

Malaria

Malaria rapid diagnostic tests



Malaria rapid diagnostic tests (RDTs) assist in the diagnosis of malaria by detecting evidence of malaria parasites (antigens) in human blood. RDTs permit a reliable detection of malaria infections particularly in remote areas with limited access to good quality microscopy services. This site provides information and guidance to malaria control programmes and health services, test kit manufacturers as well as organizations and individuals considering the use of RDTs.

What are RDTs

Overview

WHO recommends prompt parasite-based diagnosis in all patients suspected of malaria.

The role of RDTs in malaria control

RDTs can assist in making a rapid, accurate diagnosis.

How malaria RDTs work

Variations occur between products but the principles are similar.

Procuring and implementing RDTs

Selecting and procuring RDTs

Basic principles of good procurement can help secure reliable malaria RDTs.

Developing an RDT implementation plan

A sound implementation plan is composed of several essential elements.

Malaria RDTs in the private sector

The lack of availability of quality RDTs in the private sector remains a problem.

Training material

[Manuals and job-aids on the use of malaria RDTs](#)

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Quality assurance and control

WHO-FIND RDT malaria RDT evaluation programme including product and lot testing

Since 2002, WHO has developed and has been supporting an international programme to quality control malaria RDTs and generating data to inform RDT procurement and field deployment.

RDTs: suggested use of terms, labelling and instructions for use

Uniform, easy to follow and consistent terminology and labelling, aligned with international standards and appropriate for the level of the end user's education and training, is crucial.

Field trials

Malaria RDTs are designed for malaria endemic areas beyond the reach of good-quality microscopy. Field trials are helpful to confirm that high levels of performance observed in the laboratory are maintained in the field.

Malaria

Rapid diagnostic tests

Last update: 1 February 2019

WHO recommends prompt parasite-based diagnosis in all patients suspected of malaria before treatment is administered. Malaria rapid diagnostic tests (RDTs) have the potential to greatly improve the quality of management of malaria infections, especially in remote areas with limited access to good quality microscopy services.

RDTs are relatively simple to perform and interpret, they rapidly provide results, require limited training, and allow for the diagnosis of malaria at the community level.

Various types of RDTs on the market

Malaria RDTs detect specific antigens (proteins) produced by malaria parasites that are present in the blood of infected individuals. Some RDTs detect a single species (either *P. falciparum* or *P. vivax*), some detect multiple species (*P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*) and some further distinguish between *P. falciparum* and non-*P. falciparum* infection, or between specific species. Blood for the test is commonly obtained from a finger-prick and results are available within 15–30 minutes. Though there are variations among the more than 200 malaria RDT products on the market, the principles of the tests are similar.

Expansion in RDT use

In recent years, RDT testing has been significantly expanded around the world. Manufacturers surveyed by WHO for the *World malaria report 2018* reported a total of 276 million RDT sales in 2017. Most RDTs (66%) were supplied to sub-Saharan Africa. In 2017, an estimated 75% of malaria tests in sub-Saharan Africa were conducted using RDTs, up from 40% in 2010.

Quality assurance and performance testing of RDTs

To assist ministries of health in endemic countries, UN agencies and major procurers, WHO, the Foundation for Innovative New Diagnostics (FIND) and the Centers for Disease Control and Prevention established a pre-purchase (Product Testing) and post-purchase (Lot Testing)

evaluation scheme for RDTs in 2007. As a result of the periodic evaluations completed through this programme, the quality of RDTs has improved dramatically in recent years.

Since the beginning of 2018, the coordination of product evaluations is managed by the WHO Programme for the Prequalification of in vitro diagnostics (IVDs).

Further guidance on product selection and procurement

For procurement, WHO recommends that all RDTs be WHO prequalified. In the case, that no WHO prequalified test is available (or there is very limited choice) to meet procurement needs ie. settings with a high prevalence of *pfhrp2/3* gene deletions, all RDTs should meet the following minimum performance requirement:

- at least a 75% "panel detection score" for low parasite density samples from the product testing evaluation panel (HRP2 expressing and nonHRP2 expressing panels);
- a false positive rate of less than 10%; and
- fewer than 5% invalid tests.

Malaria

The role of RDTs in malaria control

Malaria rapid diagnostic tests (RDTs) can assist in making a rapid, accurate diagnosis in circumstances where demonstration of parasitaemia has previously been impossible or where microscopy-based diagnosis may be unreliable.

To enable effective diagnosis of all malaria cases, the diagnostic method used must be accurate and available at the point of care.

RDTs may be useful in:

- diagnosis by health workers distant from good microscopy services;
- remote diagnosis in organized workforces entering malaria-endemic areas (i.e. military or mining companies); and
- outbreak investigation and surveys of parasite prevalence.

RDTs can offer significant benefits in malaria management if:

- a clear plan of action has been prepared to deal with the outcomes (i.e. drug treatment or appropriate further investigation);
- a clear benefit is demonstrated in health outcomes;
- they are affordable; and
- there are adequate systems in place to ensure RDTs are used correctly and are in good condition.

Use of malaria RDTs in clinical management

The following issues are important for successful incorporation of RDTs into malaria control:

- Clear benefit is obtained by demonstrating the presence of parasitaemia.
- Accuracy of RDTs can be regularly monitored (quality control).
- A "cool chain" is in place for transport and storage.
- Good health worker training and monitoring is in place.
- A clear policy of action on results is in place.

These elements must be allowed for in the RDT budget.

Accuracy of results

RDTs should be sensitive enough to reliably detect malaria parasites at densities associated with disease. Sensitivity is determined by the quality of manufacture, species, number, viability and strain of parasites present, condition of the RDT

(including storage conditions), technique and care used in performing the test as well as reader's interpretation.

Sensitivity will always depend on the concentration of target antigen (protein) present and will therefore vary with parasite density. The same test may achieve a high sensitivity in a population in which all infected people have a high parasite density (e.g. above 10 000 parasites/ μ l), but achieve low sensitivity in areas where parasite densities are frequently below 200 parasites/ μ l; therefore, sensitivity stated by manufactures based on field trials can only be integrated if the parasite density of the study population is known.

Ultimately, it is important that both sensitivity and specificity remain high, so that both malaria and non-malarial fevers receive appropriate management. However sometimes it may be more important to have very high sensitivity even at the expense of high specificity, as a missed parasitaemia may lead to death of a patient.

Malaria

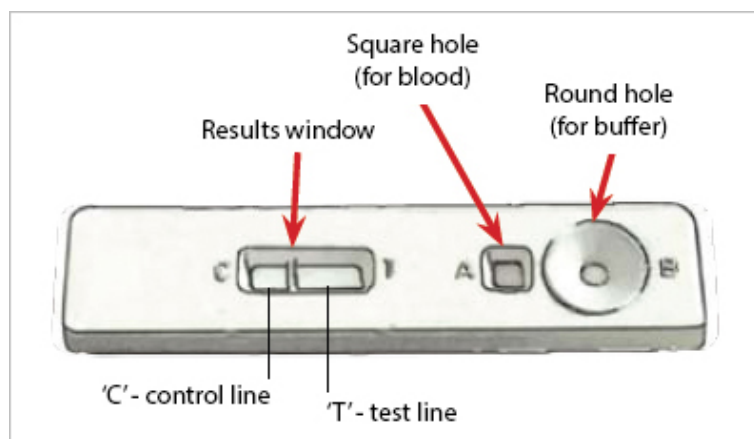
How malaria RDTs work

Malaria rapid diagnostic tests (RDTs) assist in the diagnosis of malaria by providing evidence of the presence of malaria parasites in human blood. RDTs are an alternative to diagnosis based on clinical grounds or microscopy, particularly where good quality microscopy services cannot be readily provided.

