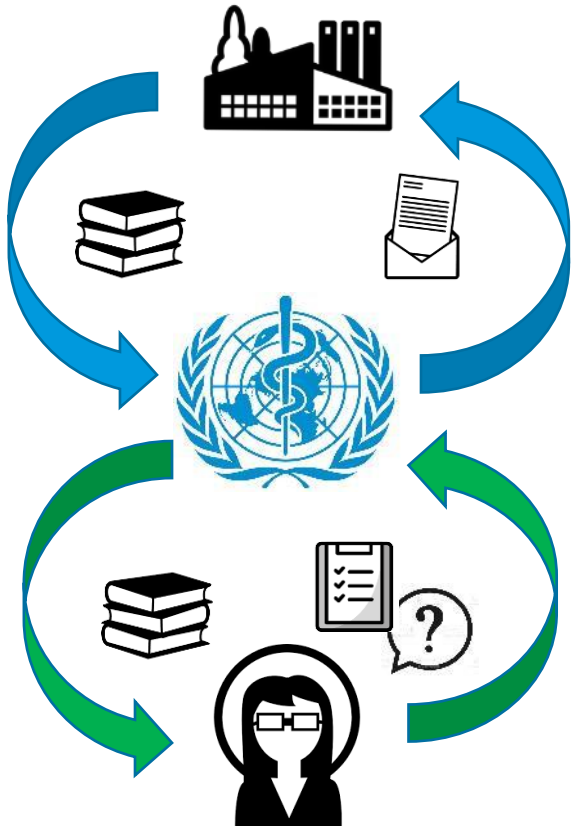
Dossier Review Process

- Dossier sent to subject matter expert for technical review
- Expert provides completed dossier review report and notes any deficiencies in the dossier
- WHO prepares dossier review letter for manufacturer requesting additional information and/or clarifications
- Manufacturer submits a corrective action plan (CAP) – Round 1
- Expert reviews new information and amends the dossier review report for WHO
- Further clarification by the manufacturer (CAP) may be required to address any additional requests – Round 2



Dossier review findings

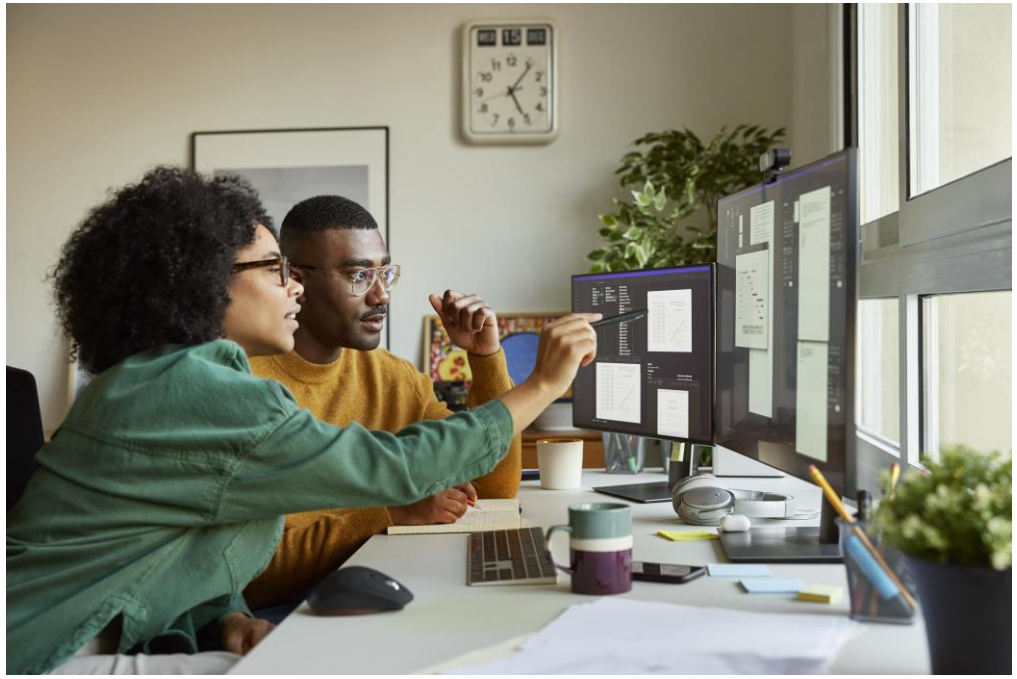
Clarification needed

- Highly summarized study protocols and/or results without the raw data
- Study acceptance criteria are not stated
- Date of design lock-down & validation studies not stated
- Unclear how specimen status was determined
  - Method used for reference results
- Confidence intervals do not match sample size
- No data on invalid results

