



2013

Malaria Diagnostics Market Landscape Update

NOVEMBER 2013

UNITAID Secretariat
World Health Organization
Avenue Appia 20
CH-1211 Geneva 27
Switzerland
T +41 22 791 55 03
F +41 22 791 48 90
unitaid@who.int
www.unitaid.org

UNITAID is hosted and administered by the World Health Organization

© 2013 World Health Organization
(acting as the host organization for the Secretariat of UNITAID)

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind either expressed or implied. The responsibility and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

This report was prepared by Jennifer Daily with support from UNITAID. All reasonable precautions have been taken by the authors to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the authors, UNITAID or the World Health Organization be liable for damages arising from its use.



CONTENTS

Abbreviations	iv
Introduction	1
Public health issue	1
Trends in malaria management and in diagnosis	2
Commodity access	4
Uptake of diagnostic tests	4
Appropriate management of fever	6
Estimating the gap in achieving universal access to testing	6
Unmet needs: diagnosis of special population groups	9
Implications of low access to testing	9
Technology landscape	10
Market landscape	10
Market growth	10
RDT demand	11
Private sector RDT markets	13
RDT prices	14
Market share and competition	14
Quality	15
Adaptability	16
Market landscape summary	16
Market shortcomings	17
Opportunities for market intervention	20
Market interventions: work in progress	20
Market interventions: new opportunities	20
Conclusions	24
Annex: Update to donor and partner landscape	25

Abbreviations

ACT	artemisinin-based combination therapy	TPP	target product profile
AMFm	Affordable Medicines Facility-malaria	UCSF	University of California San Francisco
CHAI	Clinton Health Access Initiative	US	United States
DRC	Democratic Republic of the Congo	VPP	Voluntary Pooled Procurement
GFATM	The Global Fund to Fight AIDS, Tuberculosis and Malaria	WHO	World Health Organization
GSK	GlaxoSmithKline		
GMP	Global Malaria Programme		
G6PD	glucose-6-phosphate dehydrogenase		
HWG	Harmonization Working Group		
MAP	Malaria Atlas Project		
MPAC	Malaria Policy Advisory Committee		
NMCP	national malaria control programme		
PCW	positive control well		
PMI	President's Malaria Initiative		
POC	point of care		
PQ	prequalification		
PQR	Price and Quality Reporting		
PSI	Population Services International		
QA	quality assurance		
QC	quality control		
Q4	fourth quarter		
RAcE	Rapid Access Expansion		
RBM	Roll Back Malaria Partnership		
RDT	rapid diagnostic test		
R&D	research and development		

Introduction

This report updates and highlights changes in the malaria market since the UNITAID 2012 Malaria Diagnostics Market Landscape and the UNITAID 2012 Malaria Diagnostics Technology Update.¹ It is based on a review of published reports and meeting presentations, a limited literature review, interviews with experts and feedback from five leading rapid diagnostic test (RDT) suppliers.² The focus of this update is malaria RDTs as they are driving current growth in malaria diagnostic testing. Information in this report is current as of June 2013. Further detail will be provided in the forthcoming complete UNITAID 2013 Malaria Diagnostics Landscape Report.

Public health issue

There has been little change in the public health issue or policy for malaria diagnosis. In sum:³

- Globally, 3.3 billion people were living at risk of malaria in 2011.
- There were an estimated 219 million cases of malaria and 660 000 deaths in 2010, both of which are highly concentrated: 80% of cases occurs in 17 countries, with the Democratic Republic of the Congo (DRC), India and Nigeria comprising an estimated 40% of malaria cases globally; 90% of deaths occurs in Africa.
- There are 99 countries with ongoing malaria transmission and 5 countries are in the prevention of reintroduction phase of elimination.⁴ The Global Health Group reports that 36 countries have a strategy in place for malaria elimination.⁵

Policy: There have been no recent changes in the World Health Organization (WHO) malaria diagnostic policy, and implementation of the 2010 WHO policy recommendation for parasitological diagnosis for all suspected cases is under way. In addition, in 2012, WHO launched the T3: Test, Treat, Track campaign, further underscoring the importance of scaling up malaria diagnostics as well as the paradigm shift in programme management that is possible when the data generated through testing are systematically captured and used to inform decisions and monitor progress.

1 Malaria diagnostics technology semi-annual update. Geneva: UNITAID; December 2012. Malaria diagnostics market landscape. Geneva: UNITAID; October 2012. Malaria diagnostics technology landscape. Geneva: UNITAID; December 2011 (<http://www.unitaid.eu/en/market-approach-publications?id=345>).

2 The donor funded malaria RDT market is dominated by a handful of suppliers; five of six suppliers provided feedback for this update. Source: Malaria diagnostics market landscape. Geneva: UNITAID; October 2012.

3 Unless otherwise noted, statistics are drawn from the WHO World Malaria Report 2012. Note there are wide uncertainty intervals associated with these estimates and varying approaches to estimating the burden of malaria. Source: World malaria report 2012. Geneva: WHO; 2012.

4 The WHO World Malaria Report countries in the prevention of reintroduction phase of elimination include: Egypt, Iraq, Georgia, Oman, Syrian Arab Republic.

5 The 36 countries identified by the Global Health Group at UCSF and the Malaria Atlas Project (MAP) project as moving from controlled, low-endemic malaria to elimination include: Algeria, Argentina, Azerbaijan, Belize, Bhutan, Botswana, Cape Verde, China, Costa Rica, Democratic People's Republic of Korea, Dominican Republic, El Salvador, Georgia, Iran (Islamic Republic of), Iraq, Kyrgyzstan, Malaysia, Mexico, Namibia, Nicaragua, Panama, Paraguay, Philippines, Republic of Korea, Sao Tome and Principe, Saudi Arabia, Solomon Islands, South Africa, Sri Lanka, Swaziland, Tajikistan, Thailand, Turkey, Uzbekistan, Vanuatu, Viet Nam. Source: Global Health Group and Malaria Atlas Project. Atlas of malaria eliminating countries. San Francisco: UCSF; 2011.

Trends in malaria management and in diagnosis

Notable trends and priorities that effect malaria diagnostic markets include the following situations.

Constrained donor funding and slowing of progress

Perhaps the most important concern in malaria management is the levelling off of funding for malaria, which has led to a slowing progress compared to the previous decade of gains. In particular, international donor funding appears to have levelled off and poses a real risk for malaria programmes: a recent review identified a weakening of malaria programmes following funding disruption as the single greatest cause of malaria resurgence.⁶ In particular, the uncertainty associated with the largest international funder of malaria diagnostic tests, The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), continues due to its strategic reform and unpredictable funding level. Although the GFATM new funding model has been launched, funding levels for malaria programmes and the allocation of funds between prevention and case management remain uncertain. To date, experts report no major interruptions or slowdowns in malaria diagnosis scale-up due to funding shortages. Continued progress may be partially attributed to declines in RDT prices that have stretched diagnostics budgets; however, in the future funding limitations may slow the pace of diagnosis scale-up.

Scale-up of diagnostics

In Africa, where testing rates are low, national malaria control programmes (NMCPs) and WHO are prioritizing diagnosis scale-up, largely through RDTs. In many areas, adherence to diagnostic test results remains an issue, undermining the benefits of testing. It is likely that difficulty in managing non-malaria fever contributes to the poor acceptance of malaria diagnostic tests: after years of assuming that “fever is malaria” many health workers are unaccustomed to performing differential diagnosis of fever and, furthermore, the health systems where they work may not be supportive of an alternative diagnosis. This challenge has led the malaria community to take a broader view of malaria RDTs with malaria diagnosis increasingly viewed as a service (as opposed to a commodity) that is part of improving febrile illness management. This view has catalysed work to improve the management of fever more broadly. Notable progress during the last year includes:

- WHO has been reviewing guidance and strategies for improving management of febrile illness and hosted an informal consultation on fever management in early 2013. In addition, WHO is leading RAcE (Rapid Access Expansion) 2015, a five-country implementation programme for integrated community case management of childhood illnesses.⁷
- The United States President’s Malaria Initiative (PMI) is actively working to improve fever management comprehensively. In connection with this, in late 2012, it announced the Malaria Care Project, a new US\$ 49 million five-year contract, led by PATH, to provide technical assistance for malaria case management as well as other illnesses. This project continues the work of the PMI Improving Malaria Diagnosis (IMaD) project in scaling up diagnostic testing and quality of laboratory services, and also will focus on improving the capacity of providers to manage malaria and other illnesses appropriately.

With respect to markets, the scale-up of diagnosis has created demand for RDTs and will have implications for ACT usage, which, over time, should decline where diagnosis is implemented. Work on non-malaria fever will likely impact the markets for existing health products (e.g. antibiotics, oral rehydration salts) and may create demand for products that are not yet available in resource-poor settings (e.g. diagnostics to aid management of fever).

6 Cohen JM et al. Malaria resurgence: a systematic review and assessment of its causes. *Malar J.* 2012(April 24);11:122.

7 Globally, malaria, diarrhoea and pneumonia are the leading causes of death in the postneonatal period. RAcE 2015 was launched by the WHO Global Malaria Programme in 2012. Objectives include: (i) catalysing the scale-up of community case management thereby increasing coverage of access to diagnostic treatment and referral services for the major causes of childhood mortality; (ii) generating evidence to inform WHO policy recommendations and programmatic guidance on integrated community case management; and (iii) stimulating review of the policy (in particular, diagnostic and antibiotic use at the periphery) and regulatory environment for disease management in countries, including adaptation of supply management and surveillance systems. RAcE will be implemented by selected nongovernmental organizations – Save the Children, International Rescue Committee (IRC), World Vision – with the ministries of health in a leadership position, during 2013–2017 in DRC, Malawi, Mozambique, Niger, and Nigeria (two states). RAcE is funded by the Canadian International Development Agency (CIDA) (74.5 million Canadian dollars). Source: WHO GMP website.