Variations occur between products, such as targets and formats, though the principles of the tests are similar. Malaria RDTs detect specific antigens (proteins) produced by malaria parasites in the blood of infected individuals. Some RDTs can detect only one species (*Plasmodium falciparum*) while others detect multiple species (*P. vivax*, *P. malariae* and *P. ovale*). Blood for the test is commonly obtained from a finger-prick.

RDTs are lateral flow immuno-chromatographic antigen-detection tests, which rely on the capture of dye-labeled antibodies to produce a visible band on a strip of nitro-cellulose, often encased in plastic housing, referred to as cassettes. With malaria RDTs, the dye-labeled antibody first binds to a parasite antigen, and the resultant complex is captured on the strip by a band of bound antibody, forming a visible line (T - test line) in the results window. A control line (C- control line) gives information on the integrity of the antibody-dye conjugate, but does not confirm the ability to detect parasite antigen.

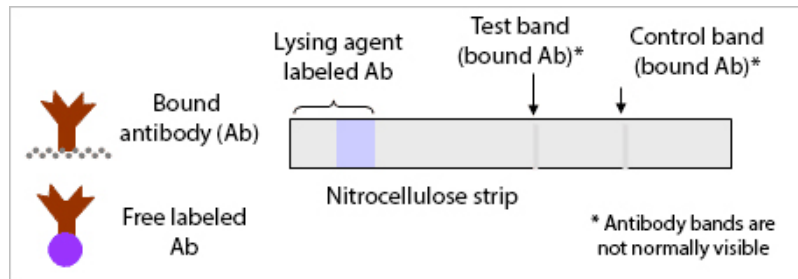
RDT cassette



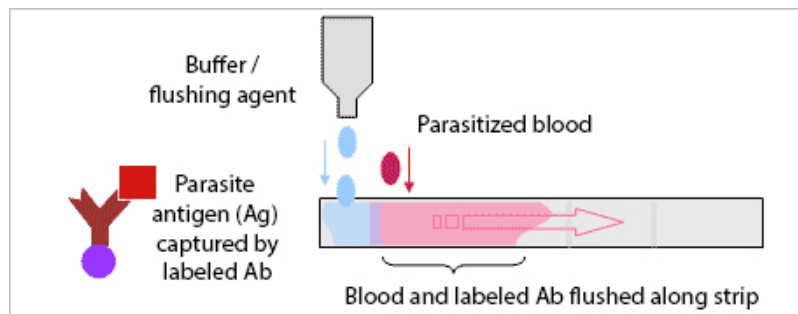
Inside the cassette is a strip made of filter paper and nitrocellulose. Typically, a drop of blood is added to the RDT through one hole (A; sample well), and then a number of drops of buffer usually through another hole (B; buffer well). Buffer carries the blood along the length of the RDT.

Mode of action of common malaria RDT format

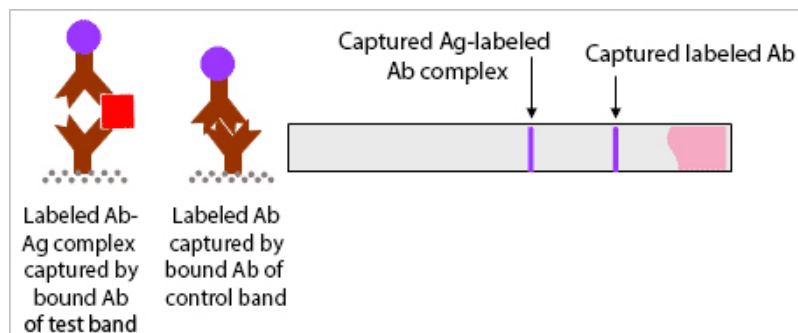
1. The first step of the test procedure involves mixing the patient's blood with a lysing agent in a test strip or well. This ruptures the red blood cells, releasing more parasite protein.



2. Dye-labeled antibody, specific for target antigen, is present on the lower end of nitrocellulose strip or in a plastic well provided with the strip. Antibody, also specific for the target antigen, is bound to the strip in a thin (test) line, and either antibody specific for the labeled antibody, or antigen, is bound at the control line.



3. Blood and buffer, which have been placed on strip or in the well, are mixed with labeled antibody and are drawn up the strip across the lines of bound antibody.



4. If antigen is present, some labeled antibody-antigen complex will be trapped and accumulate on the test line. Excess-labeled antibody is trapped and accumulates on the control line. A visible control line indicates that labeled antibody has traversed the full length of the strip, past the test line, and that at least some free antibody remains conjugated to the dye and that some of the capturing properties of the antibodies remain intact.

5. The intensity of the test band will vary with the amount of antigen present, at least at low parasite densities (antigen concentration), as this will determine the amount of dye particles which will accumulate on the line. The control band intensity may decrease at higher parasite densities, as much of the labeled antibody will have been captured by the test band before reaching the control.

Malaria

Selecting and procuring malaria RDTs

Last update: 14 July 2017

Considerations for choosing an rapid diagnostic test (RDT) product include:

- plasmodium species to be detected (*Plasmodium falciparum* only and/or non-falciparum species);
- shelf life and temperature stability in intended conditions of storage and use;
- ease of use, including format of the test (e.g. cassette, dipstick, card);
- requirement for post-treatment testing of patients;
- cost (including transport, training and quality control);
- performance in WHO Malaria RDT Product Testing (panel detection score, false positive rate and invalid rate, heat stability); and
- sensitivity and specificity.

Based on the results of the Malaria RDT Product Testing Programme, WHO recommends that selected RDTs should be in line with the following set of criteria:

- For the detection of *P. falciparum* in all transmission settings the panel detection score against *P. falciparum* samples should be at least 75% at 200 parasites/ μ L.
- For the detection of *P. vivax* in all transmission settings the panel detection score against *P. vivax* samples should be at least 75% at 200 parasites/ μ L.
- The false positive rate should be less than 10%.
- The invalid rate should be less than 5%.

By following basic principles for good procurement and product lists developed by WHO, it is possible to procure reliable malaria RDTs. However, these should be used in context of a good quality assurance system to ensure and monitor accuracy during use.

Procurement checklist

The procurement checklist below, adapted from the publication "Good practices for selecting and procuring rapid diagnostic tests for malaria", summarizes the sequence of steps in procuring quality-assured RDTs. While the steps are shown sequentially, they do not necessarily occur one after the other (some may be concurrent), and not all the steps have

to be repeated for each tender. It is most important that all the responsible bodies are well coordinated and that there is prompt, transparent information flow.

Step 1 – Requirements for selecting diagnostic tests

Select an RDT appropriate to the parasite species prevalent in the areas of use. Selection should be based on WHO and national guidelines on required performance and test characteristics for different levels of use and the results of the WHO product testing for the specific RDT.

Responsible entity: National malaria control programme

Step 2 – Estimating needs

Estimate the number of malaria cases and RDT requirements for back-up stocks at different levels of the supply chain. Estimate the order size and frequency of deliveries to maintain adequate stocks to meet requirements, avoiding stock-outs and over-stocking (with risk of unused, expired RDTs).

Responsible entity: National malaria control programme, quantification and forecasting team, laboratory department, procurement department

Step 3 – Budgeting and budget component

Consider all budget requirements to obtain quality-assured RDTs, including operating expenses (distribution, supply management, information and communication, training, supervision, quality assurance, quality control, monitoring and reporting) and not merely the cost of procuring the RDTs.

