WHO Prequalification of In Vitro Diagnostics

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WHO Prequalification of HPV diagnostic assays: pathway and recent development

27 August 2020

HPV Prevention and Control Board – Technical Meeting

Access to In Vitro Diagnostics

Access to IVDs heavily impacts the majority of medical interventions, including blood safety, surveillance, diagnosis, treatment and monitoring

To achieve such impact IVDs must be safe, of good quality and perform as expected

Changing IVDs global market

- Rapid emergence of new technologies
- Increasing expectation on quality, safety and performance
- Dynamic product lifecycle with many product changes
- Evolving regulatory landscape (nascent regulatory systems in Member States, increasing international convergence)

WHO Prequalification of IVDs

2008: shift from WHO test kit evaluations → **Prequalification of IVDs**

Standardized approach designed to assess **quality, safety and performance**

Alignment with global standards for assuring quality of IVDs

Through a rigorous process, identify IVDs that meet quality, safety and performance standards

With the purpose of providing guidance to interested UN agencies and WHO Member States in their procurement decisions.

PQ-IVD: aim, scope and impact

The aim of PQ-IVD 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 is expanding based on disease program needs

HIV

Malaria

Hepatitis C

Hepatitis B

HPV

G6PD

Cholera

Syphilis

Haemoglobin POC

Glucose meters & test strips

PQ-IVD components

PQ-IVD is a comprehensive assessment of individual IVDs through a standardized procedure aimed at determining if the product meets WHO prequalification requirements

The prequalification assessment process includes three components:

Review of a product dossier

Performance evaluation

Manufacturing site(s) inspection

Labelling review

For products that have been approved by stringent regulatory authorities, the product dossier review and manufacturing site inspection are leveraged or "abridged"

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Review of a product dossier

Purpose of the product dossier

Subset of technical documentation held by manufacturer

- Demonstrates the IVD conforms to the “Essential Principles of Safety and Performance of Medical Devices” (IMDRF),
- Product dossier including
  - Product design and manufacturing
  - Validation and verification studies
  - Labelling (Instruction for Use and labels)
  - Commercial and regulatory history
  - QMS

- WHO reference documents
  - Technical guidance series: provide guidance on how to produce required evidence
  - Technical specification series: minimum performance requirements for WHO prequalification for a specific type of assay

Product Dossier Review

Has the manufacturer considered safety and performance in WHO Member States?

Specific emphasis on issues relevant to resource-limited settings, such as:

- Stability of products
  - *e.g. heat and humidity*
- Suitable specimen type
- Labelling of products
- Ease of use

- Performance evaluated in the global population?

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Performance evaluation

Performance evaluation

Analytical, clinical and operational performance are assessed

- **Independent verification** of the performance of IVDs submitted for prequalification assessment according to standardized evaluation protocols
- Complements the verification and validation data submitted by the manufacturer in the product dossier
- Includes verification of **analytical** (e.g limit of detection, genotype detection, etc..) and **clinical** performance; and assessment of **ease of use** and **operational characteristics**
- Takes place in a PQ evaluating laboratory (currently 14 laboratories listed overall – *2 for HPV assays*)
- WHO reference document: standardized evaluation protocols

