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.
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.
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”
Review of a product dossier
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?
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:

<table>
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<tr>
<th>Category</th>
<th>Requirements</th>
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<tbody>
<tr>
<td>dossier</td>
<td>• CAP acceptance</td>
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<td>inspections</td>
<td>• CAP acceptance</td>
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<td>• Meeting acceptance criteria</td>
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- 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:

Post - Prequalification Activities

Commissions to PQ

Change Reporting

Annual Reporting

PMS / vigilance

Product lifecycle
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
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
  - careHPV Test (QIAGEN GmbH) – listed in July 2018
  - Abbott RealTime 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