

Meeting on Procurement of Laboratory Items

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Prequalification of Diagnostics, Post Market Surveillance

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Current situation

- **Scaling up interventions against major diseases of poverty**
 - Overall access to HIV ART has been a real **SUCCESS**
- Scaling up access to TREATMENT implies ...
 - Access to safe appropriate and reliable diagnostics at country level ... still a **Challenge**

Cost of diagnostics

Medicines :



First line ART regimen per adult per year :

Low Income Countries:

US\$ 125.- to 219.-

Middle Income Countries :

US\$ 160.- to 226.-

Diagnostics :

Per adult per year

HIV tests (at least two tests to confirm diagnosis)

US\$ 2.- to 10.-

CD4 tests (ideally 4 times/ year @ US\$ 10- 40)

US\$ 40.- to 160.-

VL if included (4 times/year @ US\$ 20-90)

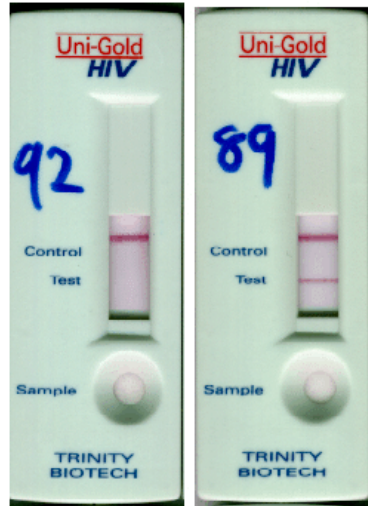
US\$ 80.- to 360.-

Total:

US\$ 122.- to 530.-



A wide variety of tests Quality ?



Situation and Challenges

Global market for Diagnostics is changing

→ Manufacturers and suppliers and Users

Trends

→ Outsourcing of production

- Move to countries with less stringent regulations

→ Confusion about licensing of products

- Re-branding of test kits (OEM)
- Same name, but different production site

→ Near patient testing

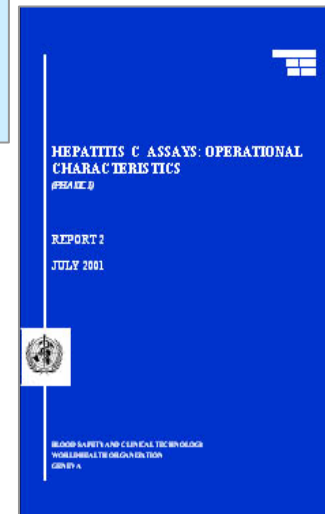
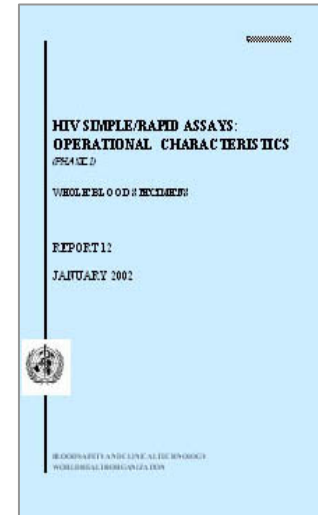
→ Easy to operate tests/methods

→ Pediatrics

Review of the "prequalification" process for diagnostics

WHO's activities

- **Assessment of the performance and operational characteristics of test kits**
 - HIV tests since 1988
 - Hepatitis B tests since 2000
 - Hepatitis C test kits since 2000
 - Chagas tests since 2002
 - Syphilis tests since 2001
 - Malaria tests since 2002.
 - CD4 technologies ad hoc in 1996 and 2003
 - Alternatives to viral load started 2005
- **Provide technical information on various diagnostics**



Prequalification of Diagnostics – Why is it needed?

