Positive control wells for quality assurance of malaria RDTs at point of use

Background on rapid diagnostic tests for malaria

Since 2010, the World Health Organization (WHO) recommended confirmation of malaria by microscopy or rapid diagnostic test (RDT) for all patients suspected of having malaria, before starting treatment with an antimalarial medicine.

The new recommendation has resulted in changes in national treatment policies and the end of presumptive treatment for malaria in many affected countries. It has also marked the start of mass campaigns to equip health workers with malaria RDTs *(see image at right)*.

Today, RDTs are used to diagnose malaria in most endemic countries worldwide, and the sales of RDTs have gone from an estimated 46 million in 2008 to 314 million in 2014.

Using a malaria RDT to test for the disease

Quality assurance of malaria RDTs: lot testing & product testing

Quality assurance of the malaria RDTs used in the public and private sectors is very important to ensure the accuracy of diagnosis for this potentially fatal disease.

In recent years, the packaging of RDTs has become increasingly user-friendly, with single packs now available with their own buffers and easy-to-read line markers showing the parasite species instead of numbers. These changes have helped to avoid misdiagnosis due to human error.

In addition, RDT product and lot quality are evaluated through quality assurance programmes run by WHO, FIND and other partners to ensure that health ministries, NGOs and other implementers are using high-quality RDTs for malaria diagnosis.

While programmes are now in place to control for product quality before procurement (product testing), and for the quality of manufactured RDT lots before distribution (lot testing), a third level of quality control is needed at the level of RDT use. Until now, there has been no method for users to ensure that RDTs are still functioning properly after poor transport or storage conditions, or when a box of RDTs is approaching its expiry date, for example. The control or “C” line that appears on an RDT confirms the presence of the dye-labelled antibodies that are part of the RDT, but this line is not an indicator of the RDT’s capacity to detect malaria parasites. This is where positive control wells can play a part.

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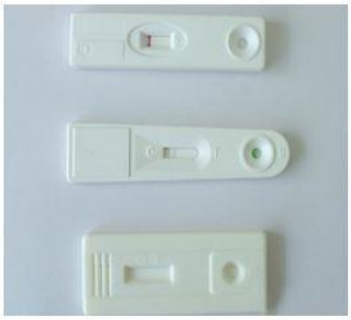

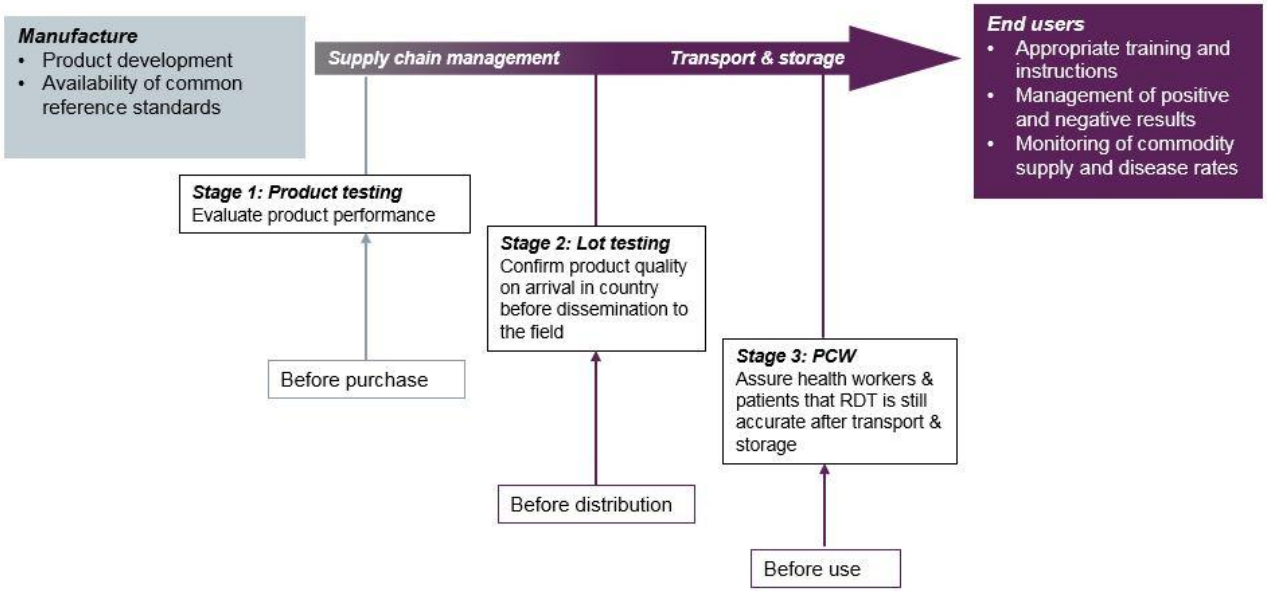

The quality assurance process for malaria RDTs, from product development to end user

PCWs: instant quality assurance of malaria RDTs by the people who use them

Positive control wells (PCWs) are a new addition to the quality assurance toolkit. They are field-stable and easy-to-use tools designed to test the performance of malaria RDTs in even the most remote settings—no laboratory equipment or electricity is required for use. They are as easy to use as the RDTs.

PCWs are a field-appropriate RDT quality control tool that can help to ensure the health provider trusts the RDT results and the patient receives appropriate care.

PCWs provide an on-the-spot quality check that can easily be used by providers with limited training to ensure that RDTs are functioning well. They have been developed, validated and piloted, but not yet introduced as part of malaria control programmes.