Dossier review findings

Specifications not met

- Studies not provided
- Study design does not support the conclusions made
- Specimen types used not appropriate or incomplete
- Insufficient number of specimens tested
- Data generated using a different product
- Usability not demonstrated for the likely end-user



Requests and CAPs

Maximum extension time for dossier = 6 months

- Dossier review letter prepared by WHO broken down into 3 modules
- A response to the requested information must first be submitted as a corrective action plan (CAP)
- For each outstanding issue listed, the plan should state:
  - Availability of the requested data
  - Date of planned submission of data and any steps (e.g., performance studies) needed to be undertaken by the manufacturer to address the issues
- The CAP is due one month from the date of the letter
  - If it cannot be provided by this date, please notify WHO before this date with a written request for a time extension, including the reasons for the request.
- To formulate the CAP the letter contains a table with the requests

Module A

- Administrative
- Submission context (Product Info)
- Analytical performance and other evidence
- Labelling
- QMS, production & service control

Module B

- Stability

Module C

- Clinical evidence

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Performance evaluation

Independent **verification** of the performance of IVDs submitted for prequalification assessment

- Assays are challenged with a focus on their use in resource-limited settings and in the context of WHO guidelines
- A standard PQ protocol is followed for the evaluation
  - May include analytical, clinical & operational performance
  - The dataset obtained complements the verification and validation data submitted by the manufacturer in the product dossier
  - Currently takes place in a WHO Collaborating Centre and/or a designated Performance Evaluation Laboratory (PEL)
- Manufacturers can choose:
  - Option 1: PEL selected by WHO & PE paid for by WHO
  - Option 2: PEL selected by Mx & PE paid for by Mx

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Option 1 / Option 2

Option 1

- Laboratory selected by WHO
- Evaluation paid for by WHO

Option 2

- Laboratory selected by manufacturer
- Evaluation paid for by manufacturer

In all cases:

- Test kits and additional reagents (e.g. controls) and equipment provided by the manufacturer
- Evaluation conducted in a Performance Evaluation Laboratory
- According to standardized protocol
- Data analysis and report reviewed by WHO
- Final report prepared by WHO

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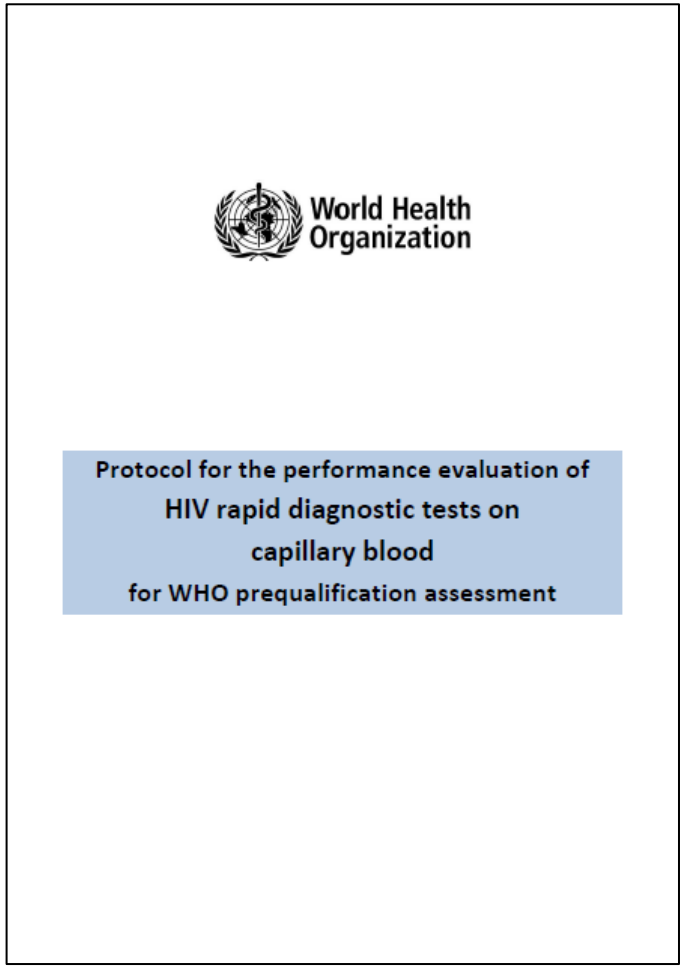
A standardized and independent evaluation

Standardized evaluation

- According to standardized protocols designed by WHO
- Using templates provided by WHO
- Where possible, same specimen panel used

Independent evaluation

- Conducted in a WHO-listed Performance Evaluation Laboratory (PEL)
- Data analysis and draft report reviewed by WHO