Responsible entity: National malaria control programme

Step 4 – Defining technical specifications

Provide comprehensive, detailed specifications for the selected product, so that the manufacturer receives a clear indication of all RDT requirements for the clinical user. Use all available supports, such as the FIND interactive guide, to ensure a detailed presentation of criteria that will enable selection of an RDT with appropriate diagnostic performance.

Responsible entity: National malaria control programme

Step 5 – Procurement method and tender documents

Assemble your requirements and technical, commercial and quality evaluation tender criteria documentation from the preceding steps, conforming with the administrative and financial requirements of the agency funding the procurement of RDTs (as appropriate), and publish the tender according to the procurement method selected.

Responsible entity: Procurement unit team members, with input on technical and quality aspects from national malaria control programme

Step 6 – Inviting tenders

Invite requests for proposals from manufacturers that have been independently assessed as having the competence and the capacity to meet the procurement requirements. The independent assessment should include the diagnostic performance of the product (preferably by WHO product testing); real-time temperature stability data on the product; long-term viability of manufacturer (to ensure continuity of supply); availability of product support; agreement for replacement of products which fail agreed quality control procedures; and box sizes appropriate to the rate of use of tests in the intended area to minimize storage time in poor conditions and limit the need to split boxes.

Responsible entity: Procurement management unit in consultation with regulatory authority

Step 7 – Evaluating bids and awarding contracts

Thoroughly check the specifications of the product offered against the requirements submitted in the tender documents. Then, check the supplier criteria (competence and capacity) with certification to

iso 13485:2003 (11) and documentation in the product dossier.
Contracts may be awarded to suppliers that meet the criteria, with clear indications of terms and conditions for deliveries and liability.
Responsible entity: Procurement management unit and national malaria control programme

Step 8 – Quality assurance in procurement

Ensure the quality of the procurement programme, including appropriate quality control, such as lot testing, through accredited laboratories.

Responsible entity: Procurement management unit

Step 9 – Quality control by lot testing

Lot testing is the most important aspect of quality control to ensure that the lots of RDTs delivered fully meet the agreed requirements.

Responsible entity: Procurement management unit, quality assurance officer

Step 10 – Transport, port clearance and receipt

Air or sea port clearance has many potential pitfalls and possible delays; careful planning is needed to avoid exposure of RDTs to high temperatures, with concerted preparation for handling at receipt, storage and distribution. Verification of the delivered product at receipt is recommended.

Responsible entity: Procurement management unit, supply chain manager

Step 11 – Monitoring

Supplier performance should be assessed in relation to the responsibilities in supply, which should be described in detail in the tender documents and contracts so that the relationship between the supplier and the manufacturer and their liabilities are clear.

Regular system audits and open communication channels are particularly important in this respect.

Responsible entity: Procurement management unit and national malaria control programme

Step 12 – Continuous improvement

Effective use of a comprehensive quality management system for information on deficiencies of any kind can result in steady, continuous improvement.

Responsible entity: Procurement management unit and national malaria control programme

Malaria

Developing an RDT implementation plan

Introducing RDT-based malaria diagnosis into national programmes

Most national programmes have relied heavily on clinical (symptom-based) diagnosis in the past, with microscopy used in larger clinics. As parasite-based diagnosis is introduced at smaller clinics and village level for case management, a large number of challenges arise in logistical management and in managing the health-seeking and health-providing behaviour of patients and health workers.

Changing practice

Many health workers and communities will have been taught that "fever equals malaria unless proven otherwise". Introducing rapid diagnostic tests (RDTs) will demonstrate that this is not the case. To have an impact on anti-malarial diagnosis and treatment, RDTs must be seen to provide an accurate diagnosis by both health workers and patients alike, as good or better than that relied on previously.

A health worker will also need a good alternative to anti-malarial medicines for the management of parasite-negative febrile patients. To achieve and maintain confidence in RDT-based diagnosis, a good quality assurance system must be in place (detailed elsewhere on this website and in the manual *Universal access to malaria diagnosis* published in 2011).

There must be good education of health workers, and widespread community sensitization. Knowledge of other causes of fever may be necessary to develop appropriate management algorithms for parasite-negative cases. Some examples are given below.

High-level planning and coordination

At the national level, regulatory requirements may need to be followed or developed to control the importation and use of malaria RDTs, and new procedures for storage, distribution and inventory management, such as those used for medicines, may need to be developed.

If changing from a different product or mode of diagnosis, an adequate phase-out plan for this must also be developed. This requires a clear strategic plan to be developed well in advance of RDT introduction, with a clear timeline to ensure that the various components of the RDT programme are in place at the right time.

A focal person, or persons, will be needed to coordinate the overall implementation plan and ensure that the various agencies that may be

involved understand the process and their particular roles. To achieve this, funding for the programme must include a significant component for planning and coordination, sensitization/IEC, training, quality assurance, monitoring and supervision, and logistics, in addition to procurement.

Without this, much of the funds expended on RDTs may be wasted, and a loss of confidence in RDT-based diagnosis may hinder the process of strengthening appropriate malaria case management.

Components of a national implementation plan

Programme planning and management

- Identify key stakeholders, and secure commitment for introduction of RDTs
- Establish working group and develop terms of reference
- Identify specific focal person(s) responsible for day to day oversight of the implementation plan

Develop a timeline, scope, and budget for implementation

- Identify human and other resource needs, and a strategy for accessing them
- Review and update, if needed, case-management algorithms for malaria and other causes of febrile illness

Policy and regulatory issues

- Develop appropriate regulatory documents if required
- Register RDT products

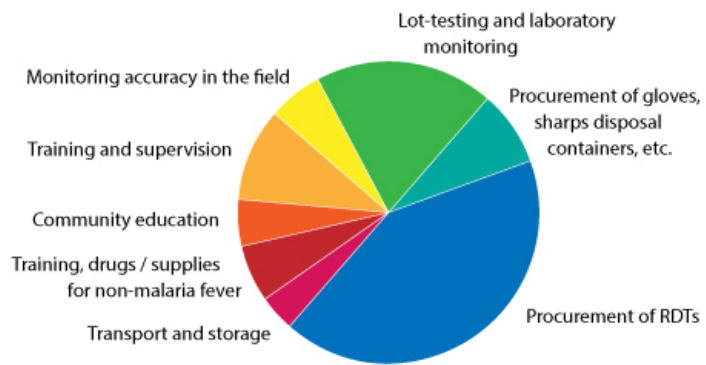
Procurement of RDTs

- Develop product specifications and packaging requirements
- Develop product short-list
- Conduct quantification (estimation of needs)
- Procure RDTs
- Procure sharps boxes, gloves etc.

Malaria RDT implementation budget

Budgeting for all the components required for introducing RDTs into a malaria programme at the outset is vital. Without adequate provision for each of these components, it is likely that an RDT-based diagnostics programme will fail to achieve its goals.

Example of components to be considered in an overall budget



Malaria

Malaria RDTs in the private sector

Last update: 14 July 2017

The availability of high-quality, inexpensive RDTs in the public sector has significantly improved and expanded diagnostic testing. However, in the private sector, where a large proportion – over 40% – of the population in endemic countries seeks care and treatment for febrile illness, RDTs are either non-existent or more expensive than artemisinin-based combination therapies (ACTs).

Success of malaria control will depend on effective diagnosis and treatment strategies in the private sector, including the introduction of malaria RDTs. These are being considered for use in a diverse private for-profit sector consisting of hospitals and clinics, local pharmacies, drug shops and itinerant drug sellers.

However, there is presently little evidence or experience to guide countries on what is required to provide locally applicable systems and regulation to scale-up malaria RDTs in private sector outlets. Furthermore, control over test sensitivity, storage and transport, and assurance that tests are working correctly, will frequently be more difficult to assess.

