RDT Quality Control and Quality Assurance

RDTs and fever case management in the private health care sector in Africa: a consultative working meeting, Entebbe 20-21 Oct 2015

Dr. Daniel Kyabayinze, Dr. Sandra Incardona, & Dr Iveth Gonzalez
Malaria and Acute Febrile Syndrome programme
The quality of RDTs can be assured!

Only good quality RDTs are procured, based on the WHO RDT Product Testing:

**Panel Detection Score (PDS):**
Score for consistent detection of parasite samples at low parasite density (200 p/ul)

**WHO procurement guidelines:**
PDS for Pf at 200 p/ul ≥ 75%
PDS for Pv at 200 p/ul ≥ 75%
False positive rate < 10%
Invalid rate < 5%

For every RDT lot coming into the country:

RDTs are Lot Tested in reference laboratories:
(RITM, Philippines and IPC, Cambodia)
ONLY RDT lots with a PASS report are released for distribution in the countries

RDTs transported and stored in the field:

Follow transport and storage guidelines:
If transport/storage is done well, risk of degradation is very low
End users
- Appropriate training and instructions
- Management of positive and negative results
- Monitoring of commodity supply and disease rates

Stage 1: Product testing
Evaluate product performance

Stage 2: Lot testing
Confirm product quality on arrival in country before dissemination to the field

Stage 3: QC at point of use (positive control wells)
Ensure that RDTs have maintained accuracy through transport and storage

Before purchase
Before distribution
Before use

Supply chain management

Transport and storage

US-CDC (Atlanta)

IPC (Cambodia)

RITM (Philippines)

End users
- Appropriate training and instructions
- Management of positive and negative results
- Monitoring of commodity supply and disease rates

PCWs field-evaluated, Pilot batches available
Malaria RDT Lot Testing [Stage 2] - current format -

- QC of RDT lots directly after purchase (pre-shipment) or in-country before distribution in the field (post-shipment)

- Two WHO-FIND reference Lot Testing laboratories:
  - closely supervised, annual EQA assessments
  - turnover of 5 days between RDTs receipt and report issue

- Lot Testing also supported in some other labs
  - Nigeria CMUL, in the frame of the ‘Private Sector RDTs project’
  - NIMR New Delhi, India, with national funding

- Institut Pasteur, Cambodia (IPC)
- Research Institute of Tropical Medicine, Philippines (RITM)
The future of the Programme – transition starting 2015/16: Testing based on recombinant panels

**Supply chain management**

**Transport and storage**

**End users**

- Appropriate training and instructions
- Management of positive and negative results
- Monitoring of commodity supply and disease rates

**Stage 1: Product testing**
Evaluate product performance

**Stage 2: Lot testing**
Confirm product quality on arrival in country before dissemination to the field

**Stage 3: QC at point of use (positive control wells)**
Ensure that RDTs have maintained accuracy through transport and storage

**Before purchase**

**Before distribution**

**Before use**

**Manufacture**
- Product development
- Availability of common reference standards

**Central evaluation lab**

**National reference labs (countries)**

**PCWs available for field QC in countries**
Moving forward with QA/QC of RDTs

It is crucial to build capacity in the countries to be able to:

- Conduct their own lot testing, and have local capacity to cross-check any RDTs failing in the field

- Do field QC of RDTs, with all the tool becoming available now (troubleshooting guide, PCWs etc.)

- Need a clear process for acting on field problems, with RDTs or also accessories
Additional slides
<table>
<thead>
<tr>
<th>Panels used for testing</th>
<th>Current Programme (Product -/ Lot Testing only)</th>
<th>Future Programme (Product -/Lot Testing + QC in the field)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Infected patient blood or cultured parasites</td>
<td>- Recombinant malaria antigens</td>
</tr>
<tr>
<td></td>
<td>- Standardized at low parasite density</td>
<td>- Standardized at concentrations equivalent to the low parasite density</td>
</tr>
<tr>
<td></td>
<td>- Stored at -70 °C</td>
<td>- Stored at room T °</td>
</tr>
<tr>
<td>Accessibility of panels</td>
<td>- Wild-type samples: only accessible to WHO-FIND labs</td>
<td>- Same recombinant panels available to all users (under different formats), including national reference labs and manufacturers</td>
</tr>
<tr>
<td></td>
<td>- Cultured samples: available to manufacturers</td>
<td></td>
</tr>
<tr>
<td>Places for testing</td>
<td>- Product Testing at US-CDC</td>
<td>- Product Testing in central lab</td>
</tr>
<tr>
<td></td>
<td>- Lot Testing in 2 WHO-FIND labs</td>
<td>- Lot Testing in national reference labs, with confirmatory testing in central lab</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Field QC by end users (positive control wells)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Development/production QC by manufacturer</td>
</tr>
<tr>
<td>Cost and sustainability</td>
<td>- High operating costs</td>
<td>- Low operating costs</td>
</tr>
<tr>
<td></td>
<td>- Requiring donor funding and unsustainable on the long term</td>
<td>- Can be supported through fees for users of the system</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Sustainable on the long-term</td>
</tr>
</tbody>
</table>
Future plans for field QC of RDTs

Tools being developed, for implementation as part of the UNITAID-funded ‘private sector RDTs project’:

1. Troubleshooting guide
2. Protocol for acting on RDT problems in the field
3. PCWs for monitoring quality of RDTs at end-users level
Troubleshooting guide

- List of issues encountered in the field, e.g. invalid tests, red background, etc.
- Recommendations on use of accessories, blood transfer devices
- Possible actions to correct any errors made by the user
- Instructions to follow in case of persistent/frequent problems (reporting to supervisors, etc.)
Proposed protocol and report forms in case of field problems with RDTs

- Defining who does what in case of field problems, e.g. troubleshooting, verification visits, cross-checking of RDT quality, reporting of confirmed problems, actions such as re-call of RDTs etc.
- Standard report forms to compile relevant info
- All to be implemented in the private sector project
- Coordination with NMCP and regulatory bodies to ensure alignment with each one’s roles and responsibilities
Acting on RDT problems

Verification n°1

RDT USER

Verifies RDTs problems with troubleshooting guide

Verification n°2

SUPERVISOR/ QA OFFICER

Fill in tally for form, inform supervisor

In- Country Testing with recombinant panels

Verification n°3

Natl. QA/QC FOCAL POINT, NRL (lab)

VERifies RDTs problems, If needed: orders NRL testing

PASS

NRL, NRA

FAIL

FIND provides TA actively for this process

NRL, MoH, NRA

Engage field actions (replacement of RDTs etc.)

Verify n°4

WHO-FIND lab do confirmatory LT and send results

PASS

Communicate to MoH, manufacturer(s), WHO PQ

FAIL

Non-conformity Alert

Acting on RDT problems
QC at end user level using Positive Control Wells (PCWs)

- Small polypropylene tubes coated with dried recombinant proteins (HRP2, pLDH and aldolase)
- Concentrations equivalent to 200 parasites per microlitre of blood
- Re-constituted with buffer using a dropstir
- Transferred to a malaria RDT using a transfer device
Prototype PCW
QC at end user level with Positive Control Wells (PCWs)

- Publishing field evaluations in Uganda and Laos

- Current status of development:
  - first batches done, ready to be packaged and shipped for field implementation

- Plans:
  - implementation in the private sector project before end 2015
  - use at the supervisors level, as a tool to assess competency, check quality of local RDT stocks, and reassure users

FUTURE PLANS: introduce PCWs also in the public sector