Susie Braniff

In Vitro Diagnostics Assessment Team
Prequalification Unit
PQ of IVDs: aim & scope

Prequalification of IVDs began in 2010

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.

Currently 103 IVDs are prequalified.

PQ List available at:
https://extranet.who.int/pqweb/vitro-diagnostics/vitro-diagnostics-lists

- HIV
- Malaria
- Hepatitis C
- Hepatitis B
- HPV
- G6PD
- Cholera
- Syphilis
- Tuberculosis NAT*
- Haemoglobin POC*
- Glucose meters & test strips*
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 inspection
- Labelling review
Review of the product dossier

Assessment of manufacturer’s data

Analyzing the relevance of the data in the dossier

- Quality data that supports the manufacturers claims of quality, safety and performance
- Appropriate & well-designed validation studies

Review of completeness, accuracy and consistency of data over IVD life-cycle

- From initial product design, through validation, manufacture, quality control and release onto the market

➢ Are the technical specifications (TSS) met?
➢ Has the manufacturer considered the use of the product in resource-limited settings?
Technical specifications (TSS)

TSS 1: HIV serology IVD performance – Manufacturer’s evidence

Analytical Performance

Includes:

- Detection of genotypes
- Seroconversion sensitivity
- Measuring range
- Precision of measurement
- Potentially interfering substances & cross-reactivity
- Stability
- Flex studies
  - Validation of reading time, operating temperature, specimen volume, etc.

Clinical Performance

Includes:

- Diagnostic sensitivity
  - Minimum 400 HIV-1 specimens
  - Minimum 100 HIV-2 specimens*
  - Minimum 50 p24 Ag specimens*
- Diagnostic specificity
  - Minimum 1000 specimens
  - At least 2 geographical settings
  - Variety of intended users
  - More than 1 manufactured lot
- Usability studies are required for self-tests
Dossier review process

Coordinated by WHO

- Manufacturer submits dossier to WHO
- Dossier screened for completeness
- Dossier sent to subject matter expert for technical review
- Expert provides completed dossier review checklist and notes any deficiencies in the dossier
- WHO prepares dossier review letter for manufacturer requesting additional information or clarifications
  ➢ Process repeated with manufacturer’s response to the dossier review letter
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
  - 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)
  - Specimen panels designed to represent a global population
Evidence of a fully implemented quality management system based on International Standards

- IVD design & manufacture meets ISO 13485
- Risk management meets ISO 14971

Consideration of the robustness of the product for WHO intended settings and users

- The products undergoing prequalification have to be in routine manufacturing
- Evidence of sufficient capacity to ensure reliable delivery
Final prequalification outcome depends on:

- A final labelling review is performed and the public report prepared
- The product is added to the list of WHO prequalified IVDs
  - IVD is eligible for WHO and UN procurement
Reports generated during IVD assessment

<table>
<thead>
<tr>
<th>Dossier Review</th>
<th>Site Inspection</th>
<th>Performance Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of manufacturer’s information:</td>
<td>On-site inspection findings:</td>
<td>Protocol &amp; data provided:</td>
</tr>
<tr>
<td>▪ Product information</td>
<td>▪ Scope of inspection</td>
<td>▪ Product provided for evaluation</td>
</tr>
<tr>
<td>▪ Design and manufacturing</td>
<td>▪ Objectives</td>
<td>▪ Specimen panels tested</td>
</tr>
<tr>
<td>▪ Product performance specifications</td>
<td>▪ Limitations</td>
<td>▪ Reference results</td>
</tr>
<tr>
<td>▪ Validation and clinical studies</td>
<td>▪ Information about the manufacturer</td>
<td>▪ Data Analysis</td>
</tr>
<tr>
<td>▪ Labels</td>
<td>▪ Inspection findings</td>
<td>▪ Results</td>
</tr>
<tr>
<td>▪ Commercial history</td>
<td>▪ Audit trails and sources of evidence</td>
<td>▪ Appraisal by laboratory technician</td>
</tr>
<tr>
<td>▪ Regulatory history</td>
<td>▪ Evaluation and conclusions</td>
<td>▪ Appendices containing data generated during the evaluation</td>
</tr>
<tr>
<td>▪ Quality management system</td>
<td>▪ List of non-conformities and observations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Grading of NCs</td>
<td></td>
</tr>
</tbody>
</table>

+ Reports for approved changes
We prequalify in vitro diagnostics

The aim of WHO prequalification of in vitro diagnostics (IVDs) is to promote and facilitate access to safe, appropriate and affordable in vitro diagnostics of good quality in an equitable manner. The focus is on IVDs for priority diseases that are appropriate for use in resource-limited settings.

WHO IVD prequalification incorporates comprehensive assessment of individual IVDs through a standardized procedure, to determine whether the product meets WHO prequalification requirements. Assessment has three components:

- review of a product dossier
- laboratory evaluation of performance and operational characteristics
- manufacturing site(s) inspection

Following prequalification post-market surveillance is undertaken. It includes reactive and proactive measures, through complaint reporting and post-shipment/pre-distribution lot testing. Post-qualification also includes mandatory manufacturer notification of changes to the product or the quality management system.
Thank you

Contact PQ-IVD Team
diagnostics@who.int

WHO

20, Avenue Appia
1211 Geneva
Switzerland