WHO participated in a systematic review that draws together published and unpublished studies on malaria RDT introduction in private sectors in 12 countries. WHO also collaborated with Population Services International, Malaria Consortium and the Foundation for Innovative New Diagnostics (FIND) in a 5-country project testing different approaches to stimulate the creation of a private sector market for malaria RDTs by:

- increasing both access to and demand for quality-assured RDTs,
- improving private providers' febrile case management skills, and
- developing and implementing a roadmap for public-private engagement that will guide policy and regulation.

The 3-year project was implemented in 5 target countries: Kenya, Madagascar, Nigeria, Tanzania (mainland) and Uganda and concluded in 2016. Findings will be released in peer-review literature and lessons learned summarized in a roadmap document jointly prepared by the project partners.

Malaria

WHO-FIND malaria RDT evaluation programme

Last update: 10 July 2017

In 2002, WHO began to develop quality control methods for malaria rapid diagnostic tests (RDTs) as part of a larger programme on quality assurance for the introduction of RDTs as point-of-care tests for malaria. This initiative, originally based at the WHO Regional Office for the Western Pacific and including the WHO Roll Back Malaria Department (now Global Malaria Programme) and the Special Programme for Research and Training in Tropical Diseases (TDR), arose from an initial WHO consultation on malaria RDTs held in 1999 in Geneva, Switzerland.

In 2006, the Bill & Melinda Gates Foundation signed an agreement with the Foundation for Innovative New Diagnostics (FIND) to partner with WHO and expand the evaluation programme (WHO-FIND Malaria RDT Evaluation Programme), accelerating the development of evaluation panels based on parasite samples collected and characterized by an international network of laboratories, and work commenced in 2003 on the development of synthetic (recombinant antigen) standards.

This 5-year award was extended in 2012, and has formed the core of programme funding until 2013, supplemented by funds from the Global Fund to Fight AIDS, Tuberculosis and Malaria, USAID, and in-kind support from partner institutions participating in the programme. Since January 2013, UNITAID has assumed the bulk of funding of the programme.

At this time, the programme consists of:

- a centralized product testing programme (WHO Product Testing), conducted at the US Centers for Disease Control and Prevention,
- a WHO-FIND lot-testing programme, based at the Research Institute for Tropical Medicine (RITM) in the Philippines and the Pasteur Institute of Cambodia (IPC),
- antigen quantitation to ensure consistency of panels, performed at the Hospital for Tropical Disease in London, United Kingdom, with other institutions (see map below) contributing parasite samples,
- job-aids and training materials appropriate for village-based health workers and trainers of village-based health workers.

Positive control wells, designed to allow village-level health workers to test RDTs in operational use in the field, are under development and

prototypes have been field tested in Uganda and the Lao People's Democratic Republic.

Steering Group

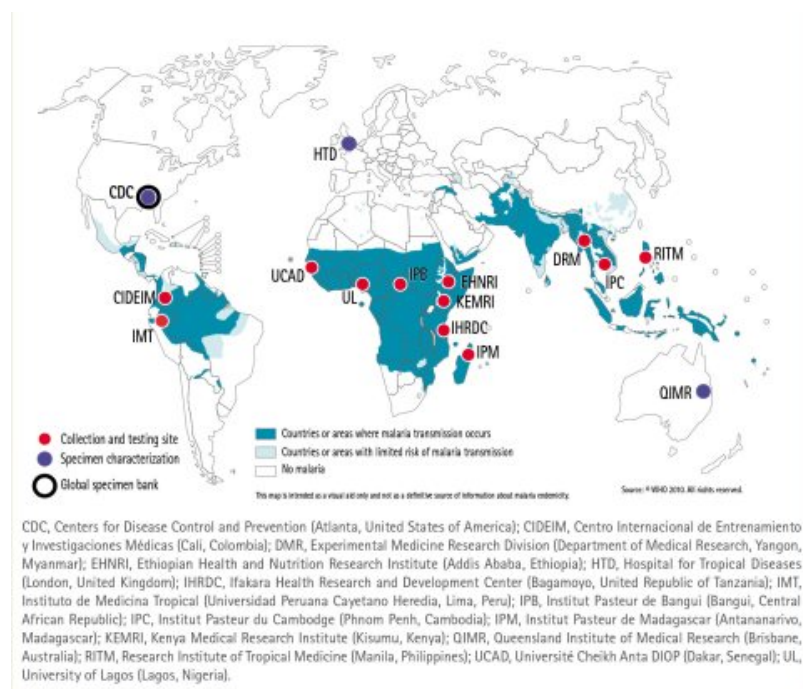
The technical and logistical aspects of the evaluation programme are overseen by a Steering Committee, functioning by teleconference and face-to-face meetings at least once per year. The Steering Committee provides recommendations to WHO on:

- development and modifications of standard operating procedures (SOPs) for specimen collection and use,
- replenishment, content, characterization and maintenance of the specimen bank,
- policy on access to the specimen bank,
- protocols for laboratory-based testing of the accuracy and stability of malaria RDTs (product testing and lot testing),
- review and approval of results of product testing prior to publication,
- transition from cryopreserved wild-type parasites to malaria recombinant antigen-based evaluation programmes and positive control wells.

Steering Group membership

- WHO/GMP (2)
- FIND (2)
- Specimen Bank(s): CDC (1)
- Collection sites (rotating): African (1), Non-African (1)
- Medicines Sans Frontières (1)
- Hospital for Tropical Disease (UK) (1)
- Army Malaria Institute (Australia) (1)

International laboratory network supporting the WHO-FIND malaria rDT evaluation programme



Malaria

The need for quality assurance

Last update: 14 April 2016

There is a need for an accurate, transparent system for monitoring the accuracy of RDTs after release by the manufacturer. The development of a comprehensive quality assurance scheme is essential to ensure that test quality is maintained, reducing the likelihood of misdiagnosis and maintaining confidence of health service providers and consumers.

Malaria RDTs are affected by various conditions of manufacture, storage and use that can impair their accuracy and reliability. WHO's T3: Test. Treat. Track initiative urges countries to scale up RDTs to universal access to aid in the management of malaria, especially in locations where laboratory-based diagnosis is unavailable. This requires a system in place to assure that service quality is guaranteed. Quality assurance (QA) should be an integral part of RDT budgets and implementation plans in the same way that it forms an important part of a microscopy-based programme.

What is a quality assurance process for malaria RDTs?

Quality assurance is defined as a total process, both in and outside the laboratory, including performance standards, good laboratory practice and management skills to achieve and maintain a quality service and provide for continuing improvement. The purpose of quality assurance is to provide reliable, relevant, timely test results that are interpreted correctly thereby increasing efficiency, effectiveness, enhancing patient satisfaction and decreasing costs brought about by misdiagnosis. This is increasingly important with the advent of combination therapies and their higher associated costs.

A quality assurance process for malaria RDTs should aim to ensure high accuracy of tests in the hands of end-users. This will include both monitoring of the technical standard of the RDTs, processes to minimize environmental insult and training and monitoring of preparation and interpretation by end-users.