Monitoring case management and malaria incidence

There is increasing concern about the inability to monitor progress in diagnosis scale-up and in case management due to weaknesses in reporting and surveillance systems. Currently, the picture of malaria is incredibly imprecise. WHO reports that existing surveillance systems capture only 10% of cases. Moreover, 41 countries, representing 85% of the malaria burden, do not have adequate systems in place to generate data that are useful for monitoring trends, identifying geographic differences and decision-making.⁸ In short, progress towards meeting malaria targets is not possible to ascertain in many countries due to a lack of data. This is due in part to the relatively recent change in policy for diagnosis: prior to the diagnosis scale-up, data on “suspected malaria cases” were not very valuable. However, now that confirmation of malaria is possible, linking diagnosis with data management systems represents a game changing opportunity to gain a realistic picture of malaria and to begin to make data-driven decisions at both the national and global levels about resource allocations. These weaknesses also result in a poor appreciation of the malaria commodity markets (e.g. estimating the global need for diagnostics, appreciating the impact of RDTs on ACT demand). These issues are highlighted in the World Malaria Report 2012 and correspond with the launch of WHO surveillance manuals and the T3: Test, Treat, Track campaign in 2012.

P. vivax

At the policy level, there is growing focus on *P. vivax*, which, for many countries outside of Africa, is the primary concern of malaria programmes. WHO has begun developing a strategy for *vivax* control and elimination.⁹ With respect to diagnostics, there is room for improvement in the sensitivity of diagnostics for *vivax* as well as a need for point of care (POC) tests to rule out G6PD deficiency, a common genetic disorder that may cause a severe reaction to primaquine, the medicine used to prevent *P. vivax* relapse. PATH has an initiative to develop target product profiles (TPPs) for POC G6PD tests.

Elimination

With the progress in malaria control over the past 10 years, malaria elimination – defined as the interruption of local transmission – is increasingly possible in areas where transmission has been reduced. Recent work in this area includes publication of case studies on malaria elimination by the Global Health Group and WHO, and increasing focus on elimination in the literature as well as in regional groups (e.g. Asia Pacific Malaria Elimination Network). With respect to diagnostics, tests that are more sensitive are needed for elimination settings, and PATH has recently launched an initiative to develop TPPs for elimination diagnostics.

Private sector

Improving access to diagnosis and treatment in the private sector remains a priority. In the past year, discussions focused on the need to target treatment in the private sector to confirmed malaria cases and activities aimed at developing the private sector markets for diagnostics intensified. While several pilots and research projects have demonstrated that it is feasible to perform testing in the private sector, several unanswered questions remain, in particular, those related to management of RDT-negative patients and financial incentives that encourage testing and appropriate fever management. Of note, in late 2012, GFATM decided not to continue its large ACT subsidy, Affordable Medicines Facility-malaria (AMFm), as a stand-alone programme, but rather to integrate it into the regular grant-making activities.¹⁰ This decision was based in part on the programme’s inability to target ACTs to people with malaria, with the GFATM Board suggesting that incorporation of diagnostic testing into a private sector programme be explored. In connection with this, the Roll Back Malaria Partnership (RBM)/GFATM AMFm Task Force is assessing the

8 World malaria report 2012. Geneva: WHO; 2012.

9 MPAC meeting website (<http://www.who.int/malaria/mpac/mpacmeetings/en/index.html>).

10 AMFm was a global health financing mechanism initiated by GFATM and aimed at increasing access to effective malaria treatments by reducing the retail price of ACTs, increasing ACT availability and use, and crowding out of ineffective treatments that contribute to drug resistance. The programme, implemented on the national scale for two years in eight countries, involved subsidizing the cost of ACTs and was supported by a pool of funds that was separate from other GFATM programmes. In late 2012, the GFATM Board decided that the AMFm activities would be integrated into its routine grant-making processes, i.e. there would no longer be a special pool of funds for subsidizing private sector case management; going forward, countries may elect to include a private sector programme in their malaria programme funding proposals.

feasibility of a catalytic RDT/ACT fund to support private sector access to diagnosis and treatment on a large scale. In addition, many operational research and pilot projects have been launched to further develop models for testing in the private sector. Large-scale implementation projects include:

- Population Services International (PSI) is leading a programme to develop private sector markets in five African countries. The specific approach will differ by country, but is likely to involve an RDT subsidy. PSI is leading work in Kenya, Madagascar and Tanzania to market RDTs to consumers and to encourage providers to stock and sell RDTs. In Nigeria and Uganda, the Malaria Consortium is leading work with RDT manufacturers to provide an RDT bundle (i.e. an RDT as well as several services such as training and medical detailing) to retailers. Currently, formative research is under way that will inform the design of these programmes.
- The Clinton Health Access Initiative (CHAI) recently launched a national initiative in Kenya and Tanzania to sell low-cost RDTs through the private sector without a subsidy. This programme includes negotiated pricing with several RDT manufacturers, agreements with local distributors that limit margins and demand generation activities. In Tanzania, the programme will include national scale-up of low-cost RDTs in the formal private sector (hospitals, clinics, dispensaries) as well as a pilot study in accredited drug dispensing outlets. The pilot will occur in two districts, and in one of the districts a subsidy for RDTs will be provided. The Kenyan programme is for national scale-up of RDTs in the formal private sector. Mid-line results are expected in late 2013.

Commodity access

In considering data on access to testing, it is important to note that access to testing starts with availability of a high-quality test and also includes the provider choosing to use the test, performing it safely and accurately and managing the patient in accordance with the results. Also critical is reporting on the test result and treatment given. Evidence from the RDT scale-up to date suggests that even when tests are available, uptake, use of results and case reporting may be problematic.

Uptake of diagnostic tests

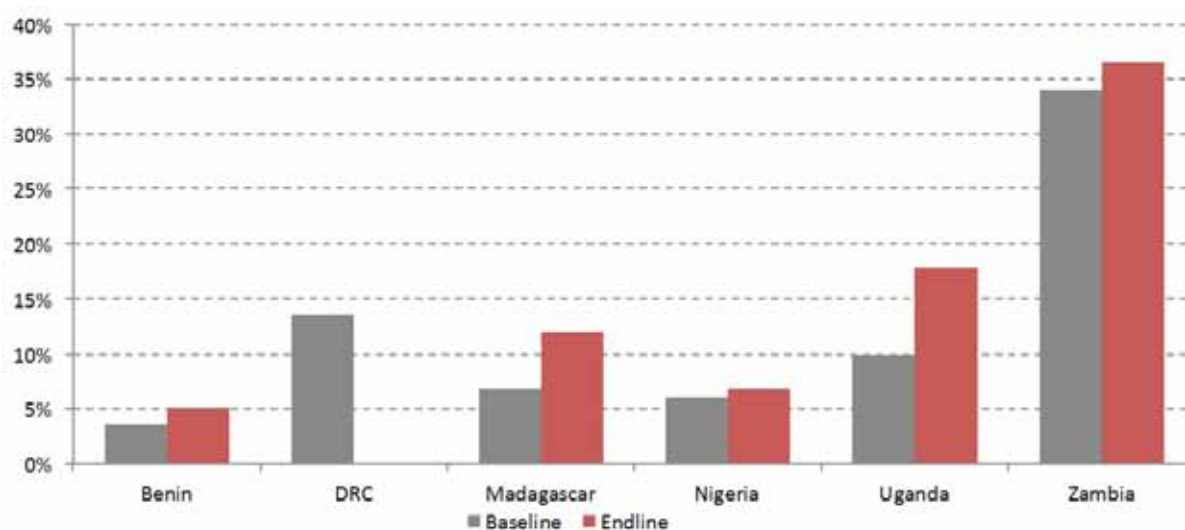
WHO reported little progress between 2010 and 2011 in public sector access to malaria diagnostics.¹¹ Globally, 77% of suspected cases in the public sector was tested in 2011, representing an increase of 1% over 2010, and of 11% since 2005. In Africa, the region with the lowest access to testing, increases in diagnostic testing rates in the public sector were minimal: 47% of cases was tested in 2011, a 2% increase over 2010. Furthermore, these figures might overestimate testing rates because countries with low testing rates may be underrepresented as they also do not report reliably.

Because many people with fever seek care outside of the public sector, universal access to diagnosis will not be achieved unless testing is expanded to the community level and private sector. Therefore, it is useful to look at household surveys to get a sense of overall testing rates in a country as these surveys capture the various treatment-seeking behaviours (i.e. public sector, private sector, no care) of individuals with fever. Figure 1 shows results of ACTwatch household surveys on the percentage of febrile children who received a diagnostic test in 2009 (baseline) and 2011–2012 (endline). Although there has been modest growth in diagnostic testing in each of the countries, even at endline, testing remained low, ranging from 5% in Benin to a high of 36.5% in Zambia.¹²

11 World malaria report 2011. Geneva: WHO; 2011. World malaria report 2012. Geneva: WHO; 2012.

12 ACTwatch Group, ABMS/Benin, ASF/DRC, PSI/Madagascar, SFH/Nigeria, PACE/Uganda, and SFH/Zambia. ACTwatch baseline and endline household survey results 2009–2012: Benin, Democratic Republic of the Congo, Madagascar, Nigeria, Uganda, Zambia. Washington DC: PSI; 2013 (www.actwatch.info).

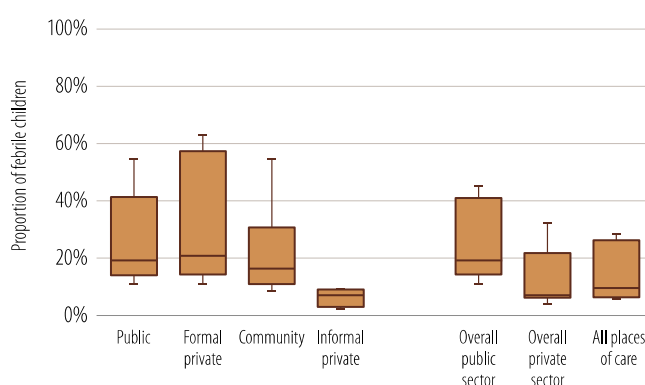
Figure 1: Percentage of children under 5 with fever in the past two weeks that received a blood test for malaria, 2009–2012



Source: Author analysis of ACTwatch baseline and endline household survey results 2009–2012: Benin, Democratic Republic of the Congo, Madagascar, Nigeria, Uganda, Zambia. Washington DC: PSI; 2013 (www.actwatch.info).