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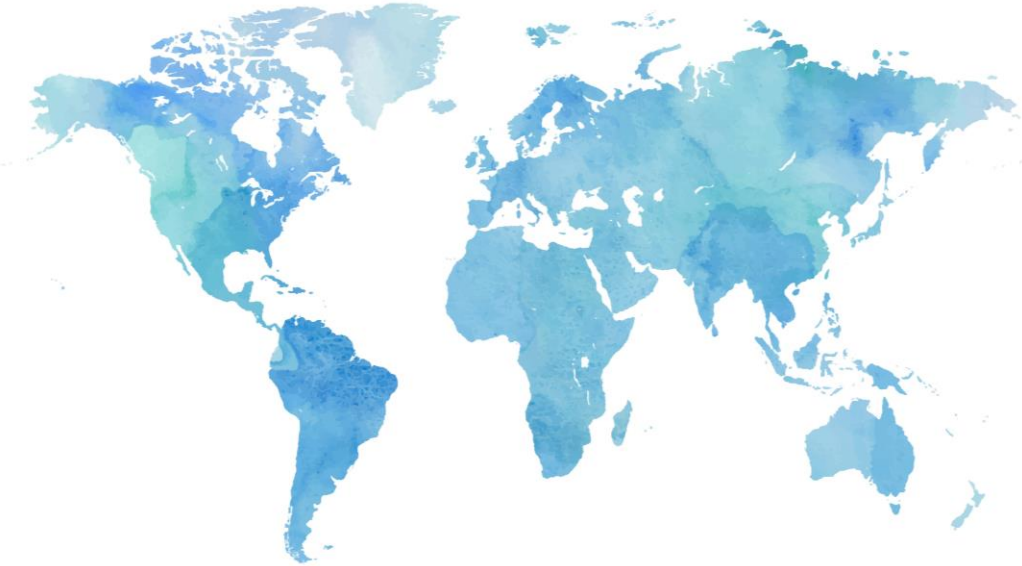
Performance Evaluation Labs (PELs)

PQ works with 15 laboratories for IVD performance evaluation

- Conduct performance evaluation according to WHO PQ protocols
    - *ensure availability of panels, conduct training, data analysis and drafting report*
- Obtain all authorizations & adhere to legal or ethical requirements
- Communication with WHO
- Record keeping
- Confidentiality
- Declaration of interest for each evaluation
- Ensure ongoing compliance with WHO requirements



Australia	India (3)	Uganda
Bangladesh	Kenya	UK (2)
Belgium	Mozambique	USA
Cote d'Ivoire	South Africa (2)	

Performance Evaluation - Key steps

WHO sends letter to manufacturer with protocol during PQ assessment process

- Option 1: after dossier screening, indicates PEL selected
- Option 2: once LoA signed, mfr to select PEL

Manufacturer ships requested number of tests to the PEL

- A specific number of tests from >1 lots
- Manufacturer may visit PEL before evaluation begins

PEL conducts the evaluation according to the PQ protocol

- Data analysis
- Draft report

WHO prepares final report and informs manufacturer of the outcome

- Data analysis and draft report review
- Comments from manufacturer

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Manufacturing site inspection

WHO PQ Inspections team will schedule the site inspection with the manufacturer

- Evidence of a fully implemented quality management system (design & development, manufacturing including quality control, storage, distribution) based on ISO 13485
- Demonstrates that the risk management meets ISO 14971 requirements
- Consideration of the robustness of the product for WHO intended settings and users
- Evidence of sufficient capacity to ensure reliable delivery

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Labelling review

- Compilation of labelling associated nonconformities identified at all the assessment stages.
- Labelling parts of the test kit –IFU, job aides, outer test kit box, inner test kit pouches, specimen transfer devices, buffer bottle, etc.
- Review of final labelling to verify if the claims are supported by evidence submitted in the technical documentation.
- Non-critical changes may be accepted as commitments e.g some cases may require approval by the Notified Bodies.
- Application may be cancelled if there are critical deficiencies and the manufacturer not willing to address them.

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Prequalification decision

For IVDs that meet PQ requirements

- The product is added to the list of WHO prequalified IVDs
- The public report is prepared & published