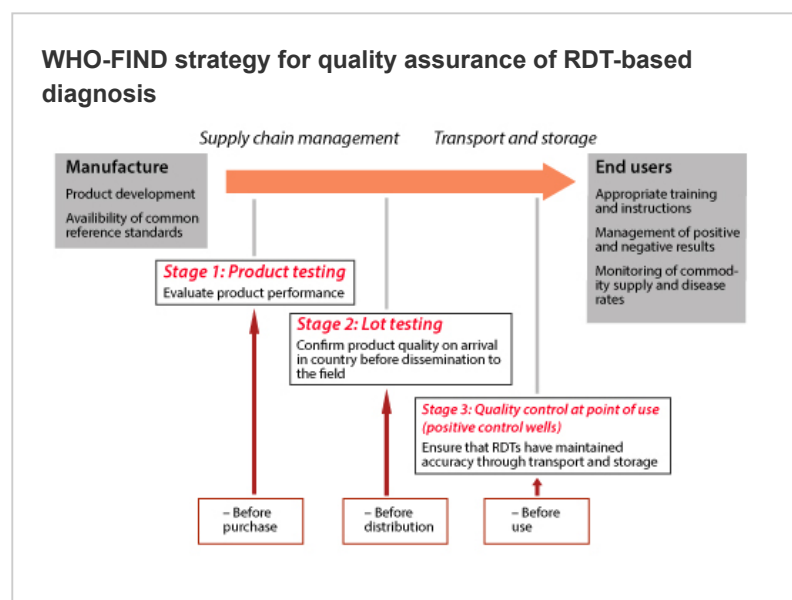
Quality control (QC) describes all the activities taken by a laboratory to monitor each stage of a test procedure to ensure that tests are performed correctly and are accurate and precise.

WHO-FIND international quality assurance scheme for malaria RDTs

Due to weak regulation in many endemic countries and the lack of easily accessible reference materials for quality controlling malaria RDTs, an international quality assurance scheme coordinated by WHO and the Foundation for Innovative New Diagnostics (FIND) was operationalized in 2008. This scheme required that manufacturers provide evidence of good quality management system (ISO 13485:2003) and offers comparative performance, thermal stability and ease of use data on RDTs (WHO product testing), to inform procurement.

The same reference materials are used to do pre-deployment quality testing (lot testing) at two WHO-FIND recognized lot testing facilities (Research Institution for Tropical Diseases in the Philippines; Institut Pasteur in Cambodia).

FIND is developing positive control wells that will facilitate clinic and end-user level quality control. Good training and regular supervision are essential for an effective programme and should be integrated as far as possible into existing health worker training and quality assurance schemes. WHO and partners have developed generic job-aids and a training manual for health workers, based on trials in Asia and Africa with several partners. These materials are available in English and French, and can be adapted to other languages and are found here.



Instructions for RDT preparation and interpretation should be clear and concise in local languages. Health workers using the tests should be trained and assessed, and systematically monitored on test preparation and interpretation. As RDTs must be read soon after preparation, this should be done on real cases rather than by review of previously prepared tests. The entire quality chain must be underpinned by appropriate handling/transport and storage practices. Responsibility for overseeing quality assurance processes should be clearly defined and coordinated from a central level.

Malaria

Lot testing

29 November 2017

Lot testing of malaria RDTs involves testing of samples of RDTs for a manufacturing lot to ensure performance reaches an acceptable standard. This can be done before or after arrival in the country.

Why is lot testing needed?

- Allows for performance assessment against highly characterized specimens that may not be available in-country, to control for lot variation, noted in most products.
- Ensures no damage during transport to country.
- Provides information on RDT stability over the shelf life, reflecting how RDTs can be expected to function under similar storage conditions in the field.
- Provides information on anomalies identified during testing that may signal a problem with a lot.
- Gives confidence to clinicians / users / regulatory authorities that the tests they are using have adequate performance for clinical use.

Producing and storing quality control dilutions of parasites obtained from field samples

Testing malaria RDTs in a laboratory setting against stored samples allows greater consistency and control of testing methods, and greater control over the parasite densities used as standards, but has the disadvantage that stored blood and parasites may react differently than fresh parasitized blood on an RDT. To guide this process, a methods manual has been produced and is updated serially.

Lot testing is readily accessible

Lot-testing capacity has been developed through a joint programme of the WHO and the Foundation for Innovative New Diagnostics (FIND). It is currently performed at lot-testing centres in the Western Pacific Region, specifically the Research Institute for Tropical Medicine (RITM, Manila) which can test for programmes globally and at the National Institute of Malaria Research, New Delhi, India and the University of Lagos, Nigeria which can test products entering their respective countries.

**Upcoming changes to the WHO-FIND Lot testing Programme
Q4 2017**

In December 2017, WHO will be implementing changes to the organization of lot testing procedures for malaria RDTs. A description of these changes is provided in an information note. Related webpages have also been updated. After 5 December, requests should be made through an email request to Malaria_rdt@who.int

Malaria

Positive control wells

Last updated: 14 April 2016

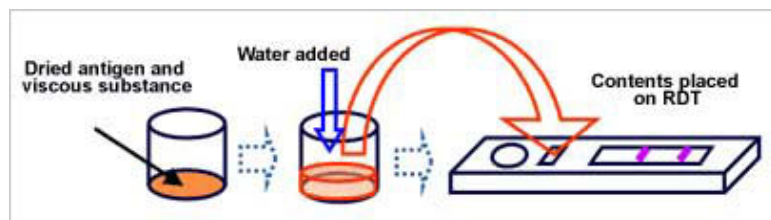
At present, users have no field-adapted method of ensuring that rapid diagnostic tests (RDTs) are still functioning properly after exposure to variable transport and storage conditions. The Foundation for Innovative New Diagnostics (FIND) and a commercial partner are developing well-calibrated positive control wells containing recombinant malaria antigens (the main targets of malaria RDTs) and designed to allow testing of malaria RDTs at clinic or village levels.

These positive control wells will enable rapid direct evaluation of RDTs performance in remote locations without the need for cross-checking against expert microscopy. Such testing has the potential to increase the confidence of health providers in the quality of RDTs after transport to remote areas or prolonged storage, allowing them to confidently manage symptoms according to the RDT result. WHO is exploring the potential role of positive control wells and different options for implementation.

Current positive control well prototype

Various prototypes of positive control wells have been developed based on inputs from health workers in endemic countries. The current prototype is a small conical shaped plastic well coated with dried recombinant proteins. Preparation of the positive control wells involves the addition of a fixed volume of water, mixing and then transfer to the sample well of the RDT. The recombinant antigen solution mimics infected blood and produces a positive test band on the RDT, indicating that the RDT batch is safe for use. PCWs can be used by health workers to ensure the validity of RDT stocks at their health facilities.

Diagram illustrating how a positive control well works



For more information regarding the research and development process for positive control wells please visit the FIND website.

Field evaluation of positive control wells

WHO has provided technical support to FIND and their collaborators at Lao Oxford Mahosot Wellcome Trust Research Unit (LOMWRU) and Malaria Consortium who have recently completed field studies in 2014 evaluating the use, utility and acceptability of positive control wells for malaria RDTs in routine health care settings in order to guide rational implementation strategies for positive control wells.

For more information regarding these studies, and the development of related training materials, please visit the FIND website.

Malaria

Lot testing: Pre and post-purchase

Last update: 29 November 2017

WHO RDT evaluation programme

WHO and other major procurement agencies recommend that all lots (batches) of rapid diagnostic tests (RDTs) be tested before deployment to the field. A 'lot' to be tested is normally defined as a production run using a particular batch of monoclonal antibodies and nitrocellulose. They are normally defined by number in this way by the manufacturer, and may vary greatly in size from 10 000 to 1 000 000 tests. Lot testing can be done:

1. before purchase, directly arranged with the manufacturer and a lot-testing centre,
2. after purchase, before distribution to the field.

Who can request lot testing?

Any national programme or organization procuring malaria RDTs may request lot testing from this programme. Lot testing is performed free of charge when arranged through the WHO RDT lot-testing programme. The requesting institution must cover transport costs for the RDTs and provide the required number of RDTs.

How to request lot testing?

At least 2 weeks before you are ready to send the RDTs, please contact the lot testing coordinator: malaria_rdt@who.int and attach a completed lot testing request form.

