

Information note on interim selection criteria for procurement of malaria rapid diagnostic tests (RDTs)

WHO Global Malaria Programme
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In view of the increasing demand of countries to scale-up malaria diagnostics following the large-scale introduction of expensive antimalarial medicines, and the decreasing malaria trends in many countries, there is a need to provide clear guidance on the criteria for selecting malaria diagnostics meeting international quality standards. This information note is addressed to managers of national malarial control programmes and other technical experts involved in making decisions for procurement of malaria rapid diagnostic tests (RDTs) and provides recommendations on the key RDT selection criteria.

WHO policy on malaria diagnosis

WHO recommends parasitological confirmation of malaria through quality assured diagnosis in all settings before treatment is started. Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible¹. Prompt diagnostic confirmation of malaria can be achieved through good quality microscopy. Since this is not feasible in many situations, quality assured malaria Rapid Diagnostic Tests (RDTs) represent suitable alternatives for the diagnosis of *Plasmodium falciparum* infections, and a number of products can also detect most cases of *non-falciparum* malaria.

The WHO product testing of malaria RDTs: Round 1

The heterogeneous diagnostic performance of more than 200 malaria RDTs available in the market is undermining the confidence of health professionals in the accuracy of these tests. The WHO product testing of malaria RDTs provides comparative data on the performance of various RDTs available in the market to guide procurement.

The first round of WHO product testing of malaria antigen-detecting RDTs was completed in November 2008. All companies manufacturing under ISO-13485: Medical devices - Quality management systems - Requirements for regulatory process were invited to submit up to 3 different products for evaluation. The RDTs were evaluated against panels of cultured *P. falciparum* parasites, panels of patient-derived *P. falciparum* and *P. vivax* parasites, and a parasite-negative panel. In addition, thermal stability of the products was assessed after 2 months of storage at elevated temperatures and humidity, and a descriptive assessment of ease of use was recorded.

The full report of the Round 1 of WHO/TDR/FIND/CDC malaria RDT product testing, with results of the 41 RDTs evaluated, is available at the following URL: <http://www.finddiagnostics.org/export/sites/default/media/press/pdf/Full-report-malaria-RDTs.pdf> . Based on these results, FIND has developed a web-based interactive guide to inform RDT selection on the basis of target malaria species, minimum detection rate² for both

¹ Laboratory confirmation of malaria should be available within two hours of patients presenting for treatment.

² The term 'detection rate' is a composite index of test positivity as well as of inter-test and inter-lot

P. falciparum and *P. vivax* at 200 parasites/ μ L, invalid rate³ and test format. The guide is available at the following URL:

http://www.finddiagnostics.org/programs/malaria/find_activities/product_testing/malaria-rdt-product-testing

Current WHO procurement criteria for malaria RDTs

Among the RDTs which have been evaluated by the Round 1 WHO product testing programme, WHO procurement has selected tests on the basis of the following minimal performance criteria:

1. **Invalid rate** less than 5%
2. **False positive rate** less than 10%
3. **Detection rate:**
 - 3.1. For RDTs targeting *P. falciparum* only:
Detection rate \geq 50% against samples of *P. falciparum* at 200 parasites/ μ L.
 - 3.2. For RDTs targeting both *P. falciparum* and *non-falciparum* species:
Detection rate \geq 50% against samples of *P. falciparum* at 200 parasites/ μ L, and
Detection rate \geq 25% against samples of *P. vivax* at 200 parasites/ μ L.

Based on these criteria, a total of 22 RDTs are considered eligible for procurement by WHO, and listed in the table below. This list will be updated based on the results of new RDT product testing rounds. The second round of product testing began in April 2009, and results will be available in April 2010. A third round is currently ongoing, following a call for expressions of interest to manufacturers published in October 2009.

Advice to national health authorities for selecting malaria RDTs

It is the responsibility of each national malaria control programme to select well performing RDTs adequate for the setting of intended use. To select malaria RDTs, experts convened at the WHO Technical Consultation on parasitological confirmation of malaria diagnosis, held in October 2009 in Geneva, provided the following advice:

A. For detecting *Plasmodium falciparum* in low⁴ and moderate⁵ transmission areas:

Select RDTs that achieve well above 50% detection rate at 200 parasites/ μ L (e.g. \geq 75%).

consistency in performance. Detection rate is not equivalent to sensitivity - see page 12 of the full report of the Round 1 of WHO/TDR/FIND/CDC malaria RDT product testing for a detailed description of this parameter.

³ Proportion of tests deemed invalid, i.e. without visible control band.

⁴ 'Low transmission' areas are hypo-endemic areas in which the prevalence rate of malaria is 10% or less during most time of the year among children from 2 to 9 years old. Here a person may attain adolescence before malaria infection is acquired and may escape acquiring a malaria infection altogether.

⁵ 'Moderate transmission' areas are meso-endemic areas in which the prevalence rate of malaria is 11-50% during most time of the year among children from 2 to 9 years old. Here the maximum prevalence of malaria infection occurs in childhood and adolescence, though still not unusual for adult life to be attained before acquiring infection.