Information on testing uptake in the private sector is very limited. The World Malaria Report 2012 includes a summary of data comparing testing in the private sector and the public sector from nine household surveys conducted in Africa in 2010 and 2011 (Figure 2). The data suggest that public sector and formal private sector health facility testing rates are similar, but that community and informal private sector testing rates are lower. Likewise, while community level diagnosis is a WHO priority, the number of countries that reported community RDT use did not increase during this time and, overall, patients tested with RDTs in the community represented a small fraction of patients who received a test.¹³

Figure 2: Proportion of febrile children who had a blood test, by place of care in nine African countries, 2010–2011



Source: Household surveys, 2010–2011, from 9 African countries (Burkina Faso, Burundi, Liberia, Madagascar, Nigeria, Rwanda, Senegal, Uganda, Zimbabwe)
Public health sector includes government and non-profit facilities; Formal private sector includes private clinics and providers; Community sector is community health workers; Informal private sector includes pharmacies, shops and traditional providers. The top and bottom of the lines are the 90th and 10th percentile, the box represents the limits of the 25th to 75th percentile or interquartile range, and the horizontal line through the box is the median value.

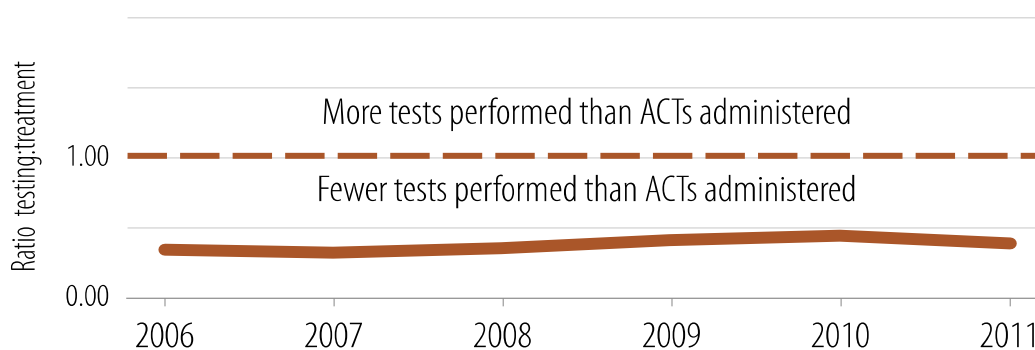
Source: World Malaria Report 2012, WHO.

¹³ World malaria report 2012. Geneva: WHO; 2012.

Appropriate management of fever

In order for diagnostics to impact health outcomes, test results must influence patient management and treatment. To date, the systems to track testing and treatment have been lacking and it is difficult to monitor the impact that the diagnostic test scale-up is having on care for febrile illness. One simplistic approach to assessing the impact of diagnostics is to compare the quantities of ACTs consumed to the number of malaria tests (microscopy and RDT) performed. The ratio of diagnostics to ACTs in most African countries continues to be the inverse of what it should be: the total number of tests in the public sector was < 1/2 the number of ACTs distributed (Figure 3). Considering case positivity rates, WHO suggests that this ratio should be > 2 times as many tests as ACTs.¹⁴

Figure 3: Ratio of RDT and microscopy performed to ACTs distributed, African Region, 2006–2011



Source: NMCP reports

Sources: World Malaria Report 2012, WHO; NMCP reports.

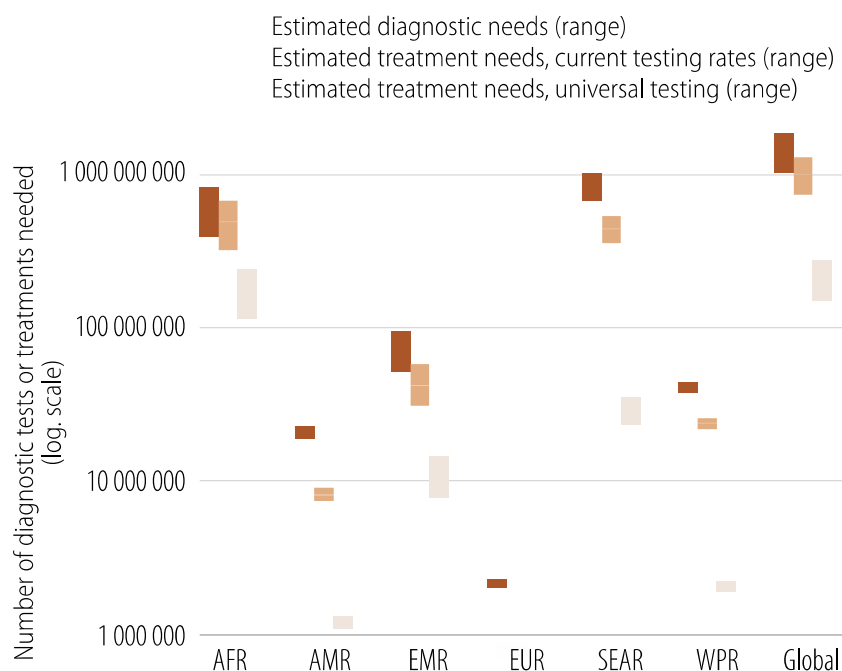
Estimating the gap in achieving universal access to testing

Refined analysis of the global gap in access to malaria testing is lacking. However, WHO has provided a rough estimate of the global “need” for diagnostic testing and the RBM Harmonization Working Group (HWG) recently analysed malaria commodity needs.

In the 2012 World Malaria Report, WHO estimated the need for diagnostic testing, (i.e. the number of suspected cases that need to be tested to achieve universal access to testing) to be well over one billion tests globally, with Africa and South-East Asia representing the greatest need. Although there are wide uncertainties associated with these estimates, it is clear that implementation of universal testing would massively decrease the need for treatment in all regions, as shown in Figure 4.

¹⁴ World malaria report 2012. Geneva: WHO; 2012.

Figure 4: Estimated malaria diagnostic and treatment needs, by WHO region, 2010



Estimated treatment needs for current and universal testing rates not shown for European Region, as below 1 000 000

Source: World Malaria Report 2011, NMCP reports

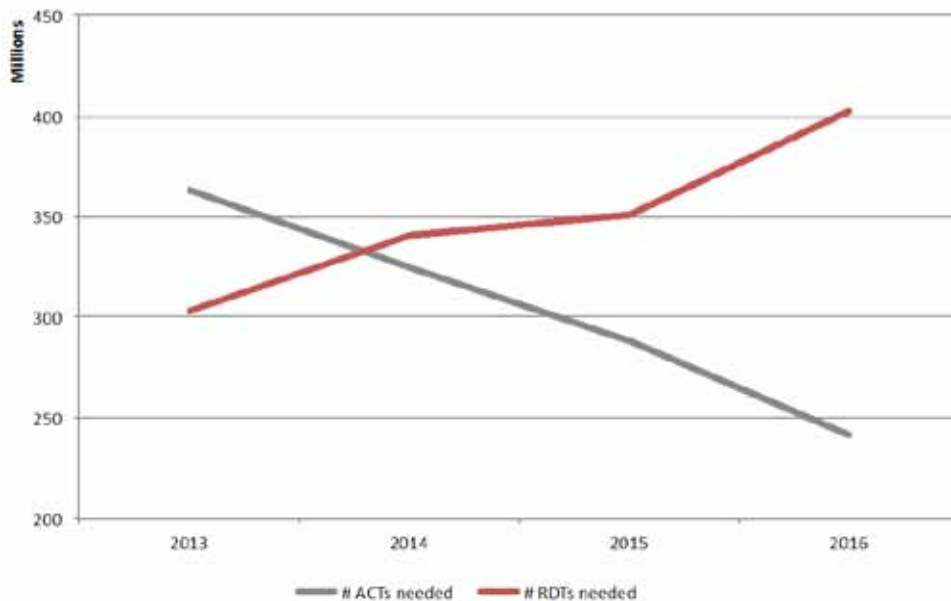
Estimated diagnostic needs = suspected malaria cases, derived from estimated confirmed cases and programme reported test positivity rates; Estimated treatment needs, current testing rates = confirmed + presumed cases, derived from the proportion of febrile persons seeking care by health sector, proportion suspected cases tested by health sector, reported test positivity rates; Estimated treatment needs, universal testing = estimated confirmed cases, 2010. Treatment needs include treatment for all Plasmodium species.

Note: AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WPR = Western Pacific Region.

Source: World Malaria Report 2012, WHO.

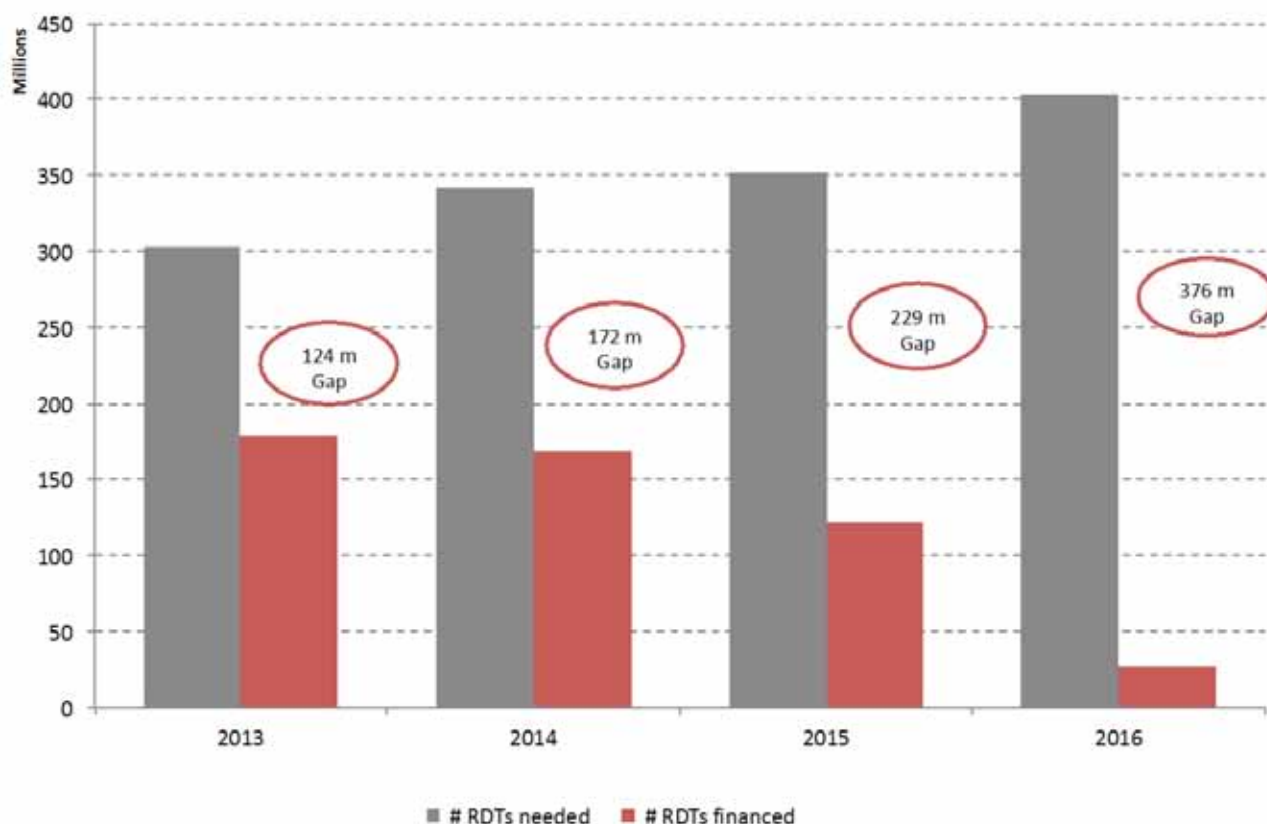
With respect to commodities, the RBM HWG has analysed commodity needs and financing for 42 African countries through 2016. This exercise, conducted in preparation for the GFATM Replenishment meetings, involved each country projecting RDT and ACT needs for the public sector, community level and private sector, taking into consideration their existing microscopy services, absorptive capacity and strategies for scaling up case management. Figure 5 illustrates a gradual decline in ACT needs and considerable growth in RDT needs, from 303 million RDTs in 2013 to 403 million in 2016, reflecting increasing scale-up in the public sector and community level and, in 16 countries, expansion of RDTs to the private sector.