How is lot testing performed?

1. Documentation and shipping

Following receipt of your request, you will be provided with details regarding the volume of RDTs required for lot testing, shipping instructions, etc. These must be followed carefully to ensure that the shipment is not held at customs.

The proper forms must be filled in accurately by the requesting institution. Failure to do so may result in shipment delays. Once the invoice is checked by the lot testing coordinator, and provided everything is in order, the goods can then be dispatched.

2. RDT sampling

It is recommended that all purchased lots be tested. The number of tests required depends on the type of RDT (i.e., a combination or a *P. falciparum* only test) and the expiry date of the product. Usually, a sample of approximately 100 *P. falciparum*-only RDTs, or 150 combined *P. falciparum* and pan-specific (or *P. vivax*-specific) RDTs is required from each lot.

3. Test evaluation

RDT lots are tested in lot-testing laboratories that have undergone quality assessment and been approved by the WHO RDT Lot Testing Programme.

An initial assessment is performed on a sample of the RDTs using panels of parasite-positive and parasite-negative blood. These panels are prepared according to the same standard operating procedures as the panels for the global malaria specimen bank. The remaining RDTs are then stored in controlled conditions at one of two temperatures (depending on the manufacturer's recommended maximum storage temperature) and re-tested 6 months prior to expiry.

Any revisions to procedures will be posted on this website and will be incorporated into subsequent versions of the *Methods manual for laboratory control testing of malaria rapid diagnostic tests*.

Interpretation of results

PASS

This means that the RDT sample detected antigens at a threshold sufficient for use in the field. The RDT lot passed the quality control assessment.

DEFERRED

This means that the RDT lot failed the initial quality control assessment and has been sent to another institution for confirmation. A final report will be issued upon receipt of confirmatory results. It is recommended that the lot be retained until a final report is received.

FAIL

This means that the RDT lot failed the initial quality control assessment and also failed confirmatory testing at another lot-testing centre. It is recommended that this lot should not be used in the field since it lacks sufficient sensitivity, and that the manufacturer be contacted and advised of the results.

4. Results

Initial results are usually returned within 5 working days of RDT receipt at the lot-testing laboratory.

A *malaria RDT lot testing quality control report form* is generated and emailed confidentially to the requesting institution. This is accompanied

by a guide for the interpretation of observations noted during lot testing. A report with the results of re-testing during shelf-life is also sent to the requester.

RDTs must detect parasite-positive panels at 200 parasites per microlitre of blood in order to pass the quality control evaluation. False positive results obtained with parasite-negative samples, as well as any unusual observations, such as poor blood clearing or incomplete test lines, are also noted. *Illustration of the comments* encountered during testing and photos of the testing are provided with the report when the testing workload allows it.

The lot testing reports and photos of the testing results cannot be released to any third party without the agreement of the requesting party. In all cases it is the requesting party that can make the report available, and not the lot testing programme. Summarized product-specific lot testing results are released every 6 months.

The programme is not responsible for final decisions to accept or reject an RDT lot by a procurement agent or malaria programme. This decision is to be taken by the requester of the lot testing. The lot testing programme aims to provide data on which this decision can be based.

Lot-testing results (2007-2017)

Biannually, lot testing results are compiled and reported on a product-specific basis. This includes results of initial and interval testing (following incubation and 6 months prior to expiry). Interval testing results are particularly useful in verifying that product performance is being maintained over the entire product shelf-life.

Malaria

WHO malaria specimen bank

Last updated: 15 November 2017

Accessible and accurate diagnosis is central to WHO's T3: Test. Treat. Track. initiative. In parallel with efforts to scale-up diagnostic testing through microscopy and rapid diagnostic tests (RDTs), WHO, in collaboration with the Foundation for Innovative New Diagnostics (FIND) and the US Centers for Disease Control and Prevention (CDC), aims to stimulate and facilitate the development and testing of new and/or improved products, to promote product comparisons (limiting the need of field trials) and to facilitate quality control of RDTs.

Well-characterized, reference materials are required to support these activities. To this end, the WHO Malaria Specimen Bank was established in 2008 and includes specimens from the following groups:

1. humans infected by malaria,
2. humans without malaria but with other specific characteristics that may influence malaria diagnostic test results,
3. human parasite-negative blood (e.g. expired banked blood),
4. culture-derived *P. falciparum* parasites,
5. recombinant or purified malaria antigens.

The clinical blood specimens have been collected from sites in various geographical locations and shipped to the CDC, which is responsible for the receipt, registration, characterization, preparation, storage, management and/or distribution of the materials.

The Malaria Specimen Bank first priority is to assist FIND and WHO in the evaluation of existing or emerging technologies. Specimens from humans infected by malaria or with conditions that may influence malaria diagnostic test results have been supporting Malaria RDT Product Testing and Lot-Testing Programmes since 2008. Due to the large demands of both of these programmes, specimens available for release to third parties are restricted to a set panel composed of cultured *P. falciparum* parasites. The panel is replenished as needed.

Characteristics of the panel of specimens available to third parties

Manufacturers panel	Antigen type and concentration			Origin
<i>P. falciparum</i> (Pf) culture lines: name of Pf strains	HRP2 (ng/mL)	pLDH (ng/mL)	Aldolase (ng/mL)	
US07F Benin I 200	14.77	29.54	2.15	Benin
US07F Benin I 2000	140.95	247.5	18.94	Benin
US10F Nigeria XII 200	10.33	12.48	1.48	Nigeria
US10F Nigeria XII 2000	107.54	129.71	11.65	Nigeria
US06F Santa Lucia 200	4.78	6.73	0.42	El Salvador, Cen. Amer.
US06F Santa Lucia 2000	59.81	66.84	4.62	El Salvador, Cen. Amer.
US07F PH1 200	2.84	10.17	0.47	Philippines
US07F PH1 2000	35.04	98.24	6.83	Philippines
US06F FC27/A3 200	12.99	15.39	1.58	Papua New Guinea
US06F FC27/A3 2000	143.04	153.47	13.95	Papua New Guinea

Note : samples characterized by microscopy, molecular species diagnosis,, and quantitative antigen ELISA.

Who can request specimens?

Scientists, test developers and/or manufacturers working towards the development or improvement of malaria diagnostics suitable for low-income settings.

Who approves the requests?

Requests for the standard panel of cultured *P. falciparum* parasites from manufacturers with a commercialized diagnostic product, enrolled or not enrolled in the WHO-FIND Malaria RDT Evaluation Programme are immediately reviewed and recommended for approval, rejection or deferral by the WHO responsible officer. In most cases, requestors granted approval are limited to one panel of samples per year.

All other requests are reviewed by the WHO-FIND Malaria RDT Evaluation Programme Steering Committee who will recommend approval, rejection or deferral, while final decision will be made by WHO.

What does it cost?

For approved requests, the requesters pay the shipping cost and any other associated fees.

How to request specimens?

Requests should be made using the Materials request form and material transfer agreement.

[Material request form and material transfer agreement](#)
pdf, 181kb

Further information

For additional information, please contact cunninghamj@who.int and c.c. malaria_RDT@who.int.

Material Request Form

WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

WHO Malaria Specimen bank

For administrative use

MATERIAL REQUEST FORM & MATERIAL TRANSFER AGREEMENT

WHO
Malaria Specimen Bank

Mail the completed original forms to:

Jane Cunningham

Technical Officer

WHO/HTM/GMP

20 Appia Avenue

Geneve-27, Switzerland 1211

Phone: +41 22 791 2230

Email: cunninghamj@who.int

To expedite review, send a scanned copy (pdf) of the original completed forms to: cunninghamj@who.int

A. Applicant¹ Information

Legal Entity Name

Principal Investigator

First Name

M. I.

Last Name

Telephone

Fax

E-mail

ext.

