Investing in our future
The Global Fund
To Fight AIDS, Tuberculosis and Malaria

Global Fund Quality Assurance for Diagnostics

AIDS MEDICINES AND DIAGNOSTICS (AMDS)
ANNUAL STAKEHOLDERS AND PARTNERS MEETING
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Dr Joelle DAVIAUD
Quality Assurance Specialist
Grant Management

Health Products Management

• Objective of Quality Assurance :

To ensure safe, effective health products and acceptable to end users.

Good Procurement Practices

Principal Recipients must procure all products in accordance with principles set out in the interagency guidelines

"A Model Quality Assurance System for Procurement Agencies".

4 critical functions

1- Prequalification of products and manufacturers
2- Purchase
3- Storage
4- Distribution

Pharmaceutical Products
(since December 2010)

Condoms
WHO Procurement Guidelines

Global Fund Quality Assurance for Health Products

Diagnostic Products
(since March 2011)

Long Lasting Insecticidal Nets, IRS
WHOPES recommendations
2012 WHO Public Health Pesticides Procurement guidelines

Background

- The Board approved the Global Fund QA Policy for Diagnostic Products in December 2010
- The QA Policy was implemented in March 2011

- The QA Policy is based on the recommendations of a group of experts on regulatory, technical, implementation issues related to diagnostics, including Manufacturers representatives.

- After 3 years of implementation, the Secretariat reviewed the policy in light of **experiences with implementation, advances in technologies, market developments, new products assessed and partners' harmonization efforts**

- Updated version adopted in February 2014

QA policy for Diagnostics - Scope

Products subject to the policy: All durable and non-durable In Vitro Diagnostic Products and important for diagnosis

- **Rapid diagnostic tests**
- **Equipment/consumables Reagents, Calibrators, Software**
- Microscopes
- Imaging equipment, for example X-ray machines

Products not subject to the policy: Products for general laboratory use: gloves, syringes, needles, general reagents, test tubes, etc…

QA Policy for Diagnostics - Principles

(a) Clinical Criteria

Product types must be selected in compliance with:

- National guidelines
- WHO guidance

(b) Quality Criteria

Manufacturing site for all products:

- compliant with ISO 13485

(except for microscopes for which ISO9000 applies)

+

Product standards for HIV RDTs as detailed later

(c) Monitoring Quality and Ensuring Adequate Use

- Adequately trained staff
- Adequate storage and distribution
- Lot testing
- Reporting of failures

Quality criteria

For Malaria RDTS

Approved by WHO after technical assessment,
After positive advice received from WHO when assessed according to requirements of authorities member of GHTF

➡ **List of Malaria RDTs**
(WHO evaluations and information note)

For HIV RDTs, ELISA, WB, CD4, VL, EID

Approved by WHO after technical assessment or
Assessed according to requirements of authorities members founder of GHTF
(not applicable to CD4)
or
ERPD recommended

➡ **List of HIV RDT**
(WHO eligible for procurement)
+ "GHTF"- approved

Phased implementation of Quality Standards

- **HIV , Malaria RDTs , reagents** : applicable since 3/2011
- **CD4, VL, EID technologies**: applicable since July 2014

Ensuring quality of use – QMS (1)

Recipients must :

1. **Develop and maintain a QA system** for the PSM and use of Diagnostics

Systematic approach to ensuring quality testing through use of

- standard operating procedures including procedures for purchasing and inventory
- management of documents and record
- implementation of quality control and external quality assessment, including proficiency testing and on-site supervisory visits.
- appropriate physical infrastructure
- equipment maintenance, customer service
- human resource management and review, including training program and appropriate number of staff

Ensuring quality of use – QMS (2)

- follow **WHO guidance** for good practice in storage and distribution of diagnostic products,

- arrange for **systematic reporting of defects**.