Manufacturing site(s) inspection

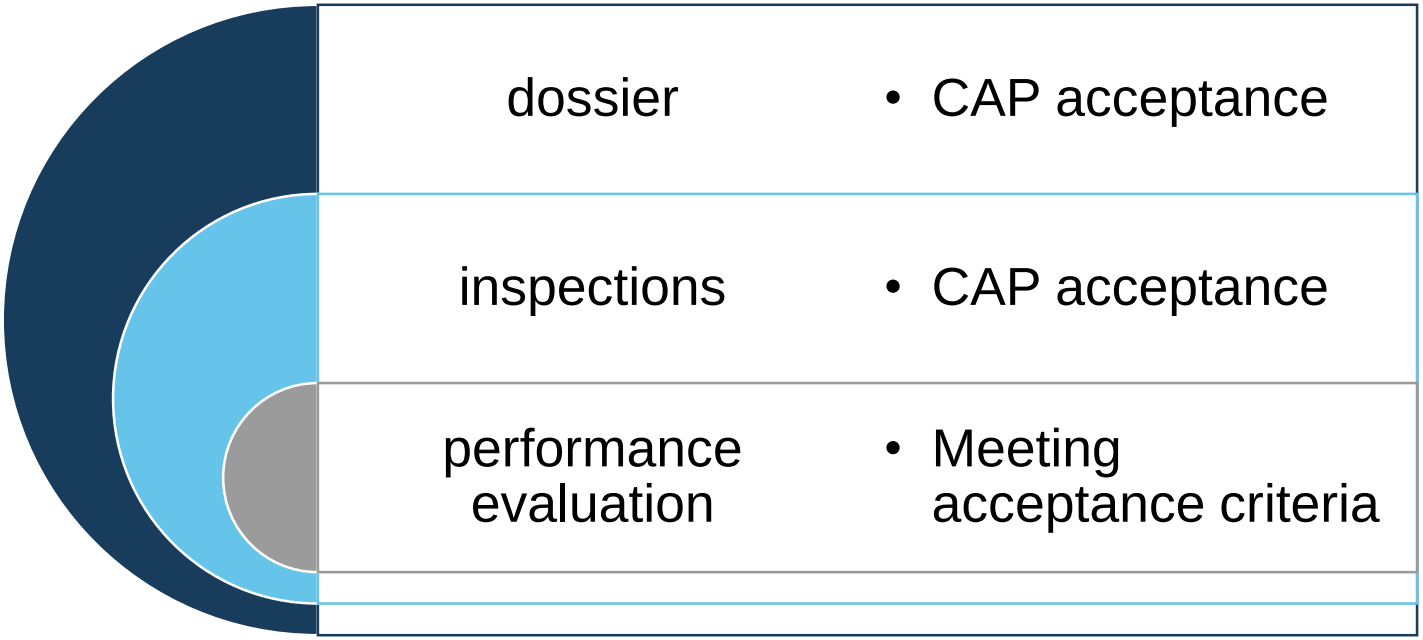
Manufacturing site inspection

All sites relevant to the IVD are considered

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

Prequalification decision

Final prequalification outcome depends on:



- Products meeting all criteria then undergo labelling review (IFU, labels)
- Product is then eligible for WHO and UN procurement