Figure 5: Projected ACT and RDT needs for African countries, 2013–2016



Source: Author analysis of RBM HWG data on commodity needs, prepared for the GFATM Replenishment meetings.

The HWG then compared the projected need for commodities already financed to estimated gaps (Figure 6). Despite the intent to scale up RDTs, sizable and growing gaps in financing exist: only 36% of the projected RDT need for 2013–2016 is currently financed. Since plans for private sector testing are very modest, the gaps will impact the public sector. The HWG estimates that full replenishment of GFATM would cover only 60% of the gap. Without financing for RDTs, the projected declines in ACTs shown above cannot be realized.

Figure 6: Projected RDT needs versus RDTs financed for African countries, 2013–2016

Source: Author analysis of RBM HWG data on commodity needs, prepared for the GFATM Replenishment meetings.

Unmet needs: diagnosis of special population groups

In addition to the general need to increase access to malaria diagnostic tests, there are several population groups that do not have adequate access to malaria diagnosis due to the lack of appropriate technologies, including pregnant women, populations in low-transmission/elimination settings and populations in *P. vivax* endemic areas.¹⁵

Implications of low access to testing

While progress has been made in expanding access to diagnostic testing in the past few years, there is still significant work to be done to achieve universal coverage. One of the major implications of low access to diagnostic testing is overtreatment with ACTs, resulting in wasted health resources. Additional benefits of scaling up diagnostic testing include improving the quality of care for febrile patients with and without malaria, reducing the potential risk of unnecessary side-effects from antimalarials and reducing the selection pressure for drug-resistant parasites. Another challenge related to the lack of diagnosis is the lack of reliable data on malaria incidence and case management, making progress towards malaria targets difficult to measure in many countries.

¹⁵ For more detailed information on these unmet needs, see: Malaria diagnostics market landscape. Geneva: UNITAID; October 2012. Malaria diagnostics technology landscape. Geneva: UNITAID; December 2011 (<http://www.unitaid.eu/en/market-approach-publications?id=345>).

Technology landscape

Two technologies are currently used for routine malaria diagnosis: microscopy and malaria RDTs. Microscopy has been the standard for malaria diagnosis since it was first introduced over 100 years ago. In expert hands and ideal settings, it performs well. However, a general lack of sustained investment in microscopy services means that the quality of results varies greatly; under typical field conditions, the performance of microscopy is compromised.

Malaria RDTs are POC disposable tests that detect antigens produced by the malaria parasite. They are simple to perform and require no laboratory infrastructure. RDTs may detect one or multiple species of malaria (the latter being “combination tests”). While the quality of products on the market varies, recent evaluations have shown that there are many commercially available RDTs that perform as well as if not better than operational microscopy.

The malaria diagnostic pipeline includes a number of technical approaches to detecting malaria, and is described extensively in the UNITAID 2012 Malaria Diagnostics Technology Landscape and subsequent update.¹⁶ The pipeline includes improvements to existing technologies (e.g. higher performing RDTs, urine-based RDTs, automated microscopy and simplified versions of complex reference tests) as well as platforms based on novel approaches for malaria (e.g. spectroscopy and hemozoin detection). While some of these technologies are intended for routine diagnosis, others are designed to be field applicable reference methods. Given the acute nature of malaria disease, tests for routine case management should be both accurate and rapid. Other priorities for malaria diagnostic test research and development (R&D) include affordability and the ability to widely deploy the test (i.e. tests must be portable, able to withstand high heat and humidity and be simple to perform). The ideal characteristics of tests for elimination settings, pregnant women or for *vivax* malaria may differ and have yet to be defined in detail.

Two of the tests reported on in the last version of the Malaria Diagnostics Technology Landscape have come to market: a commercial LAMP kit (Eiken, FIND) and the Truelab Real-time Micro PCR System (Tulip Group and Bigtec Labs). These are expected to be used primarily in health facilities with laboratories to supplement RDTs or microscopy use for research or for surveillance. In addition, Fio has launched Fio-net, a system comprising an RDT reader that guides users through protocols and captures patient and quality assurance (QA) data as well as a cloud database that aggregates data and a portal for analysis and report generation.

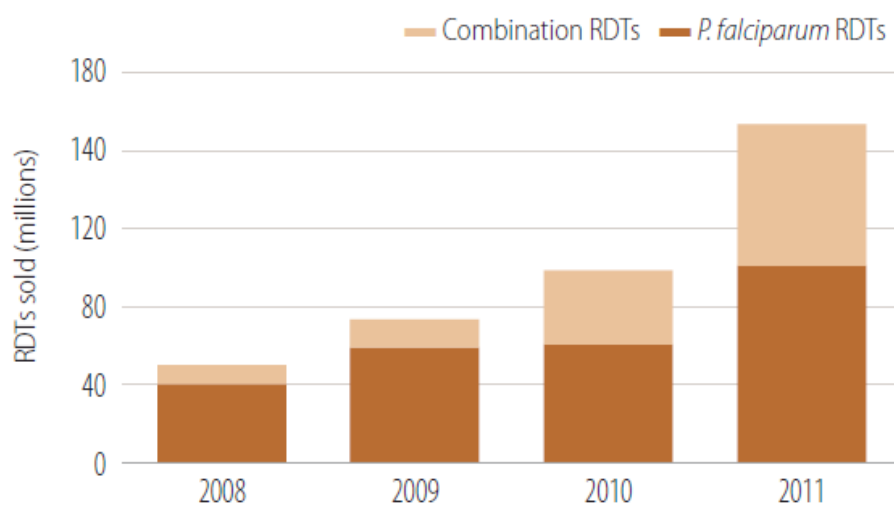
Market landscape

Market growth

The malaria RDT market continues to grow rapidly, reaching 155 million RDTs in 2011, an increase of 67 million RDTs over 2010¹⁷ (Figure 7). Growth stems both from *P. falciparum* RDTs as well as combination tests. Despite growth in testing, the need for testing is several times current demand.

¹⁶ UNITAID, Malaria diagnostics technology semi-annual update. Geneva: UNITAID; December 2012. Malaria diagnostics technology landscape. Geneva: UNITAID; December 2011 (<http://www.unitaid.eu/en/market-approach-publications?id=345>).

¹⁷ World malaria report 2012. Geneva: WHO; 2012.

Figure 7: Malaria RDT market

Sources: Analysis based on responses from manufacturers participating in the WHO Malaria RDT Product Testing Programme; World Malaria Report 2012, WHO.

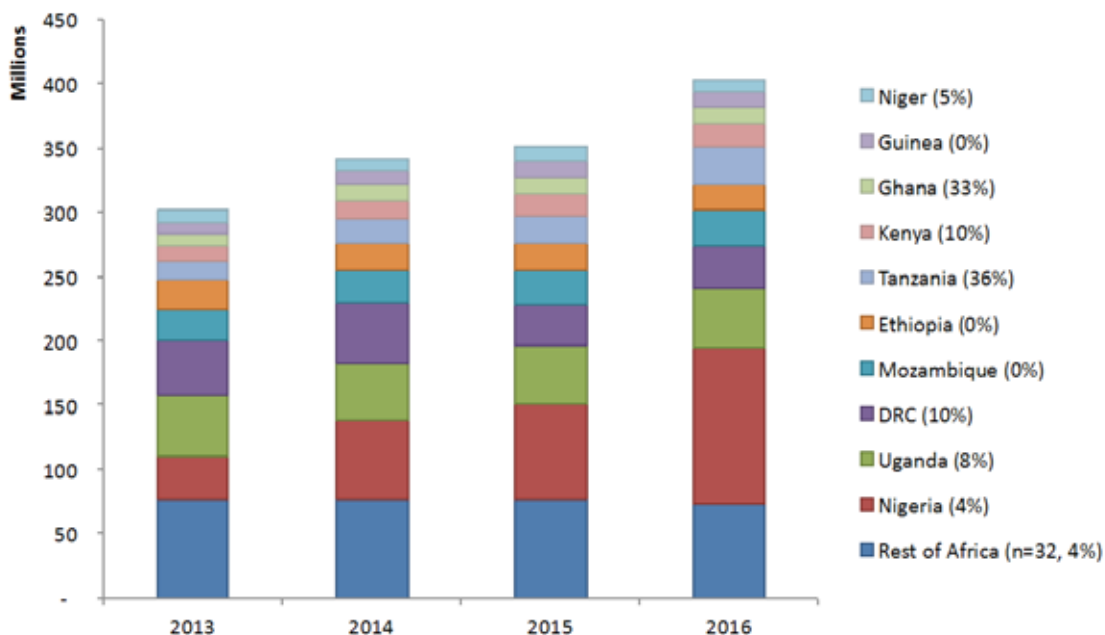
RDT demand

The public sector scale-up of RDTs is under way and driving demand growth, although it is more advanced in some countries than others. Conversations with manufacturers and reporting by NMCPs to WHO of RDTs distributed indicate that Africa is the largest market for RDTs, followed by South-East Asia. Most of the increase in testing in the African Region is attributable to the increase in use of RDTs, which accounted for an estimated 40% of all cases tested in the region in 2011.¹⁸

The RBM HWG projection of RDT needs and financing for African countries sheds some light on how countries plan to move forward with diagnostic scale-up as well as high-level insight into RDT demand. The total need for RDTs in Africa for 2013–2016 is projected to be 1.4 billion with Nigeria, Uganda, DRC, Mozambique, Ethiopia and Tanzania having the greatest needs (Figure 8).