B. Collaborator(s)² - if multiple, attach separately

Legal Entity:

Principal Investigator or other Focal Point:

First Name

M. I.

Last Name

Telephone

Fax

E-mail

ext.

Department

Building

C. Product Information (if applicable)

Company name	Product name	Species targeted	Target	Format ¹ Dipstick: Cassette: Card:	Packaging (Individual or bulk).	Number of tests per box	Required material not included with test kit.
	A						
	B						
	C						
	D						
	E						
	F						
	G						
	H						

¹ Applicant must be from the receiving laboratory or institution housing the receiving laboratory

² Any third party, collaborating (financially, technically or otherwise) with the Applicant on the proposed project. By completing this Form, the Applicant confirms that any agreements which Applicant may have concluded with any such third party are consistent with, and will not in any way prejudice, Applicant's obligations under this Form (if WHO approves the release of the requested materials to the Applicant).

D. Shipping Information

N.B: **All shipment costs are paid by the applicant.** The requesting party will be responsible for arranging the courier services, and ensuring the courier liaise with the WHO Malaria Specimen Bank Repository, the United States Center for Disease Control (CDC).³ The distribution of specimens to applicants must be performed under UN guidelines for shipping infectious material, Category B.

Organization Name

Department

Street Address (P.O. Boxes are not acceptable)

City

State/Province

Other

Zip/Postal Code

Country

Telephone

Fax

E-mail

ext.

E. Manufacturer's Panel

At this time only cultured *P. falciparum* parasites are available as a set 'manufacturers' panel. 10 aliquots (50µl) are provided with each culture line and concentration (200 parasites/µl and 2000 parasites/ µL).

The panel is provided free of charge⁴.

³ Research & Development Laboratories Unit, Malaria Branch: Jeffrey Glenn - khi2@cdc.gov

⁴ This may change in the future depending on the demand and availability of public funding.

Description of panel for release

MANUFACTURERS PANEL	Antigen type and concentration			Origin
	<i>HRP2</i> (ng/mL)	<i>pLDH</i> (ng/mL)	<i>Aldolase</i> (ng/mL)	
<i>P. falciparum</i> (Pf) culture lines: name of Pf strains				
US07F Benin I 200	14.77	29.54	2.15	Benin
US07F Benin I 2000	140.95	247.50	18.94	Benin
US10F Nigeria XII 200	10.33	12.48	1.48	Nigeria
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US06F Santa Lucia 2000	59.81	66.84	4.62	El Salvador, Cen. Amer.
US07F PH1 200	2.84	10.17	0.47	Philippines
US07F PH1 2000	35.04	98.24	6.83	Philippines
US06F FC27/A3 200	12.99	15.39	1.58	Papua New Guinea
US06F FC27/A3 2000	143.04	153.47	13.95	Papua New Guinea

Note : samples characterized by microscopy, molecular species diagnosis,, and quantitative antigen ELISA.

F. Scope of Use

Panels of specimens from the WHO Malaria Specimen Bank are intended only for use in research, product development, testing, quality assurance and/or evaluation of new malaria diagnostics, which are appropriate for use and affordable in developing countries.

In the space below (and on an additional sheet, if necessary), describe the Research and/or Diagnostic Development and/or Diagnostic Evaluation and/or Laboratory Quality Management activities for which you are requesting malaria specimens. What are the expected outcomes and impact of this work. If applicable, please reference any previously published articles or abstracts with information concerning the diagnostic assay being developed and/or evaluated. **For commercialized products please attach a product/package insert to this application.**

G. GENERAL TERMS AND CONDITIONS

The specimens/panels described in Section E above (hereinafter referred to as "the Material") and any information relating thereto (hereinafter referred to as "the Information") are provided on the following conditions.

Scope of Use

1. The entity requesting and receiving the Material and Information (the "Recipient") will use the Material and Information exclusively for the purpose of the Research and/or Diagnostic Development and/or Diagnostic Evaluation and/or Laboratory Quality Management of Malaria diagnostics, described under Section F above. On completion of the aforesaid Research and/or Diagnostic Development and/or Diagnostic Evaluation and/or Laboratory Quality Management of Malaria diagnostics, the Recipient will cease to use and destroy any remaining quantities of the Material, Replicates and Derivatives, and any and all copies of the Information unless WHO advises the Recipient otherwise in writing. The authenticity of the Material is restricted to storage at -80°C for 2 year.
2. The Material and Information are supplied by WHO to the Recipient solely for the use and subject to the restrictions on use as set out in this document. The Recipient shall not distribute, sell, offer for sale or otherwise transfer the Material and/or Information without the prior written authorization of WHO.
3. Unless agreed to in this Material Request Form and Material Transfer Agreement, the Recipient will not permit the Material and/or Information, or any part or modifications thereof, to come into the possession or control of any other entity or person, except those who are engaged in the above-mentioned Research and/or Diagnostic Development and/or Diagnostic Evaluation and/or Laboratory Quality Management of Malaria diagnostics at the facility and under the supervision, of the Recipient and who have accepted the same obligations of confidentiality and restrictions on use in respect of the Material and Information as set forth in this document.
4. Recipient agrees that WHO has no control over the use that is made of the Material and Information by the Recipient, or parties collaborating with Recipient. Consequently, Recipient agrees that WHO shall not be liable for such use.

Ownership of the Material and Intellectual Property

5. All rights and title in the Material and Information is, and will remain, solely and exclusively vested in WHO. Other than explicitly provided herein, this Material Request Form and Material Transfer Agreement will not be construed as conveying to the Recipient any rights or title to the Material and/or Information.
6. **Inventions and Patents made by Recipient through the use of Material.** Recipient is free to file patent application(s) claiming inventions made by Recipient through the use of Material. In order to avoid prejudice to proprietary rights of WHO or parties collaborating with WHO, the Recipient shall provide WHO with a copy of intended patent applications and other related disclosures for review in accordance with paragraph 9 below, prior to their submission or presentation to any patent office or other third party. Recipient will retain ownership of any such inventions and corresponding patents or patent applications. Recipient agrees to acknowledge WHO, the WHO Malaria Specimen Bank and any contributors thereto (as indicated by WHO) in all patent applications that reference the Material.

7. **Commercial Purposes.** Without the prior written authorization by WHO (which WHO shall be free to grant or refuse, in its sole discretion), Recipient shall not make or allow others to make any commercial use of the Material. "Commercial use" as aforesaid means any large scale manufacture and for-profit or not-for-profit distribution other than for research purposes. In addition, Recipient agrees to ensure that any commercial use of the results obtained through use of the Material shall be designed to achieve that any resulting product shall be made widely available to the public, including to the public sector of developing countries on reasonable terms.
8. **Publications** Recipient may publish or otherwise publicly disclose the results of the work with the Material. Prior to publication or presentation of any results using the Material, the Recipient will provide WHO with a copy of such intended publication or presentation for the purposes of ensuring that it contains no disclosure of proprietary Information. Any objection to publication or presentation for the aforesaid reason will be notified by WHO to the Recipient within a period of sixty days of receipt of the draft copy. In the absence of such an objection within that sixty-day period, the publication or presentation may proceed. Recipient agrees to provide WHO with 5 free copies of any such publications or presentations.
9. All such intended publications and presentations of the results using the Materials will contain an acknowledgement of WHO, the WHO Malaria Specimen Bank and any contributors thereto as indicated by WHO and include a reference to the WHO *Plasmodium falciparum* ID numbers. The Recipient agrees to consult WHO with regard to giving appropriate acknowledgement as aforesaid, before such publication is published or presentation is made.