→ IVD is eligible for WHO and UN procurement & CRP

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Post-PQ assessment

Commitments to PQ

Outstanding but non-critical issues may be made commitments

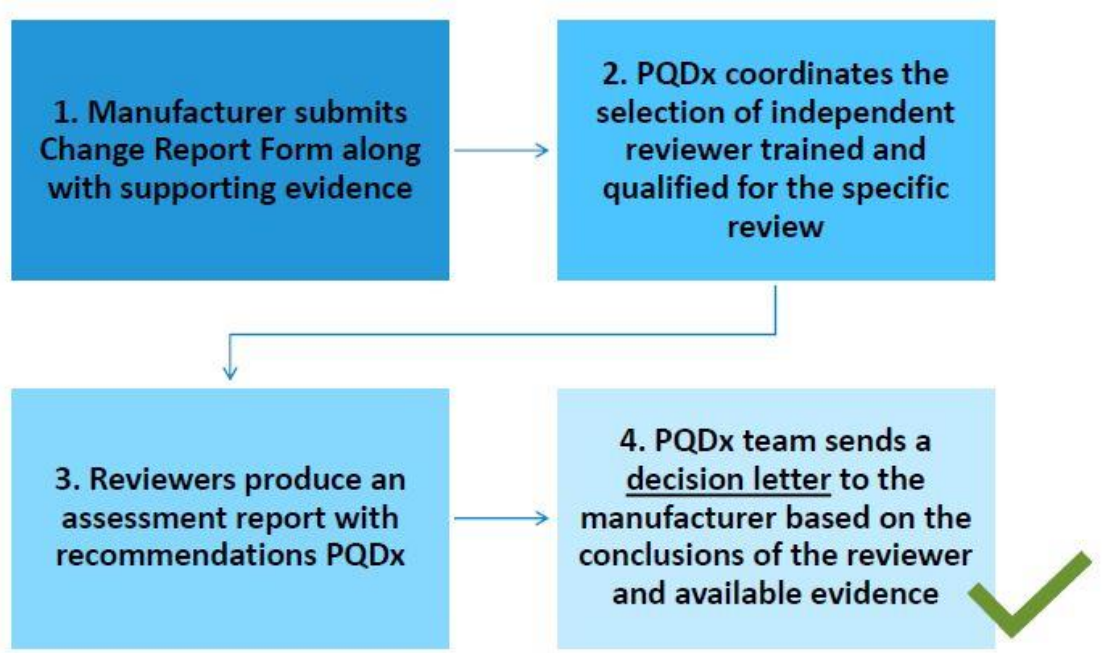
Prior to PQ manufacturer agrees to a plan & timeline for addressing these issues

Failure to meet commitments can lead to de-listing

May be addressed at follow-up site inspection or by document review

Manufacturer will be informed by letter when commitments have been met

Change Requests



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Collaborative Registration Procedure

Aims to accelerate country registration of prequalified IVDs through information sharing between WHO PQ and National Regulatory Authorities

PRINCIPLES

- Voluntary for Mx of prequalified IVDs
- Product sameness must be guaranteed
- Confidentiality of data shared
- Target timeline: **90 days** for NRA decision

WHO PQ REPORTS SHARED

- Dossier review & Change requests
- Site Inspection
- Performance Evaluation

Target time for NRA decision: **90** days

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Keep updated with the PQ-IVD webpage

https://extranet.who.int/prequal/vitro-diagnostics

World Health Organization | Prequalification of Medical Products
IVDs, Medicines, Vaccines and Immunization Devices, Vector Control

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IVD **In Vitro Diagnostics**

- About In Vitro Diagnostic & Male Circumcision Device Prequalification
- What We Do
- Documents A-Z
- Prequalified In Vitro Diagnostics
- Prequalified Male Circumcision Devices
- In Vitro Diagnostics Under Assessment
- IVDs Eligible for WHO Prequalification

In Vitro Diagnostics

Rapid advances in development of medical devices are generating challenges in quality assurance for manufacturers and regulators, and in both quality assurance and product selection for procurers. Launched in 2010, WHO prequalification of in vitro diagnostics provides a valuable service to each of these groups.

Procurers can procure prequalified IVDs secure in the knowledge these products are not only quality-assured but also appropriate for their intended setting of use. Manufacturers who attain prequalification of their products will be able to offer those products for supply to procurement agencies and organizations that apply quality

Information for

- Manufacturers
- Regulatory agencies
- Performance evaluation laboratories
- Procurement agencies

Workshop for Asian manufacturers of IVDs: from QA to procurement

20 to 23 January 2025

The Westin Jakarta Hotel, Jakarta, Indonesia

REGISTRATION IS OPEN: To secure your spot for 4 days' workshop, please register now: INDICO Registration

The World Health Organization Prequalification of In Vitro Diagnostics cordially invites you to attend the Workshop for Asian manufacturers of IVDs: from QA to procurement in T**he Westin Jakarta Hotel, Jakarta, Indonesia**, from **20 to 23 January 2025.** The workshops is specifically intended for IVD manufacturers based in Asia. The programme will include days dedicated to quality assurance, procurement and support projects. Manufacturers interested in participating to this event are invited to register as soon as possible. Participation is limited to two (2) representatives from each company and there are 200 seats available. We strongly encourage participation from the director QA/QC and the company CEO. Manufacturers may register until 1 December 2024.

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Thank You

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