¹⁸ World malaria report 2012. Geneva: WHO; 2012.

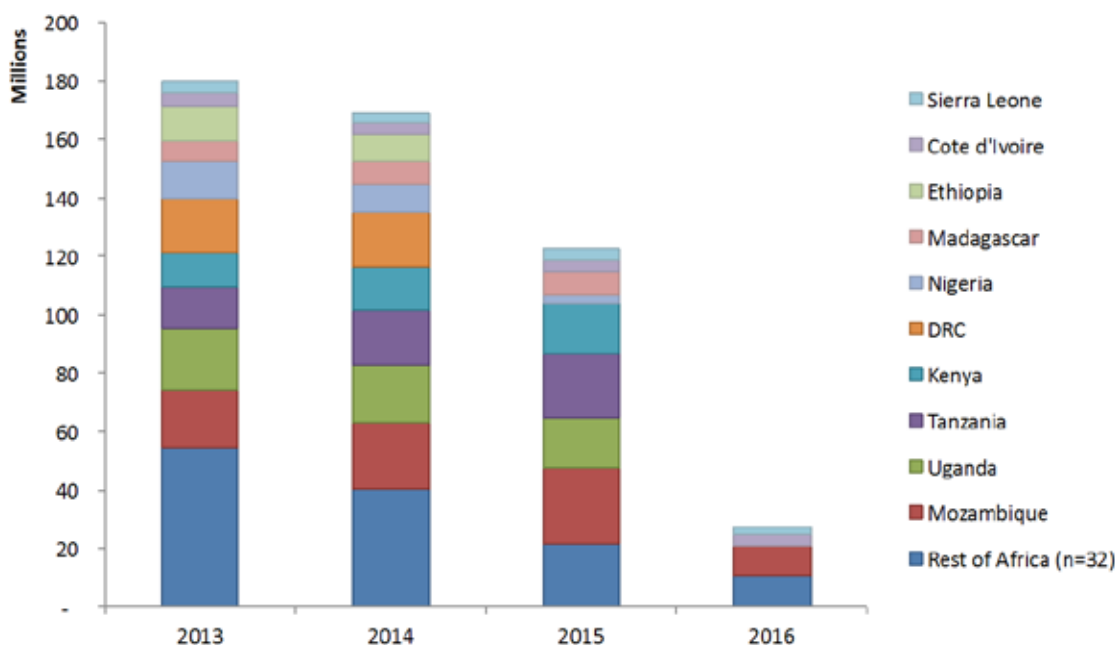
Figure 8: RDT needs in African countries by % of need from the private sector, 2013–2016



Source: Author analysis of RBM HWG data on commodity needs, prepared for the GFATM Replenishment meetings.

However, there is often a significant difference between RDT needs and actual demand, with funding being a major factor influencing whether or not demand is realized. As such, RDT financing may be more indicative of actual future demand. Figure 9 shows that there were 498 million RDTs financed through 2016. In addition, need does not correlate with financing; for example, in Nigeria and DRC, two countries with significant RDT needs, less than a quarter of the need is actually financed.

Figure 9: RDTs financed in African countries, 2013–2016

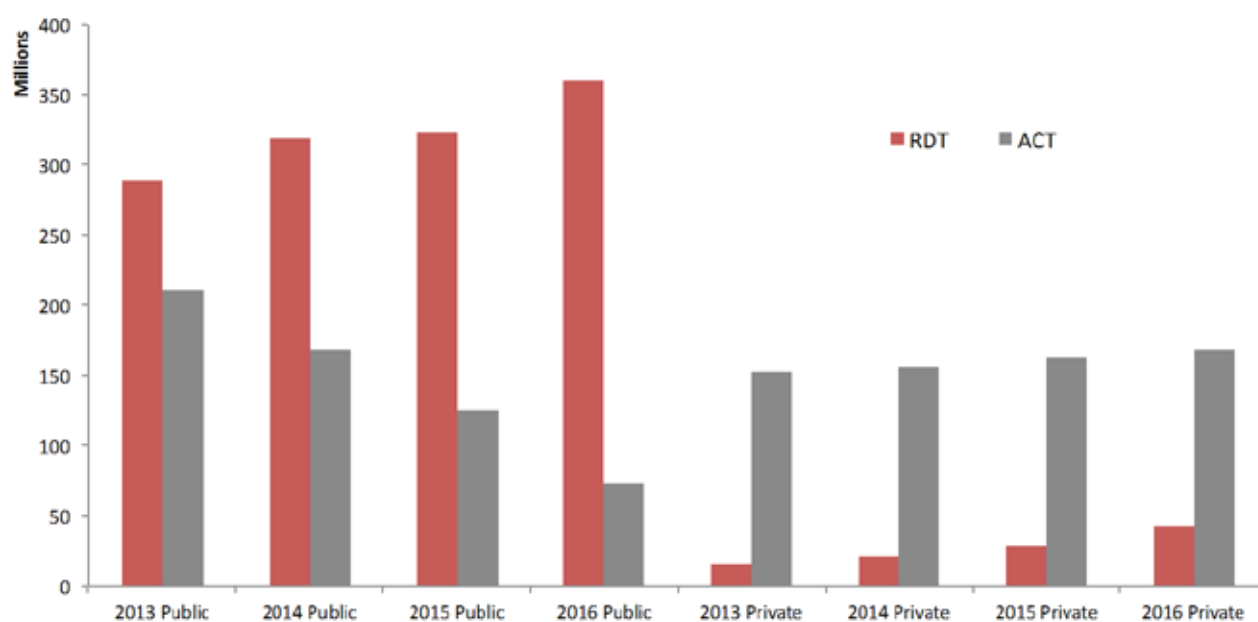


Source: Author analysis of RBM HWG data on commodity needs, prepared for the GFATM Replenishment meetings.

Private sector RDT markets

The HWG data in Figure 10 show how countries are planning to scale up RDTs in the public/community sectors compared to the private sector, and what impact they expect RDTs to have on ACT needs. While in the public sector RDT needs continue to grow as ACT needs decline, the reverse is true in the private sector, where ACT needs are slowly increasing and remain significantly above RDT needs, suggesting a slow implementation of diagnosis in the private sector.

Figure 10: RDT and ACT needs by sector for 42 African countries, 2013–2016



Source: Author analysis of RBM HWG data on commodity needs, prepared for the GFATM Replenishment meetings.

Several operational research projects are under way to better understand the potential private sector market for diagnostics and to add to the limited information that is currently available. Interviews with experts have highlighted several areas of progress in understanding potential private sector markets for RDTs as well as areas requiring more study. In sum:

- In general, these research projects have demonstrated the feasibility of testing in the private sector. They also are revealing the heterogeneity of this sector, both between and within countries. The heterogeneity makes generalizing from any one study challenging and suggests that a nuanced approach to developing the private sector may be needed.
- RDT availability in the private sector is low, although diagnosis is more common in outlets staffed by trained providers (clinics, pharmacies) as opposed to informal outlets such as drug shops, groceries and kiosks. When tests are available, ACTwatch and independent evaluation data indicate that prices vary, from less than US\$ 1 to several dollars per test. Information on the type or quality of the tests is not available.
- Operationally, many studies have demonstrated that it is feasible to safely and accurately diagnose malaria in the private sector using RDTs, even in the less formal drug shops. However, cost-effective means of training retailers (especially in light of high staff turnover) and providing QA remain a challenge.

- Experts suggest that awareness of RDTs among consumers is often low, although many are aware that fever may be caused by diseases other than malaria and seem open to the idea of malaria testing. Only a few publications on willingness to pay for RDTs are available, but they suggest that consumers may be willing to pay for an RDT and that willingness to pay varies considerably (e.g. in Uganda a mean of US\$.53 willingness to pay compared to US\$ 3.53 in Benin).¹⁹
- As in the public sector, operational research projects suggest that adherence to RDT results varies; many individuals with negative RDTs buy antimalarials.
- In Cambodia, the only country that has had a national RDT programme for over 10 years, availability, uptake and adherence to diagnostic testing was still moderate, suggesting that activities to support retailers and to promote diagnosis among consumers may need to be ongoing.
- In many countries, policies and regulations relating to testing may lead to low availability of diagnostics in the private sector.

With respect to areas needing additional research, experts suggest that activities to increase awareness of testing and adherence to results would be beneficial, although the optimal strategies for doing so are unclear. Also, more work is needed to understand pricing and to overcome affordability challenges, in particular consumer willingness to pay, how providers set prices and provider incentives to diagnose, treat and refer non-malaria fever illness. Many experts feel that a subsidy will be required in order to achieve affordable retail prices for RDTs, but the structure and amount of subsidy are undefined. Other high priorities for private sector market development include strategies for management of non-malaria fever in the private sector (e.g. referrals, observation periods), appreciating the degree of programmatic support needed to ensure optimal health outcomes and how to implement QA activities at scale, in particular when the public sector QA is weak or non-existent.

RDT prices

Downward pressure on RDT pricing continues. The GFATM Price and Quality Reporting (PQR) database shows a low price of US\$.27 for RDTs and US\$.33 for combination RDTs.²⁰ Conversations with suppliers and procurement groups indicate that in larger competitive tenders *falciparum*-only RDT pricing is in the mid-twenties. However, there is continued wide variation in pricing for the same product, with competitive bids often resulting in lower prices.²¹ From a donor perspective, there is increasing pressure on country programmes to plan procurement so as to avoid costly emergency orders and to allow for less expensive shipping (e.g. by boat as opposed to air).