- **Diagnosis of HIV infection is important both for prevention and care. There is an urgent need to expand access to accurate, reliable, and cost-effective diagnostic technologies**
- **Increasingly diagnostics are produced in less regulated countries aimed at market of LIC and MIC**
- **There are many new manufacturers producing HIV rapid tests of variable quality**
- **Many diagnostic technologies are not assessed by stringent regulatory authorities**
- **Often the performance and appropriateness of the diagnostics are not assessed for their intended use setting (e.g. resource limited settings)**

The aim of WHO's Prequalification of Diagnostics

- To promote and facilitate access to safe and appropriate diagnostic technologies of good quality in an equitable manner.
- To increase country capacity to effectively regulate diagnostics and diagnostics manufacturers and to monitor the quality of diagnostics on their market

Prequalification of Diagnostics - How do we approach it ?

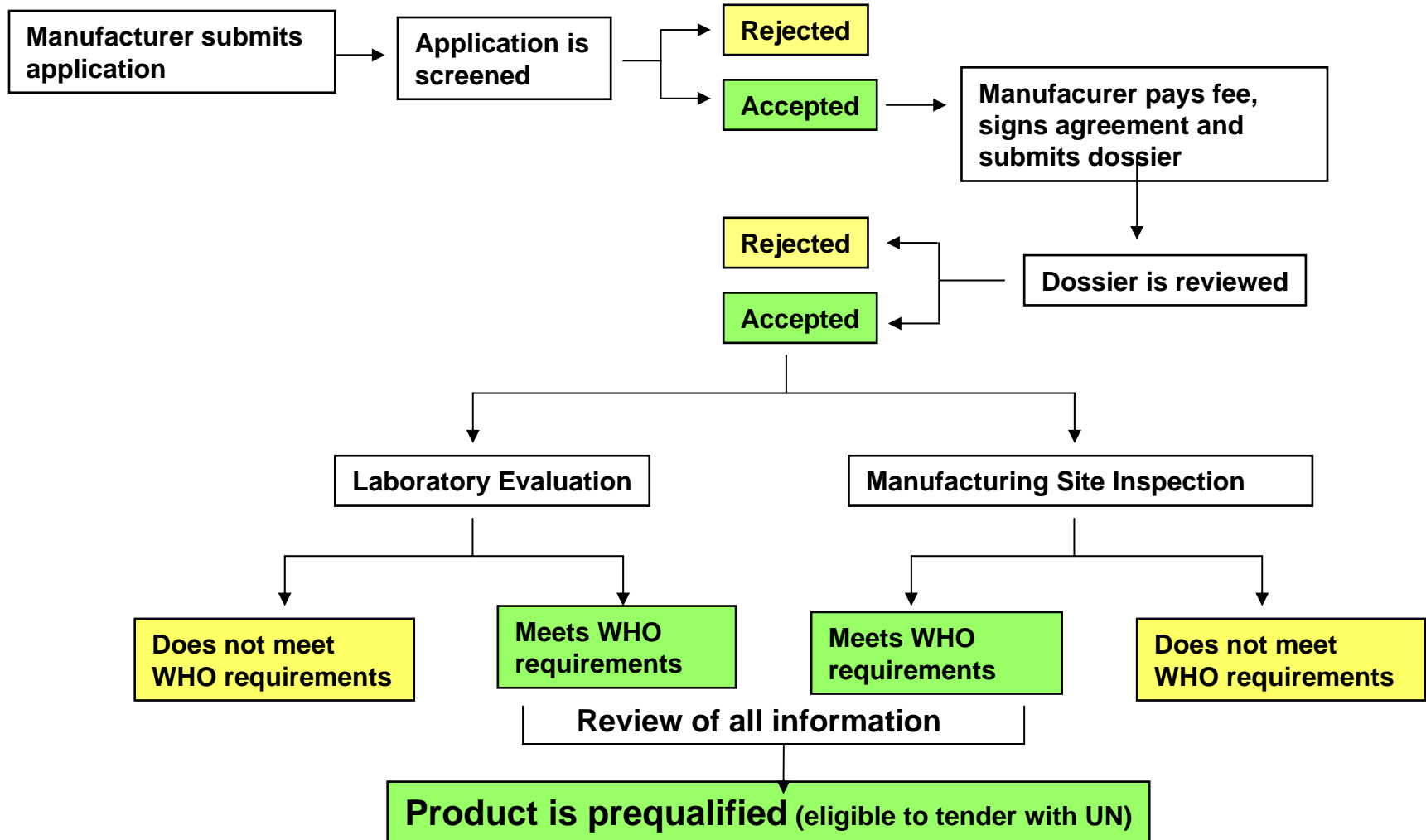
- Through a rigorous process identify diagnostics that meet the quality standards
- Harmonize the WHO prequalification process
 1. More stringent dossier assessment of diagnostics
 2. Inspection of QMS compliance at production
 3. Laboratory assessment of performance characteristics
 4. Building capacity at country level (NRA and NRLs) for post market surveillance of diagnostics
- Partnering with well known regulatory authorities and with key technical partners