Confidentiality Obligations of WHO

11. Any information provided by the Recipient to WHO under, or in connection with, the Material Request Form, will - if marked 'confidential' - be treated by WHO as confidential and proprietary to the Recipient, for a period of five years after the disclosure of such information to WHO. In this connection, WHO will only use and disclose such information for the purpose of evaluating such information and determining (in WHO's sole discretion) the merit of releasing Material for Research and/or Diagnostic Development and/or Diagnostic Evaluation and/or Laboratory Quality Management of Malaria diagnostics - activities by the Recipient.

However, there will be no obligations of confidentiality and restrictions on use, to the extent that WHO is clearly able to demonstrate that the aforementioned information or any part thereof:

- I. was known to WHO prior to their disclosure by the Recipient hereunder; or
- II. has been independently devised, or arrived at, by or for WHO without access to the disclosure made by the Recipient hereunder; or
- III. was in the public domain at the time of disclosure hereunder, or becomes part of the public domain through no fault of WHO; or
- IV. becomes available to WHO from a third party, who is not in breach of any obligations of confidentiality owed to the Recipient.

Safety; compliance with laws

12. The Recipient will ensure that the Material will at all times be stored, used and handled (including any possible disposal and transportation) in compliance with all relevant laws, rules and regulations (foreign and domestic) applicable to the use of infectious substances and other biological materials. Recipient will take all appropriate safety and handling precautions to minimize health or environmental risk.

Shipping

13. The Material will be packaged and shipped in accordance with all applicable laws and regulations, including (but not limited to) the UN guidelines for shipping infectious material, Category B "Diagnostic specimens" UN3373. The Material will be shipped Free On Board (FOB) point of shipment, via carrier of the Recipients choice. Recipient agrees to inform the Repository of plans to schedule a shipment and WHO electronically of the date of receipt and any loss or damage to the Material within three (3) working days of receiving the Material.
14. The Recipient is responsible for ensuring that all permits required for the Recipient to receive the Material, are obtained.

Insurance

15. The Recipient agrees to obtain and maintain liability insurance in an adequate amount to cover third party claims (including by WHO) for death or bodily injury, or loss or damage to property, arising from or in connection with: (i) the possession, use, storage and/or disposal of the Material and/or Information, and/or (ii) Recipient's activities under this Agreement.

The Recipient furthermore agrees to obtain and maintain adequate workers' compensation or equivalent insurance for its staff to cover claims arising from or in connection with: (i) the possession, use, storage and/or disposal of the Material and/or Information, and/or (ii) Recipient's activities under this Agreement.

Indemnification

16. The Recipient agrees to assume full responsibility for, and to hold harmless WHO, the Repository and other contributors to the Repository from any and all claims, costs, expenses and liabilities resulting from, or otherwise related to: (i) the possession, use, storage and/or disposal of the Material and/or Information; and/or (ii) Recipient's activities under this agreement.

Limitation of liability

17. WHO and persons and entities collaborating with WHO make no warranty of merchantability or fitness of the Material or Information for any particular purpose, or any other warranty, either express or implied (including but not limited to any warranty that the use of the Material and/or Information does not infringe on the intellectual property or other proprietary rights of others).
18. WHO, the Repository and other contributors to the Repository disclaim any and all responsibility and liability for any damages of any kind in connection with or arising out of the Material (whether in contract, tort, negligence, strict liability, statute or otherwise)

Termination

20. On completion of the Research and/or Diagnostic Development and/or Diagnostic Evaluation and/or Laboratory Quality Management of Malaria diagnostics using the Material and Information, or on expiration or earlier termination of this Agreement, the Recipient will cease to use any remaining quantities of the Material and Information for any purpose. Recipient understands that WHO may terminate this Agreement at any time with written notice to Recipient.

Miscellaneous

21. Any dispute relating to the interpretation of application of this Material Request Form and Material Transfer Agreement will, unless amicably settled, be subject to conciliation. In the event of failure of the latter, the dispute will be settled by arbitration. The arbitration will be conducted in accordance with the modalities to be agreed upon by the parties or, in the absence of agreement, with the rules of arbitration of the International Chamber of Commerce. The parties will accept the

arbitral award as final. The arbitration shall take place in Geneva, Switzerland, unless the Parties agree otherwise.

22. Nothing in or relating to this Material Request Form and Material Transfer Agreement shall be construed as an obligation on the part of WHO to submit to any national legislation or jurisdiction, and/or as a waiver of any of the privileges and immunities enjoyed by WHO under any national or international law, convention or agreement.

23. This Material Request Form and Material Transfer Agreement sets forth the entire understanding between the parties and supersedes any prior agreements, written or verbal. It shall only be capable of change by written amendment executed by duly authorized officers of the parties.

Signed for and on behalf of WHO

Signed for and on behalf of Recipient

Name:

Title:

Global Malaria Programme

Date:

Principal Investigator

Name:

Title:

Date:

Responsible Administrative Authority

Name:

Title:

Date:

INTERNAL USE ONLY

For Level II requests:

Approved by WHO/GMP Responsible Officer:

1. Standard Manufacturer's Panel

Yes ☐ No ☐ (complete 1.1)

1.1 Modifications to Standard manufacturers panel

Sample ID	Volume of each aliquot	Number of aliquots

Signature:

Name:

Title:

Date:

For Level I and III Requests:

Approved by WHO Malaria Specimen Bank Steering Committee

1. Standard Manufacturer's Panel

Yes ☐ No ☐ (complete 1.1)

1.1 Modifications to Standard manufacturers panel

Sample ID	Volume of each aliquot	Number of aliquots

Signature:
Name:
Title:
Date:

Comments:

Malaria

RDTs field trials

Malaria rapid diagnostic tests (RDTs) are designed predominantly for use in malaria endemic areas beyond the reach of good-quality microscopy. The ultimate test of their performance is therefore accuracy attained in such an environment, after enduring probable conditions of transport and storage, in the hands of the intended end-users, in high-quality field trials.

Performance in such conditions may be affected by the quality of manufacture and packaging, exposure to high temperatures, preparation and interpretation by the end-user, and characteristics of the host population and parasites in the area where they are used.

Requirements and limitations of field trials

Field trials are useful in confirming that high levels of performance observed in the laboratory is maintained in the field, and in investigating certain aspects of RDT use such as ease of use and safety, or outcomes in populations with specific characteristics, such as pregnant women. Good field trials are relatively expensive to implement and are unsuited to comparison of many RDTs in parallel and variation within the study population makes testing in series inappropriate.

Field trials of malaria RDTs are further limited by the requirement for a reference standard that is clearly better performing than the expected performance of the RDT under evaluation. This is difficult to achieve with light microscopy, as RDTs may potentially out-perform microscopy in some aspects of parasite detection. The use of more sensitive methods, but less widely available methods such as polymerase chain reaction (PCR) is usually necessary to obtain reliable estimates of sensitivity and specificity.

Good design, conduct and reporting of diagnostic evaluations

In order to allow comparison of results between various field trials, it is essential that field trials of malaria RDTs are planned, performed and documented meticulously according to the standards necessary for comparative trials of any diagnostic method. Without strict adherence to standardized protocols and clear documentation of conditions and standards used, it is difficult or impossible to draw firm conclusions from results.

Well planned, performed, and documented trials can be of major benefit to public health. The basic procedures for designing and conducting diagnostic evaluations are provided in the document *Methods for field trials of malaria rapid diagnostic tests* and guidance on reporting of

results of diagnostic evaluations have been developed by the STAndards for the Reporting of Diagnostic accuracy studies (STARD) initiative.

Last updated: 6 March 2015