Market share and competition

Competition on price is intense: suppliers report the current prices are unsustainable and the first signs of supplier exit are emerging, with at least one formerly dominant supplier reducing capacity. Low prices likely represent strategic attempts by RDT suppliers to capture and penetrate new markets as well as efforts to ensure capacity utilization (e.g. avoid costs associated with shutting down production) and use inventory. Logistics, raw materials inventory management and operations are important factors in this market where large orders must be filled within a few weeks and finished goods inventory is minimal.

In-depth analysis of procurement data has not been conducted at this time. However, review of GFATM PQR data and discussion with PMI suggests that although there are many RDT suppliers meeting WHO recommendations, the market is increasingly consolidating around a few companies. Barriers to entry exist, especially in the large public sector market segment, including: (i) participation in WHO product testing, which can take two years; (ii) working capital and capacity to deliver large public sector orders

¹⁹ Hansen K et al. Willingness to pay for a rapid malaria diagnostic test and artemisinin-based combination therapy from private drug shops in Mukono district, Uganda. *Health Policy and Plan.* 2013;28(2):185–96. Rennie W et al. Willingness to use and pay for a new diagnostic test for malaria in children under 5: results from Benin, Peru, Tanzania. Bethesda: Center for Human Services; 2009. Uzoichukwu BS et al. Willingness to pay for rapid diagnostic tests for the diagnosis and treatment of malaria in south-east Nigeria: ex post and ex ante. *Int J Equity Health.* 2010(15 January);9(1):1.

²⁰ GFATM PQR database (www.theglobalfund.org/en/procurement/pqr; accessed 10 April 2013).

²¹ GFATM VPP and John Snow Inc, procurement agent for PMI, personal communication, May 2013.

rapidly; and (iii) WHO prequalification (PQ), which is not yet required, but is a lengthy process that may be prioritized by donors and policy-makers in the future.

Quality

The WHO FIND Malaria RDT Product Testing Programme remains the most important quality standard in this market, and forms the basis of the WHO recommendations for RDT procurement and major donors' RDT procurement standards. Round 4 of product testing results were released in December 2012 and over 10 new RDTs were added to the WHO list of RDTs acceptable for procurement, in particular an increase in the tests that can differentiate between *falciparum* and *vivax* malaria. However, the number of high-performing products targeting pLDH antigens produced by *falciparum* malaria is limited and, given the geographic variation in HRP-II, alternatives for *falciparum* detection are needed.

Round 5 of testing is now under way and should be completed by the end of 2013, with a report available in early 2014. One notable change to the programme is a new requirement that manufacturers resubmit their tests to product evaluation every five years in order to continue being listed in the Product Testing Report and be eligible for WHO procurement. This means that 22 tests originally evaluated in Round 1, and not subsequently reevaluated, must participate in Round 5 to remain listed in the Product Testing Report.

In 2012, FIND received a grant from UNITAID to continue the Product Testing Programme and to transition it to recombinant-based panels as opposed to the expensive human derived samples currently used. The transition is expected to reduce reliance on donor funding by lowering the cost of product testing and introducing a user fee. Additionally, it should improve the turn-around-time for product testing and create a common standard in the market for RDT performance evaluation and quality control (QC) activities. The recombinant technology has been in development for several years and its equivalency to the current product testing panels is being evaluated. The transition to recombinant technology and changes to the programme will take place from 2013 to 2016 and will involve consultation with stakeholders and manufacturers. It is expected that recombinant QC panels will be available for manufacturer purchase and to country programmes for QC activities (e.g. lot testing at national reference laboratories as opposed to international reference facilities).

There are limited QC activities in the field; in particular, there is little information on RDT quality and stability after tests have been distributed beyond the central level. At the central level, lot testing is required by donors and is increasingly common. In 2012, 567 lots underwent testing through the FIND WHO Lot Testing Programme, an increase of 55% over the previous year²² and represents an estimated 30–50% of all RDT lots produced. This programme is designed to detect major flaws in RDTs, and the vast majority of RDTs pass.

Positive control wells (PCWs) are QCs for malaria RDTs intended for use at the point of service to check that RDTs are working acceptably. FIND is developing PCWs based on recombinant antigens that are undergoing field trials to demonstrate that they are technically sound and well adapted to end-users. Results of these trials are expected in late 2013, and the WHO Policy Malaria Advisory Committee (MPAC) is expected to review the evidence on PCWs in 2014.

Although the WHO PQ Programme is reviewing malaria RDTs, only two RDTs are WHO prequalified and this programme does not yet have an impact on RDT procurement. Although the concept of stronger upstream quality standards (i.e. dossier review, site inspections) is generally accepted by donors, policy-makers and manufacturers, malaria RDT manufacturers have not been progressing through the PQ system. For RDT suppliers, achieving PQ status has been a challenge, often requiring multiple inspections and additional investment in quality systems and staff. In 2012, Notices of Concern issued by the PQ Programme for two dominant manufacturers caused some apprehension in the market. The slow pace of progress and lack of clarity on PQ processes and when PQ status becomes a standard for RDT procurement are growing concerns. The current PQ timelines and uncertainties also create a disincentive for investment in new capacity and innovation, both for potential new entrants and for existing suppliers.

22 FIND malaria RDT lot testing results website (http://www.finddiagnostics.org/about/what_we_do/successes/malaria_rdt_lot_testing_results/).

Adaptability

In general, the process for performing an RDT is similar across brands: a drop of blood is transferred to the test, after adding buffer and waiting 15–25 minutes results appear as a visible line. However, among different manufacturers there are differences in the format of the RDT, labelling, components included in the test kit and the test procedures. These differences can present a challenge for test operators who often need to be familiar with more than one product type, for example, when multiple products are deployed in a country or when a programme wishes to change products. The RBM Procurement and Supply Management Working Group is supporting work by the Institute of Tropical Medicine in Belgium to further analyse the degree of similarity between RDTs and to assess potential options for harmonizing RDTs so as to improve quality, user-friendliness and ease of switching between products.

Market landscape summary

In summary, malaria RDT competition remains intense, characterized by: (i) buyers who have limited ability to monitor and differentiate product quality; (ii) strategic pricing by suppliers to gain market share/penetrate new markets; and (iii) competition around price, lead times and logistics. The declining margins for malaria RDTs are increasing the relative importance of economies of scale. The first signs of supplier exit are emerging, with at least one supplier reporting capacity reductions.

While competition continues to drive prices lower, the sustainability of these prices (e.g. US\$.25) is a risk to the RDT market and leads to cost reduction efforts on the part of suppliers. However, gains are minimal in light of limited leverage with their input suppliers and limited sources of monoclonal antibodies and quality nitrocellulose. In some markets, there is a move to automation to reduce labour costs, increase capacity and improve quality. In other instances, manufacturers are shifting production to lower-cost labour environments and/or locations closer to customers. Given the limited ability of the market to monitor quality, and current market conditions, there is risk of product quality deterioration and of quality suppliers exiting the market.

The private sector represents a significant market in many countries given how many people access treatment for fever there; however, developing these markets is challenging, given limited awareness of diagnostics among providers and consumers as well as the likely affordability issues. In addition, because a large proportion of customers would not have malaria, finding the appropriate incentives for retailers to offer testing and appropriate treatment/referral for non-malaria fever will be important to ensuring uptake of tests and good health outcomes.

With respect to quality, the majority of donors, policy-makers and RDT suppliers believe that the market would benefit from additional quality standards; however, the current format of WHO PQ is problematic due to several factors, chief among them: (i) uncertainty about when PQ will be required by major RDT buyers; (ii) lack of clarity on the PQ processes and standards; and (iii) limited experience of RDT manufacturers with rigorous quality reviews such as WHO PQ. The uncertainty, along with the lengthy timelines for both PQ and product testing, create disincentives for innovation as well as investment in new capacity.

Market shortcomings

Table 1 summarizes the market shortcomings in the malaria diagnostics market and reasons for these shortcomings.

Table 1: Market shortcomings in the malaria diagnostics market

Market shortcoming	Description of market shortcoming	Reason for market shortcoming
Quality	No practical QC technologies for RDTs: current programmes for malaria RDT QC are expensive and complex due primarily to reliance on human derived specimens; suitable replacements for human derived specimens (i.e. recombinant antigens for QC) have yet to come on the market	<ul style="list-style-type: none"> • Little incentive for private sector investment in QC technologies • Little prioritization and/or awareness of need for QC by buyers, donors and policy-makers, in particular as the RDT market was first developing
	Limited information on the quality of malaria RDTs; the market has little ability to monitor product quality, in particular manufacturing and field-level quality ¹	<ul style="list-style-type: none"> • No formal regulatory and postmarket surveillance processes in resource-limited countries that consume RDTs; no incentive for manufacturers to undergo an alternative stringent regulatory process (e.g. United States Food and Drug Administration) • WHO PQ not functioning optimally: slow progress; standards unclear • Limited experience of RDT suppliers with robust quality standards due to lack of regulations in markets where RDTs are produced or sold • Suppliers reluctant to invest in stronger quality management systems due to thin margins and inability of the market to recognize and value upstream quality • Market developed in absence of standards; buyers, donors and policy-makers did not initially prioritize QA/QC due to limited experience with diagnostics QA; lack of consensus on standards for QA • Practical QC technologies do not exist (see above)
Delivery	Uncertainty about consistent uninterrupted supply of quality RDTs in light of rapid increases in demand, market consolidation and intense price competition	<ul style="list-style-type: none"> • Uncertainty about scale-up manufacturing quality systems commensurate with rapidly scaling production, especially in light of large orders and short delivery time frames • Uncertainty about the effects of cost-reduction measures on quality taken by suppliers in response to price competition • Market consolidation increases reliance on a handful of suppliers, thus quality issues at a single manufacturing site (e.g. product recalls) could result in major market disruption • Thin margins and the market's relative inability to monitor quality create little incentive for supplier investment in manufacturing quality systems
	Compared to the global need for fever testing, insufficient uptake of diagnostics and concern about potential slowing of scale-up in the public sector	<ul style="list-style-type: none"> • Implementation weaknesses, including weak supply chain management, inadequate training of health-care workers, lack of supervision and QA • Insufficient investment in behaviour change communications to increase demand for testing and to improve awareness and acceptance of RDTs • Potential reductions in global funding for malaria that may limit diagnostic test budgets and the scale-up of malaria diagnosis

¹ While product testing and lot testing have shaped the market significantly, their focus is limited: product testing demonstrates manufacturers' ability to produce two high-performing batches of RDTs; it does not address the ability to manufacture quality batches at scale. Lot testing covers only 30–50% of the market and it aims to identify major deficiencies; standards are not as rigorous as product testing.