WHO PQ public report

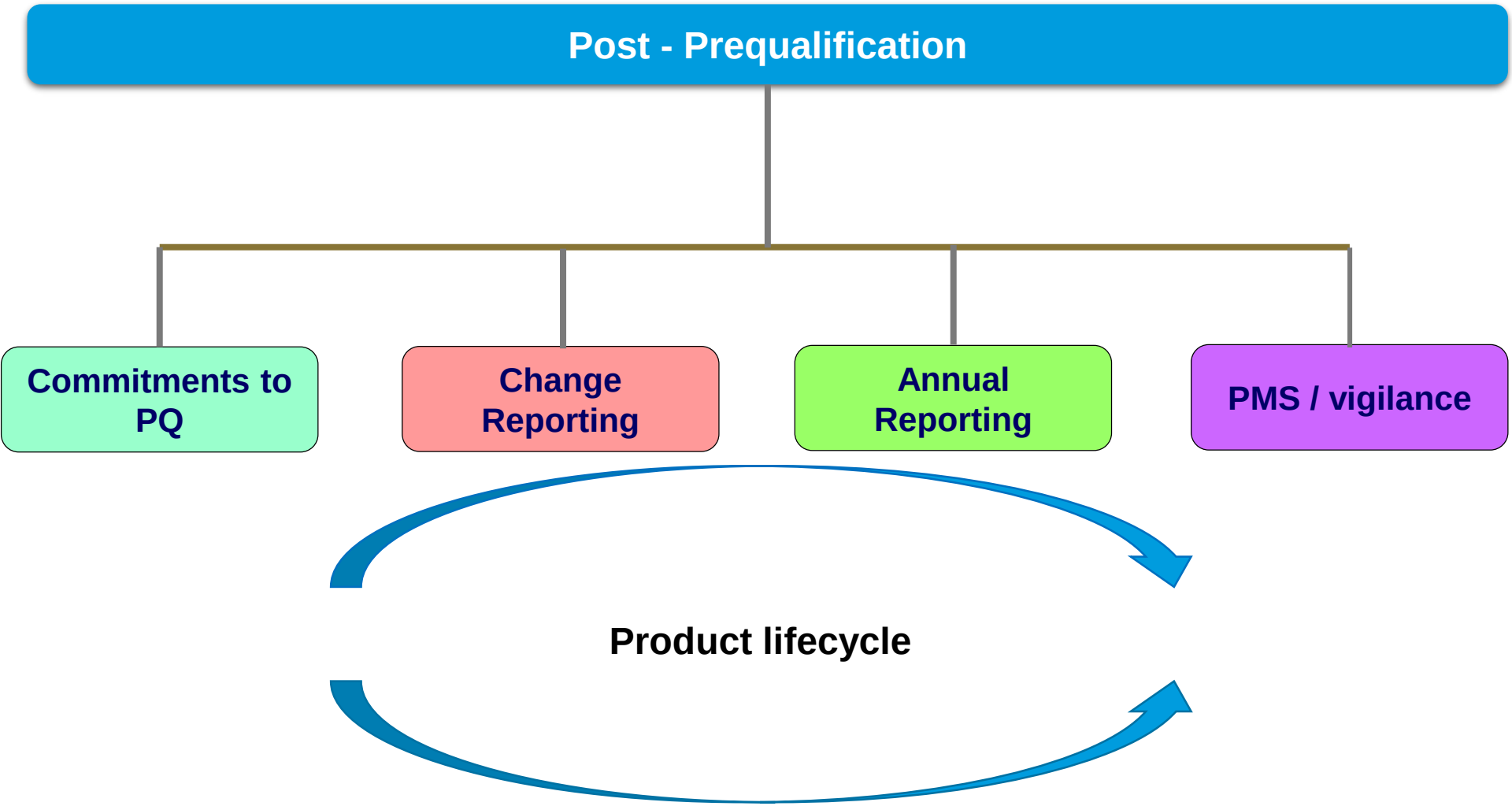
Published on WHO website

- Available on WHO website for all PQ-ed IVDs
- Clearly identifies:
  - product name
  - manufacturing site(s)
  - product codes
  - product regulatory version
- Summary of the prequalification assessment for a specific product, dates when the assessments were conducted and the outcomes of the assessment

For HPV assays:

https://www.who.int/diagnostics_laboratory/evaluations/pq-list/public_report_hpv/en/

Post - Prequalification Activities



Prequalification of HPV assays

Dossier requirements

TSS-4 describes the minimum requirements for product dossiers submitted by HPV assays manufacturers:

- Analytical performance (e.g. specimen stability, precision, genotype detection, interfering substances, etc.)
- Clinical performance
- Usability for self-collection and/or POC testing

Technical Specifications Series for submission to WHO Prequalification – Diagnostic Assessment

TSS-4 In vitro diagnostic medical devices (IVDs) used for the detection of high-risk human papillomavirus (HPV) genotypes in cervical cancer screening

Prequalification of HPV assays

Performance evaluation

2 PQ evaluating sites (Scottish HPV Reference Laboratory, UK and National AIDS Research Institute, India)

Protocol under revision in collaboration with K. Cushieri and M. Arbyn, with support from NIBCS:

- Analytical evaluation using material developed by NIBSC
  - Limit of detection using NIBSC International Standard
  - Within-laboratory reproducibility
  - Genotype detection
  - Cross-contamination / carry-over
- "Virological" evaluation
  - Not a proper clinical evaluation but comparison with a validated assay
  - Possible comparator assays: assay independently validated and shown to fulfil Meijer 2009 criteria

Prequalification of HPV assays

Current status

3 HPV assays prequalified

- Xpert HPV (Cepheid AB) – listed in December 2017
- *care*HPV Test (QIAGEN GmbH) – listed in July 2018
- Abbott *Real*Time High Risk HPV (Abbott GmbH&Co.KG) – listed in October 2019

2 HPV assays under assessment

- cobas 4800 HPV Test (Roche Molecular Systems, Inc.)
- cobas HPV (for use on cobas 6800/8800 Systems) (Roche Molecular Systems Inc.)

Thank you

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