B. For detecting *Plasmodium falciparum* in high⁶ transmission areas:

Detection rate should be at least 50% at 200 parasites/μL. Since the extent of such areas is likely to decrease with effective malaria control, detection rates well above this level should become the basis for product selection in the future years.

C. For detecting *Plasmodium vivax*:

Selection criteria for *P. vivax*-detecting RDTs should be at least equivalent to those for *P. falciparum*-detecting RDTs. Please note that this advice recommends a more stringent performance level than the minimal criteria described under 3.2 in the previous section.

In addition to the above criteria, national health authorities should take the following factors into consideration when selecting appropriate malaria RDTs for procurement:

D. Stability requirements at temperatures of intended storage, transport and use;

E. Ease of use and training requirements by the health workers.

Once all these factors have been considered, other parameters should be also evaluated, such as completeness of the kits (e.g. inclusion of lancets and alcohol swabs) and price. Price alone should not be the determining factor for the procurement of RDTs.

Programs which are planning the introduction of RDTs should consider selecting tests with the highest performance, indicated in bold in the Table below. In countries with heterogeneous levels of transmission, programs should consider selecting RDTs with higher detection levels to cover all areas, including those with low to moderate transmission.

Programs which are already implementing RDTs on a large-scale should continue to deploy a test listed in the Table, including those in regular font (not in bold), until a decrease in malaria transmission will require introduction of RDTs with higher detection levels at low parasitaemias. Subsequent plans to replace RDTs should be made with consideration of all corresponding training and programmatic requirements. In addition, production capacity and expected delivery time for orders of the new RDTs should be assessed as part of the decision-making process.

The performance of individual products is likely to vary between lots over time. It is therefore recommended that all production lots of procured products be checked for quality through lot-testing prior to large-scale deployment in the field and that a process of monitoring RDT performance in the field⁷ should be put in place. This should be applied to all RDTs eligible for WHO procurement (see below table) as well as products no longer in this list. Full information on WHO procedures for RDT lot testing is available at: http://www.wpro.who.int/sites/rdt/who_rdt_evaluation/lot_testing.htm.

⁶ 'High transmission' areas are hyperendemic and holo-endemic areas in which the prevalence rate of malaria is over 50% during most time of the year among children from 2 to 9 years old. In these areas by late infancy or early childhood practically all individuals are infected.

⁷ P.11 <http://www.wpro.who.int/NR/rdonlyres/9F42AF75-AC81-48E5-AAA2-0FB9B630425C/0/RBMGFATMRDTApr17Fin2.pdf>

List of malaria RDTs eligible for procurement by WHO.	
Product	Manufacturer
<i>P. falciparum</i> only	
Advantage P.f. Malaria Card *	J. Mitra & Co. Pvt. Ltd.
CareStart Malaria HRP2 (Pf) *	Access Bio, Inc.
First Response Malaria Ag HRP2 *	Premier Medical Corporation Ltd.
ICT Malaria Pf Cassette Test *	ICT Diagnostics
Immunoquick Malaria Falciparum *	Biosynex
Malaria Plasmodium falciparum Rapid test Device (Whole blood) *	ACON Laboratories, Inc.
Malaria Rapid Pf	Vision Biotech (Pty) Ltd.
Paracheck Pf Rapid test for <i>P. falciparum</i> Malaria (Device)	Orchid Biomedical Systems
Paracheck Pf Rapid test for <i>P. falciparum</i> Malaria (Dipstick)	Orchid Biomedical Systems
Parahit-f Dipstick for Falciparum Malaria *	Span Diagnostics Ltd.
SD Bioline Malaria Ag Pf *	Standard Diagnostics, Inc.
<i>P. falciparum</i> & Pan/ <i>P. falciparum</i> & <i>P. vivax</i>	
Advantage Mal Card	J. Mitra & Co. Pvt. Ltd.
AZOG Malaria pf (HRP-II)/pv (pLDH) Antigen Detection Test Device	AZOG, Inc.
CareStart Malaria HRP2/pLDH (Pf/PAN) Combo Access Bio, Inc. °	Access Bio, Inc.
First Response Malaria Ag Combo (PLDH/HRP2) °	Premier Medical Corporation Ltd.
Immunoquick Malaria +4	Biosynex
OnSight – ParaQuick (Pan, Pf) Test	Amgenix International, Inc.
Parascreen Rapid Test for Malaria Pan/Pf (Device)	Zephyr Biomedicals
SD BIOLINE Malaria Ag Pf/Pan	Standard Diagnostics, Inc.
Wondfo One Step Malaria Pf/Pan Whole Blood Test	Guangzhou Wondfo Biotech Co., Ltd
Pan only	
Advantage Pan Malaria Card	J. Mitra & Co. Pvt. Ltd.
CareStart Malaria pLDH (PAN) °	Access Bio, Inc.

* RDTs with $\geq 75\%$ detection rate of *P. falciparum* at low parasite densities for areas with low-to-moderate transmission.

° RDTs with $\geq 75\%$ detection rate of both *P. falciparum* and *P. vivax* at low parasite densities for areas where both species are prevalent.