Market shortcoming	Description of market shortcoming	Reason for market shortcoming
	Little demand for RDTs in the private sector despite this being a significant market for treatment	<ul style="list-style-type: none"> • Lack of awareness among customers and retailers of benefits of diagnosis and of malaria RDTs • High prices of RDTs due to supply chain mark-ups • Limited incentives for private sector suppliers to sell RDTs • Customers may have limited incentives to purchase RDTs • Local regulations may prohibit performing RDTs in the private sector • Supply chain weakness; interruptions in supply of quality RDTs
	Insufficient information on malaria diagnostics markets to serve as an evidence base for market monitoring and to inform future decisions, including limited information on: access to testing; monitoring supply and demand dynamics; understanding potential private sector markets for diagnostics	<ul style="list-style-type: none"> • Intrinsic uncertainty about malaria incidence due to lack of investment in surveillance and weakness in case reporting systems • Few systems for aggregating information on RDT purchasing (donor or country level); where it is available (e.g. GFATM PQR), data may be unreliable • Large number of products (>200) on the market from many companies makes monitoring supply side difficult • Little dialogue between suppliers, policy-makers and purchasers to identify challenges and to provide qualitative insight into market issues • Complexity of the private sector markets for malaria commodities; limited research undertaken to date
	Inadequate malaria surveillance; diagnostics scale-up presents opportunity to improve data quality, in particular case reporting	<ul style="list-style-type: none"> • Historically, limited use of malaria diagnostic tests led to low-quality case reporting data,² resulting in de-prioritization of surveillance by programmes, donors and policy-makers • No clear guidance until recent (April 2012) WHO surveillance guidelines released • Need for coordination across different departments in the public health system to improve case reporting at the facility level • Weak implementation systems • Record keeping and reporting is often paper-based, little use of digital/information technology solutions
Availability	No tests for pregnant women, elimination settings and <i>P. vivax</i> (liver stage detection and POC G6PD test)	<ul style="list-style-type: none"> • Lack of TPPs and limited work to better define the needs or market for such products • Limited philanthropic and private funding for malaria diagnostics R&D • Malaria diagnostics are complex and costly to develop, in particular to evaluate performance • Lack of clarity regarding regulatory pathway and quality standards for malaria diagnostics, as well as the adoption process for global health products, creates uncertainty and risk at the investment level
Acceptability/adaptability	Low acceptance of RDTs, even when available RDTs may not be used, and negative results are often ignored	<ul style="list-style-type: none"> • Low awareness of declines in malaria prevalence and of benefits of diagnosis • Difficulty in changing long-standing clinical practices around fever and malaria • Lack of alternative diagnosis for non-malaria fever due to lack of training, protocols and diagnostics to assist with non-malaria fever • Low availability of commodities for non-malaria fever • Mistrust of RDTs; lack of QCs

² For example, health facilities might have reported the number of cases of malaria, but it would not be clear if these were “suspected” cases or “confirmed” cases (or a mix of the two). Suspected cases would overestimate the malaria burden.

Market shortcoming	Description of market shortcoming	Reason for market shortcoming
	<p>Suboptimal RDT adaptability:</p> <ul style="list-style-type: none"> • RDTs could be more consumer friendly to reduce training needs and ease difficulty in switching from one RDT to another • RDT kits may not be well adapted for retail channel sales 	<ul style="list-style-type: none"> • Specifications for improving ease of use and interchangeability have not been developed/communicated; little dialogue between buyers, policy-makers and suppliers • Optimal specifications for test kits sold through retail channels have not been developed
Affordability	RDT prices in the private sector are likely to be unaffordable	<ul style="list-style-type: none"> • Add-on costs (mark-ups, taxes, transport, etc.) throughout the distribution chain • Patients who test positive or negative must also be able to afford the appropriate treatment (ACT or alternative)

Opportunities for market intervention

There are a number of potential market interventions and opportunities to improve access to malaria diagnostics and contribute to better quality fever management in resource-poor settings. These include initiatives focused on assuring the quality of malaria diagnostic tests, improving delivery and availability of RDTs in the public and private sectors, supporting development of new technologies targeting populations for which current technologies are inappropriate, improving the acceptance of RDTs and increasing market knowledge. The following is a description of interventions that have recently begun to be followed by new opportunities.

Market interventions: work in progress

There has been a significant increase in malaria diagnostics market-shaping work in recent years. A number of projects that address the market shortcomings described above are already under way or are planned for the near future. The progress is notable, however, since in many areas, such as development of private sector markets for diagnostics, there is scope for additional work or refinement of existing programmes. Table 2 provides an overview of various market initiatives, many of which have been noted previously in this report.

Table 2: Planned and ongoing initiatives in the malaria diagnostics market

Description	Market shortcoming addressed	Lead implementer
Development of private sector markets for diagnosis and treatment	Delivery, affordability	<ul style="list-style-type: none"> PSI, CHAI Various pilots and operational research efforts (e.g. ACT Consortium, UCSF/ Society for Family Health, PMI)
Transition product and lot testing to more sustainable business model, including development of recombinant QC panels	Quality	FIND; WHO
Develop QCs for field use (PCWs)	Quality	FIND
RDT harmonization: review of RDTs currently on the market; development of optimal specifications and opportunities for standardization	Adaptability	Institute for Tropical Medicine (Belgium)
ACTwatch II: monitor uptake of ACTs and diagnostics	Market intelligence	PSI
ACT and RDT forecast	Market intelligence	UNITAID issued a request for proposal; implementer to be determined
Development of TPP elimination diagnostics	Availability	PATH
Development of TPP for POC G6PD test	Availability	PATH
Strategies to reduce pricing variability in the RDT market, e.g. longer-term supply agreements	Delivery	Major donors are planning to explore appropriate strategies in the coming year(s)
Mapping the market for malaria RDT raw materials (monoclonal antibodies)	Market intelligence	William Davidson Institute

Market interventions: new opportunities

Several examples of potential new opportunities for market intervention are described below, although this list is illustrative and not comprehensive.

Fund to achieve appropriate RDT:ACT ratios fund (near-term): market shortcomings addressed: delivery; acceptability; market intelligence

A fund for RDTs and ACTs that aims to accelerate the growth in demand for RDTs, thereby correcting the size of the RDT market relative to ACTs, and to develop intelligence for capturing data on what the “appropriate” ratio of diagnostics (RDTs + microscopy) to ACTs should be. Such a programme would include two components:

- Funding for procurement of commodities to be accessed by national programmes: for every 1 ACT, there must be > 1 RDT (as appropriate for the setting). Procurement of ACTs and RDTs though this fund would incorporate market-shaping activities to ensure affordability and sustainable supply of quality RDTs and ACTs. “Light touch” criteria would be in place to access funding, including demonstrated ability to absorb additional ACTs and RDTs and the existence of programmatic components to support case management, in particular activities aimed at raising awareness, uptake and adherence to RDTs.
- Funding for market intelligence data collection activities, either on a national scale or across representative geographies, seasons and settings (rural versus urban; hospital versus informal drug shop), that would provide insight into the appropriate ACT:diagnostic ratio (i.e. what is relative “demand” for diagnosis and ACTs in a particular market and how will these change over time) and would monitor progress towards appropriate case management.

Strengthening incentives for manufacturing quality (medium-term): market shortcoming addressed: quality

With respect to quality, stronger upstream incentives for quality are needed. Among possible interventions are strengthening of a programme such as WHO prequalification and/or adoption of alternative standards (e.g. revised CE mark requirements for malaria diagnostics are likely to be more stringent than existing ones) for diagnostics quality with a focus on the manufacturing level. This could be coupled with support to RDT manufacturers (mock inspections, dossier reviews, onsite technical assistance) who have relatively little experience with robust quality standards systems. In the near term, expansion or adaptation of the product and lot testing programmes to create stronger incentives might be beneficial.

PCW scale-up (medium-term): market shortcomings addressed: quality; availability; acceptability of RDTs

Currently, there is little QC of malaria RDTs in the field and, therefore, little information on their quality and stability after they have left the central level where lot testing can be conducted. This is due to the lack of practical tools to enable QC at the POS. PCWs are QCs intended for use at the health facility level to check that the RDTs are working acceptably. FIND has been developing PCWs, which are currently undergoing field trials to assess whether they are technically sound and well adapted to end-users. The WHO MPAC is expected to review the evidence from these trials in late 2014 and make a policy recommendation. Assuming a positive outcome, when they are available, a project to catalyse the adoption and scale-up of PCWs would involve funding for their procurement coupled with demand side work (e.g. local policy work, development of usage recommendations and end-user training).

Market intelligence projects (near-term): market shortcomings addressed: delivery; market intelligence

The lack of market intelligence in malaria diagnostics leads to uncertainty in the commodity markets, constrains management of programmes and limits monitoring and evaluation. There is a range of activities that would be meaningful to commodities markets as well as provide public health value. Among them are:

- Case management: data gathering efforts to better appreciate the uptake of malaria diagnostics; what the correct ratio of ACTs to diagnostics (RDTs + microscopy) should be; the extent of appropriate targeting of ACTs; and causes of non-malaria fever.

- Private sector: there is scope for a range of work to better inform development of private sector markets, for example: work concerning economic bundling and incentives for retailers to stock and sell RDTs and ACTs appropriately; better understanding of consumer demand, including willingness to pay; and further insight into effective demand generation/communication strategies.
- Supply side market intelligence: on the supply side, several experts prioritized an RDT-costing exercise that would inform negotiations about sustainable RDT pricing and enable a better appreciation of the costs associated with implementing robust manufacturing quality systems.
- Monitoring supply and demand: stronger systems for capturing and aggregating RDT procurement data (order size, price, lead time, shipping method, etc.) are needed to monitor trends in the market.