How PCWs work

A positive control well is a small plastic tube containing small amounts of dried recombinant, malaria parasite antigen. To test the quality and function of a box of RDTs, one RDT from the box is tested using a PCW. Water is added to the PCW tube to dissolve the recombinant antigens, and the resulting antigen solution is applied to the RDT well where the user normally puts the patient's blood sample, using the same blood collection device that the user normally uses for patient blood.

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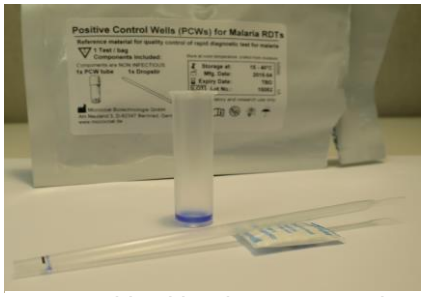
If the RDT is functioning properly, the solution should produce a positive test result. If the test result is negative, it indicates that the RDT is of poor quality, or has deteriorated and is no longer functional. By extension, this result applies to the other RDTs from the same lot with the same expiry date having been exposed to the same storage and transport conditions.



PCW kit with tube, straw and desiccant

Why are PCWs needed?

Effective use of malaria RDTs requires that both health workers and patients are confident in the reliability and accuracy of the tests. Confidence in the test result ensures that health workers only give antimalarial drugs when the test is positive for malaria. It also ensures that patients believe they have received a correct diagnosis with regard to malaria, whether the test is positive or negative.

Not all health providers trust the results of malaria RDTs. This has been particularly true when front-line health workers have switched from using presumptive treatment (i.e. assuming all fevers are malaria and treating them accordingly) to using a diagnostic test, and when health workers have switched from using microscopy to RDTs for malaria diagnosis, and can no longer physically see and count the parasites.

When health providers lack confidence in RDT results, they may disregard test results, which can lead to:

- Over-prescription of antimalarial drugs;
- Inappropriate treatment of non-malarial illness;
- Poor patient outcomes;
- Unnecessary waste of diagnostic tests and medicines;
- Increased costs to patients and the health system.

When patients do not have confidence in RDT results:

- They may not follow an appropriately prescribed treatment;
- They may pressure health workers to provide antimalarial medicines, despite a negative test result;
- They may seek care from another provider in the belief that they have malaria.

Have PCWs been field-tested?

In 2013, the PCWs developed by FIND in partnership with ReaMetrix Inc. were field-tested in a study that evaluated the use of PCWs by health care providers who routinely used malaria RDTs in their work.

Nearly 560 health workers and village health volunteers in Laos and Uganda received a half day of training on using PCWs to identify RDTs with inadequate sensitivity.

After training, about 90% of participants correctly identified “good” and “bad” RDTs with PCWs, and 89% reported appropriate follow-up action. These results were largely maintained six months later without refresher training during that time.


Health workers in Uganda receive training to use PCWs with the support of job aids

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What is needed to introduce PCWs for point-of-use quality control of malaria RDTs?

To move PCWs from validated product to commercially available tool, and to develop context-specific guidance for their use, there are several next steps to be taken:

Determine the best scenarios for using PCWs in the public and private sectors

PCWs could be used by health providers and private sector vendors to test RDTs when they have doubts about RDT quality or to routinely test one RDT out of every new box received. Alternatively, or in addition, routine checking of RDT quality could be conducted by national or subnational quality assurance focal points before distribution of RDTs to health facilities and private sector outlets. Likewise, PCWs could be used by district supervisors as part of periodic assessments of health provider competence in the correct use and interpretation of malaria RDTs. The most appropriate uses, in both public and private sectors and in different country contexts, need to be determined.

Implement PCWs in the public and private sectors

Implementation will involve training on the correct use of PCWs in line with national case management guidelines, developing procedures for monitoring RDT quality and what to do when the PCW result shows problems with an RDT, and aligning the use of PCWs with case management supervision processes in the public and private sectors. Implementation will vary by country context and by sector, and it is important to learn from each.

Determine the best way(s) to procure, package, distribute and price PCWs

PCWs could be sold separately or included in each box of RDTs by manufacturers. Certain options may be more attractive to health workers and private sector providers but less viable for manufacturers, so these options need to be tested. In addition, market analysis is needed to better understand what will define the most effective pricing structure, distribution systems and demand forecasting. These may differ between the public and private sectors.

Assess the acceptability of PCWs by providers and patients

Any health-care provider or medicine vendor asked to use a new product must be convinced of its value and trust its quality. In order to effectively encourage a health provider to use a new product, we need information on what they think about it and what will encourage them to use it – or deter them. Likewise, for those seeking a diagnosis, including those who go to kiosks or informal drug shops, focus group discussions and key informant interviews will provide clear insights into the acceptability of PCWs by providers and patients. They will also help to identify factors that influence the treatment behaviour of providers. Once PCWs have been implemented, it will be important to assess provider confidence in RDTs and any behaviour changes associated with the use of PCWs.

Support the registration of PCWs for post-market surveillance of malaria RDT quality

Data are needed from implementing countries to submit to the WHO Prequalification Department to seek approval for the use of PCWs as reference standards for malaria RDT quality control. In addition, support may be needed for national regulatory bodies to facilitate the registration of PCWs as an approved health commodity and to gather the evidence required for WHO prequalification of PCWs as RDT kit components.

For more information about PCWs, please contact Christian Nsanzabana at Christian.Nsanzabana@finddx.org

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FIND, Campus Biotech, Chemin des Mines 9, 1202 Geneva, Switzerland

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