Technical guidance

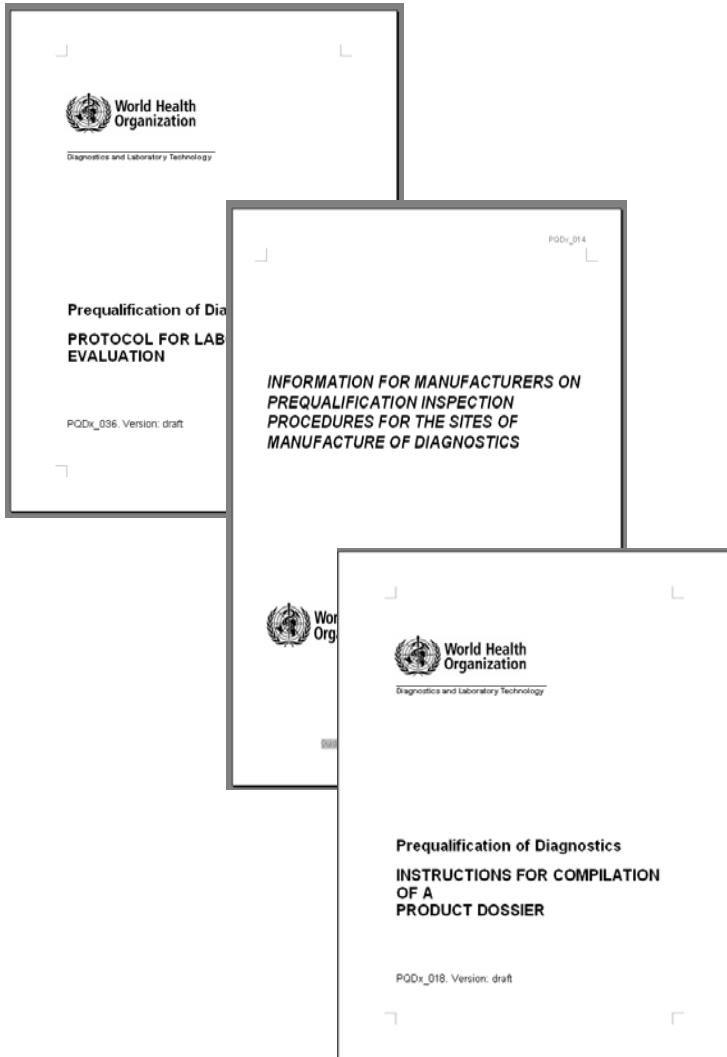
The process WHO uses to identify appropriate diagnostics needs to be

- Impartial
- Transparent
- Scientifically sound

Prequalification of Diagnostics Process



Quality Process in Place



DOSSIER

Prequalification of Diagnostics - Application Form

Instructions for Completion of the Application Form

Dossier Preparation guidelines

IT business requirements for web based PQ of Dx process

MANUFACTURER - INFORMATION

Guidelines for documentation of Quality Management Systems for manufacturers of diagnostics

Overview of the inspection process

Interim Inspection Report _ Final Inspection Report

Information for PQDx Stability Testing

INSPECTION

Information for inspectors on the inspection process

Checklist Inspection Diagnostics - Quality System and Process

Confidentiality agreement for inspectors – Declaration of interest

External Inspection Report

LABORATORY EVALUATION

Laboratory Evaluation Protocols

DLT INTERNAL QUALITY MANAGEMENT SYSTEM

DLT Post Inspection Internal Report

SOP's for all Prequalification of Diagnostics processes

What is a Product Dossier?