Recommendation to PR
Laboratory systems capacity to be evaluated and monitored especially when Viral Load scale up is considered

Global Fund HIV Diagnostics List

The Global Fund
To Fight AIDS, Tuberculosis and Malaria

Version-5
August 2014

List of Diagnostic test kits for HIV and HIV equipments classified according to the Global Fund Quality Assurance Policy

According to Global Fund Quality Assurance Policy for Diagnostic Products (http://www.theglobalfund.org/en/procurement/policy), in force since 1st March 2011, Grant Funds may only be used to procure HIV RDTs if they have been:
(1) recommended by WHO for use in HIV/AIDS programs, based on a technical review of quality and performance indicators,
OR
(2) approved by authorities founding member of Global Harmonization Task Force (US, EU, Canada, Japan, Australia) (GHTF)

criteria 1 applicable currently to HIV Rapid Diagnostics, Immunoassays and after 1st July 2014 also applicable to CD4 and Virological Technologies (VL and EID)
criteria 2 applicable currently to HIV Rapid Diagnostics, Immunoassays and after 1st July 2014 also applicable to Virological Technologies (VL and EID)

The list is an overview of HIV RDTs to assist Principal Recipients (PRs) of Global Fund grants to identify the status of HIV RDTs according to the Global Fund Quality Assurance Policy. It includes products recommended for use after technical evaluation by WHO Prequalification of Diagnostics Programme and GHTF founding members.

The list is not exhaustive; PRs can procure product(s) not listed below as long as PRs demonstrate that the product is compliant with one of the above mentioned requirements.

The list is adapted from the lists posted in the following websites:
List of HIV diagnostics eligible for procurement by WHO: http://www.who.int/diagnostics_laboratory/procurement/purchase/en/
(which has also the products prequalified by WHO :http://www.who.int/diagnostics_laboratory/evaluations/PQ_list/en/

The list is updated regularly based on evidence received by the Global Fund.

HIV Simple assays/Rapid Diagnostic Tests (RDTs)

Manufacturer Product Catalogue number	Product Name	Number of tests per kit	Initial Sensitivity	Final Specificity	Manufacturer	Analyte	Specimen Type	Shelf life (months)/ Storage temperature	Comments	Eligibility WHO or GHTF countries
IHI-T402.	ABON™ HIV 1/2/O Tri-Line Human Immunodeficiency Virus Rapid Test Device	40	100.00%	99.70%	ABON Biopharm (Hangzhou) Co. Ltd. Hangzhou, PR China	Discrimination between HIV-1 and HIV-2 antibodies	Whole Blood/ Serum/Plasma	24 months 2 to 30°C	If whole blood: lancets, alcohol swabs, and heparinized capillary tubes with 50 µL mark line and dispensing bulb.	WHO PQ http://www.who.int/diagnostics_laboratory/evaluations/140822s_public_report_abon_hiv_triline_rdt_v1.pdf?ua=1
ITP02002-TC40.	Advanced Quality™ HIV Rapid Test	40	99.40%	98.80%	InTec Products, Xiamen, PR China	HIV1/2 antibodies combined	Serum, Plasma and whole blood	18 months 2 to 30°C	If whole blood: lancets, alcohol swabs.	WHO PQ
7D2342.	Alere Determine™ HIV-1/2	20	100%	99.40%	Alere Medical Japan, Matsudo, Japan	HIV 1/2 antibodies combined	Serum, Plasma and whole blood	14 months 2 to 30°C	If whole blood: lancets, alcohol swabs, chase buffer (7D2211), EDTA capillary tubes (7D2222). If serum/plasma: requires precision pipette plus tips.	WHO PQ http://www.who.int/diagnostics_laboratory/evaluations/111125_00033_013_00_public_report_final.pdf
7D2343.		100								
7D2643.	Alere Determine™ HIV- 1/2 Ag/Ab Combo	100	100%	98.80%	Alere Medical Japan, Matsudo, Japan	Discrimination between HIV 1/2 antibodies combined and HIV1- p24 antigen	Serum, Plasma and Whole blood	10 months 2 to 30°C	If whole blood: lancets, alcohol swabs, chase buffer (7D2211),EDTA capillary tubes (7D2222). If serum/plasma: requires precision pipette plus tips.	WHO PQ http://www.who.int/diagnostics_laboratory/evaluations/120320_00324_013_00_final_public_report_version2.pdf
7D2346	Alere Determine™ HIV-1/2	20	100%	99.75%	Alere Medical Japan, Matsudo, Japan	HIV 1/2 Antibodies combined	Serum, Plasma and Venous/capillary whole blood	14 months 2 to 30°C	Lancet, sterile gauze, antiseptic wipes Biohazard waste containers On order separately for whole blood procedure: Chase buffer 1x1.5ml (7D2243) EDTA capillary tubes (7D2222) or Microsafe capillary tubes (7D2223)	CE marked
7D2347		100								