Surveillance: market shortcoming addressed: delivery

The scale-up of diagnostics represents a potential paradigm shift for malaria surveillance and programme management; however, at present the potential gains in these areas are not being realized. Currently, diagnostic test results are not plugging into data systems and, therefore, data-driven decision-making is not possible in malaria. Improved data on malaria are critical for programmatic decision-making, especially in a context of increasing focus on value for money. In addition, elimination of malaria is only possible when surveillance systems provide real time feedback on malaria cases. Although improving malaria surveillance would require significant programmatic work, there is likely scope for market intervention to accelerate adoption of technologies to streamline surveillance activities. Investment in this area could start with understanding the barriers, mapping of potential technical solutions and eventual scale-up of technology solutions to streamline data collection, reporting and analysis.

Improving fever management: market shortcomings addressed: delivery; acceptability of RDTs

It is thought that one of the primary reasons for poor RDT acceptance is difficulty in managing non-malaria fever. Clinical practice is difficult to change, and the 2010 policy of universal diagnosis represents a major paradigm shift for individuals who have for years been treating fevers presumptively as malaria. In addition, declines in malaria incidence and recognition that many fevers are not caused by malaria have catalysed work to improve the management of fever more broadly.

Commodity access is one of several challenges to improving fever management; significant programmatic work also will be required to improve outcomes, for example: refining algorithms for fever based on epidemiological studies of fever cause; improving referral systems; behaviour change communications; health worker training; and supply chain strengthening. Despite the need for programmatic work, it is worthwhile exploring potential market interventions aimed at improving fever management practices and acceptance of RDTs, for example, procurement of key commodities (e.g. RDTs, ACTs, antibiotics, oral rehydration salts, zinc) combined with market-shaping interventions to improve supply, adaptability and quality of these commodities might be beneficial. In the longer term, work to develop new products for non-malaria fever indications could start with studies to better understand causes of fever and thereby inform demand for new diagnostics, other products or new clinical protocols, as appropriate. This would be followed by development of TPPs, investment in R&D and comprehensive scale-up programmes when products come to market.

Market catalyst for G6PD testing and treatment for radical cure of *P. vivax* (medium/long-term): market shortcomings addressed: availability of POC G6PD tests; adaptability of medicine for radical cure

Vivax malaria is currently largely undertreated, primarily due to poorly adapted medicines (primaquine) for radical cure of *vivax* and the lack of POC diagnostic to rule out G6PD deficiency.²³ Both POC G6PD tests

²³ Two medicines are needed to cure *P. vivax* malaria: a drug to treat the blood stage infection (e.g. chloroquine or an ACT) and a drug to treat the liver stage infection which causes relapse. Currently, a 14-day course of primaquine is recommended for relapse prevention; however, it is grossly underutilized because: (i) it is not safe for people with G6PD deficiency and POC G6PD screening tests are not available; and (ii) compliance is low due to the length of the regimen. Extremely low utilization of primaquine has two consequences: at the individual level, relapse of a potentially severe illness occurs; and at the community level, onward transmission of *P. vivax* occurs. A new shorter course drug targeting the liver stage, tafenoquine, is currently being developed by GSK (2016–2017 launch). Although more acceptable to patients than a 14-day drug, tafenoquine will also be contraindicated in patients with G6PD deficiency and require G6PD testing.

and an improved medicine (tafenoquine) are in development. A scale-up programme for a radical cure of *vivax* would involve large-scale scale-up of G6PD testing and treatment across many countries and would aim to reduce prices for testing and medicines through economies of scale. The programme would include procurement of G6PD tests and treatments as well as programmatic work on policy, improving diagnosis of *vivax*, training health workers, communications and monitoring and evaluation. In some countries, there would be a significant private sector component.

Currently, PATH has an initiative to evaluate the G6PD pipeline and tafenoquine is being developed by GlaxoSmithKline (GSK) and Medicines for Malaria Venture. The work of PATH involves development of TPPs for POC G6PD tests, development of evaluation standards for G6PD products, setting operational research priorities and evaluating tests in the pipeline. Future work may include working with technology developers to optimize products in the pipeline. Currently, one POC RDT by AccessBio is in the late phase of development; it is undergoing evaluations, with results expected in late 2013. While there may be other POC G6PD tests in the development pipeline, none is as advanced as the AccessBio product. Tafenoquine is undergoing clinical trials and would launch in 2016–2017, though it is expected that it would not be marketed without a POC G6PD test.

Market catalyst: new high-performing malaria diagnostics (long-term): market shortcoming addressed: availability

The currently available diagnostic tests are not optimal for malaria elimination settings. Diagnostic needs for elimination settings include very sensitive POC tests for screening asymptomatic infections as well as high throughput tests for conducting large-scale surveys. The PATH DIAMETER project aims to further define the diagnostic needs unique to malaria elimination so as to enable development of cost-effective tests for these settings. The DIAMETER project includes development of use scenarios and TPP, landscaping and mapping technologies in the pipeline to the TPPs and development of laboratory evaluation standards. The TPPs are expected to be complete in 2014.

Currently, there are devices in the malaria diagnostic pipeline that may fit some of the needs for elimination settings (and possibly high endemic settings, e.g. POC devices that speciate and quantify parasitaemia, with minimal operator input). The extent to which these new products will be relevant depends largely on performance data, cost and the degree to which they are POC (i.e. require minimal training and little operator input and are durable). At this point, it is too early in product development to judge. In the longer term, market interventions in this area would involve funding or incentives for product development and scaling up new products as they come to market, including support for evaluations, procurement, policy work, supply chain planning and training of health workers.

Conclusions

While the use of RDTs continues to grow, given the overall need for testing, access to malaria diagnosis remains low, in particular in Africa where only 47% of patients in the public sector is tested and significantly fewer tested in the private sector. Further diagnostics scale-up and future demand for RDTs will depend on financing for malaria diagnostics: although half a billion RDTs are financed in African countries through 2016, sizable gaps remain. In the coming years, changes at GFATM and their impact on malaria budgets will be important to monitor. Given the lack of experience with private sector markets and uncertainty around funding for malaria programmes, demand from this sector is likely to grow at a slower pace unless large-scale interventions are made. At the same time, the market for malaria RDTs remains intensely competitive, with declining prices, increasing consolidation and the first signs of supplier exit. Given these conditions, and the market's inability to monitor RDT quality, continued supply of quality RDTs is at risk.

Recently, several malaria diagnostics market-shaping activities have begun, including efforts to address gaps in the quality of RDTs, plans to develop private sector markets and initiatives to increase market knowledge. Potential new opportunities include further work to increase the uptake of RDTs and to improve their quality. With respect to unmet needs in malaria diagnosis, preliminary market-shaping work has begun through the development of TTPs and preliminary market analysis for diagnostic tests for elimination and *P. vivax*. Surveillance remains a major gap in malaria management, and while diagnostics represents a game changing opportunity to improve the reliability of data, the potential gains in this area are not being realized. Due to the lack of reliable basic data on malaria (i.e. the number of fevers needing testing, positivity rates, treatment provided), it is currently difficult to assess progress in case management and to monitor markets for malaria commodities.

Annex: Update to donor and partner landscape

GFATM and PMI have been the primary funders of malaria diagnostic test procurement and as such their policies have a significant influence on diagnostic markets. This section provides a brief update on these donors.

GFATM

In connection with its 2012–2016 strategy, in 2012, GFATM adopted a new funding model that changes the grant application, approvals and grant management processes. The model is designed to help GFATM invest more strategically and provide countries with more flexibility with respect to timing and predictability around funding levels.

The model was launched in early 2013 and will be implemented in a phased manner until it is fully operational in 2014. To improve predictability, GFATM will indicate to each country the total amount of money they can expect, called “indicative funding”, which is based on disease burden, need, ability to pay and other qualitative factors. GFATM will provide guidance on how this funding should be allocated among HIV, tuberculosis, malaria and health systems programmes; this guidance will be discussed during a country dialogue process. In addition to this funding, countries may receive further funding from a competitive pool for high-impact programmes (called “incentive funding”). In the new model, countries will apply for funding on a rolling basis, as opposed to the rounds-based system. Country dialogue forms the basis of a concept note, which is the new process of applying for a grant, with opportunities for early feedback from GFATM to ensure that the programme is technically sound and to increase the likelihood of success. In addition, early involvement of GFATM during the application process will help minimize delays in programme implementation once the grant is approved.

Also, as noted above, the GFATM Board decided in late 2012 that AMFm operations will be integrated into the routine grant-making programme and will no longer operate as a separately funded programme.

GFATM is the leading funder for malaria RDTs; in 2010, 5.2% of its malaria programme grants was used for diagnosis, including RDTs.²⁴ With respect to quality, the GFATM current RDT selection criteria are in line with WHO procurement recommendations and it maintains a list of eligible RDTs on its website. With respect to procurement, the GFATM Voluntary Pooled Procurement (VPP) mechanism reports that it procured 41 million RDTs in 2012 and expects to procure > 50 million RDTs in 2013. Because RDT prices are falling, the value of VPP procurement is not growing as rapidly. Current priorities for VPP include concern about pricing variability and standardization of RDTs to improve interchangeability and competition. VPP also has found that procurement planning can save significant costs, in particular when sufficient lead times allow for shipping by boat instead of air. In the future, VPP is likely to explore long-term supply agreements for malaria RDTs.

PMI

PMI performs malaria RDT procurement on behalf of countries, primarily through the United States Agency for International Development (USAID) DELIVER project. Currently, the PMI criteria for RDT quality are in line with WHO recommendations; in addition, manufacturers must agree to pre-shipment lot testing. PMI reports that the volumes of RDTs procured are increasing: in fiscal year 2012, it procured nearly 29 million RDTs,²⁵ and it expects to procure even more in 2013. PMI maintains a list of preselected RDT suppliers through an expression of interest process. Like VPP, PMI also is concerned about pricing variability for similar products and is considering new procurement strategies.

As noted above, in 2012, PMI awarded the Malaria Care technical assistance contract to PATH as well as to PSI, Save the Children and Medical Care Development International. The focus is on scale-up of diagnosis and case management at the facility and community levels, in both the private and public sector; QA of laboratory services; and improving the capacity of clinicians and community health workers to manage

24 Zhao J et al. Adoption of rapid diagnostic tests for the diagnosis of malaria, a preliminary analysis of the Global Fund programme data, 2005–2010. *PLoS ONE*. 2012;7(8):e43549.

25 GFATM Supplier Meeting. ACT and RDT procurement (presentation). Geneva, PMI; 10 July 2013.