Product Dossier

(Global Harmonization Task Force)



World Health
Organization

Purpose of the Dossier Review

- Prequalification Decision Point
 - Understanding the Product
 - Understanding the Manufacturer

Elements of the Dossier

- Description of product
- Instructions for use (and labels)
- Shelf-life and stability (transport)
- Performance
- Sites of manufacture and key suppliers
- Manufacturing process
- Commercial and regulatory history
- Quality management system



Dossier Review Report

- Provides a recommendation
- Report used by WHO inspectors
- Report used by WHO scientists

Purpose of the Inspection



- Verify that a quality product is produced in a consistent manner
- Based on international recognised standards (ISO 13485)
- Strengthen national regulatory capacity NRA staff
- Beneficial for the manufacturer

What is inspected?

ISO13485:2003

1 Scope

2 Normative references

3 Terms and definitions

4 Quality management system

including documentation requirements

5 Management responsibility

including customer focus, quality policy

6 Resource management

including human resources, work environment

7 Product realization

including production and service provision, control of monitoring and measuring devices

8 Measurement, analysis and improvement

including control of nonconforming product, improvement



ISO 13485:
A Path to the
Global Market

This medical device standard is the
common denominator for international
compliance.



Laboratory assessment

- **Laboratory Testing at WHO CC or field sites**
 - WHO clinical specimen panel + additional panels
 - Technician's Appraisal
 - Safety aspects
- **Data Analysis**
 - Sensitivity -Specificity
 - Ease of use - operational aspect – suitability for use in resource limited settings
- **Reporting**
 - Individual reports to manufacturers
 - Manufacturer right of reply to report
 - Summary reports

The PQ communication strategy

- **Communications mapping and analysis**
- **Prequalification web pages**
 - Information on diagnostics that are in the PQ process
 - FAQs
- **Prequalification of Diagnostics Updates (quarterly)**
- **Annual stakeholders meeting /Annual report**
- **Communications specific for**
 - manufacturers
 - NRA - NRL
 - Users
 - procurers

PMS for prequalified diagnostics_

Why is it needed ?

As a prequalified diagnostics are placed on the market it is necessary to make sure that:

- They continue to meet all safety and performance requirements and standards that were required for the PQ approval
 - Any problems with the use of the product are dealt with and reported through appropriate channels
- The post-market phase of a diagnostic product is as important as the assessment and evaluation performed within the prequalification process

post-market surveillance _key players

- Manufacturers of diagnostics
- National programmes
 - Donor agencies/ mechanisms
 - Procurement agencies, (supply chain)
- National Regulatory Authority
- National Reference Laboratories
- End users

Manufacturers

- Requirements for a PMS system establishment by the manufacturer:
 - ISO 9001:2000 Quality management systems - Requirements
 - ISO 13485:2003 Medical devices – Quality management systems – Requirements for regulatory purposes
 - ISO 14971:2000 Medical devices – Application of risk management to medical devices
- PMS provides a continuous feedback on the diagnostic on the market and helps the manufacturer to maintain a high standard of product quality and customer satisfaction

NRA's _ NRL's and end users

- Strengthening national regulatory capacity
 - Registration of diagnostics
 - Review batch release data
- Strengthening national reference labs
 - Batch release testing
 - Sampling and testing of test kits from field
- End users
 - QMS

WHO post-market surveillance system for priority diagnostics

- Vigilance system:
 - Event/Incident
 - Notification _ alert
 - Performance assessment
 - Corrective action, if applicable

PMS - Batch release testing

- **Reasons :**

- Difference in quality between batches of the same diagnostic may occur
- Inappropriate transport and storage conditions (temperature, humidity, exposure to sunlight...) may affect diagnostic's performance
- A high level of reliability can only be guaranteed through testing of each batch procured in a country

- **Purpose**

- Ensure that the diagnostics delivered to the Member State meet the prequalification requirements and the manufacturer's claims on product's performance
- Ensure that only batches of satisfactory quality are distributed to laboratories all over the country.