- Rapid Diagnostic Tests (RDTs)
- Enzyme Immunoassays (EIAs)
- HIV Supplemental assays
- CD4 Enumeration technologies
- HIV virological technologies

Procurement - principles (1)

Taking into account the local context and ensuring a competitive and transparent approach, procurement must align with the following recommendations:

For Malaria RDTs:

Recipients might continue to procure a selected RDT/from a short list of RDTs provided

1. a competitive selection process had been performed within, at least, the previous 3 years, and
2. evidence of:
   - continued compliance of the product with the quality criteria defined in the Global Fund QA Policy ;
   - evidence of adequate performance in WHO-FIND Lot testing;
   - absence of reports of failure in the field.

Procurement - principles (2)

For HIV RDTS: 2 situations

1. One or several testing algorithm(s) for the diagnosis of HIV infection defined and validated within the last 5 years

Products selected as part of the validated national testing algorithm(s), compliant with the QA criteria

- PR to follow the recommendations of the validated algorithm(s)
- to order the products without competition, for the validity period of the algorithm

Products selected as part of the validated national testing algorithm(s), not compliant with the QA criteria defined in the Global Fund QA policy

- PR inform the National HIV Programme and request a replacement HIV assay.
- Selection through competitive process

2. No testing algorithm defined and validated: selection through competitive process

Procurement - Selecting appropriate Diagnostic Test Kits

- In country-studies to determine performance (sensitivity specificity) of the RDTs are not recommended as a primary basis for product selection.

- Ease of use assessments in local conditions may be highly relevant in informing procurement decisions within a short list of RDTs.

- Choice of RDTs
  - In line with national guidelines
  - Guided by programmatic needs: training requirements for health workers, completeness of the kits, and ease of use, previous experience in use of RDTs, and level of deployment in the country

Procurement - Total Cost of Ownership

Expected additional costs must be compared against estimated procurement cost :

- unit price of eligible RDTs, including all the components needed to perform the test
- Additional costs related to the introduction of a new RDT: re-training, or re-design of job aids.
- Maintenance of equipment and costs of consumables, and reagents for durable products.

RDTs Lot Testing

1. Routine lot testing : not mandatory

- Pre-shipment lot testing: check a QC lot release certificate issued by the manufacturer or an independent regulatory body,

- Through WHO-FIND Lot Testing of Malaria Rapid Diagnostic Tests and its recognized laboratories.

2. In case of suspected quality problem

- Quarantine suspected faulty Diagnostic Test Kits,

- Inform the national reference laboratory for preliminary investigation,

- Inform Global Fund PSM and WHO for guidance.

Compliance monitoring through PQR

- It is mandatory to report procurement transactions for diagnostic tests, CD4, Viral load, Genexpert machines and associated consumables in the Price Quality Reporting on line system (PQR) http://www.theglobalfund.org/en/procurement/pqr/

- The Secretariat monitors compliance with QA requirements:
  - Compliance criteria
    - Procurement of WHO-PQ , SRA authorized or ERPD products
    - Notification request sent/ Non Objection for ERPD products procured
  - Monthly compliance review

In case of non-compliance, follow up and potential corrective measures

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The Expert Review Panel mechanism

Expert Review Panel for Diagnostics (ERPD)

Risk/ benefit assessment :

- Mechanism integrated in the QA Policy for Diagnostics based on previous experience with ERP for medicines.
- Joint Global FUND/UNITAID initiative
- Volontary application by manufacturer in response to the EOI
- Scope of products: products which may have a high public health impact, but have not yet undergone a stringent assessment, either by WHO Prequalification or by a SRA.
- Step towards a WHOPQ/full regulatory review.: does not replace WHO PQ/SRA assessment
- Impact: should help expediting access to innovative diagnostic products, if the associated risks are deemed less than the potential benefits.