PMS_ Field sampling and testing

- Reasons

- Inappropriate transport and storage conditions after procurement (in country distribution) may affect the assay's performance at the end user level
- Do the stability claims of the manufacturer hold

- Purpose

- Get an oversight of the performance of the tests sampled in laboratories at different levels within the country therefore bringing additional information on the quality of the assay when distributed to end users
- Testing of samples from the field in combination with batch release testing guarantees the monitoring of assay quality throughout the distribution chain thus ensuring that only quality assays are used by end users

PMS: The vigilance system

- The vigilance procedure:
 - Vigilance notifications submitted to WHO will be assessed
 - Manufacturer's investigation will be monitored
 - Information exchange will be undertaken with relevant parties as appropriate
- Reporting forms for manufacturers, end users and NRAs and instructions for fulfilment of these forms have been developed for vigilance data exchange with WHO

PMS: The impact on diagnostics procurement

- PMS will monitor the consistency of the quality of the PQDx on the market
- Unsatisfactory PMS data will be dealt with in cooperation with the manufacturer and the relevant players
- Removal from the list of prequalified diagnostics will be undertaken, if necessary, to protect public health

Prequalification of Diagnostics - What will be the impact at country level? (1)

- Prequalification of HIV/AIDS, TB and malaria diagnostics provides the evidence for:
 - transparent selection of diagnostic test of good quality
 - Adapted to the intended use conditions in low and middle income countries.
- Who will benefit from prequalification ?
 - Regulatory authorities, national reference laboratories, manufacturers, donors and patients

Prequalification of Diagnostics - What will be the impact at country level? (2)

- A range of good quality diagnostics appropriate for all levels of the health system in resource limited settings
- Increased access to quality diagnostics at reduced prices
- Improved access to impartial technical information on diagnostics
- Improved capacity at country level to monitor the quality of diagnostics on their market

Prequalification of Diagnostics - What will be the impact at country level? (3)

- Streamlined and fair procurement tenders
- Simplified procurement and supply management
- Sustainable and secure markets for manufacturers, with some healthy competition
- Better services for users of diagnostics, including maintenance and repair of equipment
- More standardized diagnostic practices, facilitates training and implementation of quality assurance.

WHO web pages

www.who.int/diagnostics_laboratory

www.wpro.who.int

e mail: diagnostics@who.int



World Health Organization

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Contributions to universal access

Prequalification of diagnostics

Procurement of diagnostics

Quality assurance

Guidance and training

Country projects



The goal of the diagnostics and Laboratory Team is to promote and facilitate access to safe, reliable and appropriate diagnostic technologies and laboratory services in an equitable manner through:

- Prequalification of diagnostics for high burden diseases;
- Capacity building of national regulatory authorities and national reference laboratories;
- Facilitation of procurement of affordable and appropriate diagnostics ;
- Policy, guidance and advocacy to Member States;
- Provision of quality assurance programmes to countries;
- Training and technical support including country projects;

"Accelerated progress further depends on broad investments in human resources and health infrastructures, including procurement systems and supply chains, and laboratory services."
Dr Margaret Chan Director-General of the World Health Organization
Remarks by at the UN General Assembly High Level Meeting on AIDS, New York, June 2008

RELATED LINKS

[Maputo Declaration 2008 \[pdf 299kb\]](#)

UPDATES

Prequalification of Diagnostics

Update

[Q1 2008 \[pdf 153kb\]](#)

[Q2 2008 \[pdf 401kb\]](#)

PUBLICATIONS

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Thank you