ERPD: Operationalization & Membership

- Funded by UNITAID & The Global Fund, hosted by WHO
- Managed according to Terms of Reference (TORs) developped under the oversight of The Global Fund and UNITAID with inputs from partners (MSF, OGAC, UNICEF, USAID, WHO).
- Organized for **selected** diagnostic technologies according to agreed upon timelines: **4 month timeline**

An **independent technical body** :

- Established and administered with guidance from WHO Essential Medicines and other Health Products Department, leading the technical implementation.
- Composed of external technical experts: representatives from a wide range of expertise in the field of *in-vitro* diagnostics medical devices

ERPD Mechanism

WHO	WHAT		On/To	Timeline
Global Fund/ UNITAID	Publication of EOI	Define the scope of products to be submitted	**GF, UNITAID website**	T0
Manufacturer	Application as per EOI requirements (product questionnaire + other doc)	According to eligibility criteria: regulatory status and QMS system in place	**GF Secretariat**	2 months
GF Secretariat	Review the completeness of applications	Submit complete dossier Inform manufacturer about status of application	**ERPD coordinator** **Manufacturer**	2 weeks
ERPD coordinator	Organize the review of applications	Finalize ERPD reports and provide conclusions	**GF and UNITAID**	2 months
ERPD experts	Review applications	Provide reports to ERPD coordinator	**ERPD coordinator**	
GF	Review ERPD reports	Communicate ERPD advice and conclusions	**Manufacturer/ UNITAID**	2 weeks

ERPD: Risk classification

Classification of products in 4 risk categories:

- **Risk Categories 1 and 2**

  products may be considered for time-limited procurement.

- **Risk Category 3**

  products may be considered for time-limited procurement only if there is no other option

  And

  if the risk of not diagnosing and/or making treatment decisions is higher than the risk of using the product.

- **Risk Category 4**

  products may not be considered for procurement under any circumstances.

ERPD Implementation

4 MONTH PROCESS

ERPD steps	Pilot Round	ERPD round 1
GF/UNITAID EOI : selected products	POC HIV EID	POC CD4/ VL/ EID lab-based molecular VL techniques using DBS
EOI publication	13 Feb 2014	4 July 2014
Manufacturer's submissions to GF	8 April 2014	29 August 2014
Number of submissions received	2	15
ERPD review	Mid April- mid June 2014	Mid September- Mid November
Conclusion letters sent to Manufacturers	20 June 2014	Last week of November

QA policy: Implementation challenges

- Quality assurance for products/EQA
- Selection of products by country programmes: national algorithms/products non interchangeable/suitability of technology
- Post marketing surveillance
- Forecast of needs vs forecast of purchase
- Placement of equipment/commodities/contracting models/mark ups by distributors
- Affordability/access/Inconsistent pricing policies
- Country readiness for adoption of new products/lab systems
- Registration in countries/barriers to market entry

Conclusion

MAIN DRIVING FORCES for the Global Fund

- Work with partners towards QA harmonization
- Extend scope of products submitted to the GFQA policy
- Increase number of available products through the operationalization of the ERPD
- Work on the Total Cost of Ownership in which maintenance and servicing are considered
- Ensure Quality of Use, not only Quality of Products
- Support countries for the implementation and scale-up of new testing (CD4/ Viral load) through
  - strong quality assurance program,
  - better EQA system,
  - clear and simple guidance for HIV testing algorithms

Guidance documents available on the Global Fund website

- Global Fund's QA policy for Diagnostic Products
- List of HIV Diagnostics tests
- Price and quality reporting
- Guidance for best practice
- Global Fund Guidance for Procurement and Use of HIV Diagnostic Test Kits with Global Fund Grants
- "Technical considerations for expansion of viral load testing"; WHO, PEPFAR, CDC, Global Fund, ASLM
- "Programming of laboratory investments with a focus on viral load testing"; Global Fund
  http://www.theglobalfund.org/en/procurement/quality/diagnostics/

THANK YOU

QUESTIONS?????