act for performance

End of Project Evaluation of the Foundation for Innovative New Diagnostics (FIND) project on sustainable Global and National Quality Control for Malaria Rapid Diagnostic Tests (RDTs)

Evaluation report

Submitted to :

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LIST OF ACRONYMS

ACT	Artemisinin-based Combination Therapy
CDC	Centres for Disease Control and Prevention
DMR	Department of Medical Research
EQA	External quality assurance
FIND	Foundation for Innovative New Diagnostics
GF	The Global Fund to Fight Aids, Tuberculosis and Malaria (Global Fund)
GTS	Global Technical Strategy for Malaria 2016-2030
HarT	MRDT Harmonization Task Force
HTD	Hospital for Tropical Diseases
IPC	Institut Pasteur du Cambodge
LT	Lot testing
mRDT	Malaria rapid diagnostic test
MoH	Ministry of Health
MoU	Memorandum of Understanding
MSF	Doctors Without Borders
NCE	No-cost extension
NMCP	National Malaria Contol Programme
PMI	President's Malaria Initiative (PMI)
PT	Product testing
QARDT	Quality assurance rapid diagnostic test
RITM	Research Institute for Tropical Medicine
RDT	Rapid diagnostic test
UoL	University of Lagos
WHO	World Health Organization
WHO/GMP	WHO Global Malaria Programme
WMR	World Malaria Report

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Our sincere appreciation is extended to all of the experts and other associated partners who generously gave their time to answer our questions. The evaluation team acknowledges the support and advices provided by Unitaid regarding the approach, findings and recommendations of this evaluation, as well as the oversight and direction provided.

EXECUTIVE SUMMARY

The purpose of this evaluation was to conduct an end-of-project evaluation of the Foundation for Innovative New Diagnostics (FIND) project on sustainable global and national quality control of malaria rapid diagnostic tests (mRDTs).

Starting in 2013, Unitaid provided support to FIND and to other collaborative partners such as WHO to establish sustainable standards to ensure quality-assured malaria RDTs used to support rational treatment of malaria in endemic countries (grant of $US 9.4 million).

The project involved 12 countries : Ethiopia, Uganda, Republic of Tanzania, Kenya, Madagascar, Rwanda, Mozambique, Malawi, Zimbabwe, Myanmar, Cambodia and The Philippines, and aimed to produce four outputs:

i. product testing and evaluation, implemented with manufacturers;
ii. RDT lot-release and field deployment, implemented and based on lot-testing data and performance findings;
iii. introduction of operational malaria recombinant antigen-based RDT product testing programme, funded by manufacturers;
iv. market created for malaria RDT quality control, based on recombinant antigen technology.

This evaluation provides a learning opportunity for Unitaid and the partners, and reports on the implementation of the project, with a particular focus on the project's overall progress and impact. The objectives are:

- Assess the programmatic implementation of the project, with a particular focus on the project's overall progress and impact achieved against set objectives and where possible against Unitaid's strategic key performance indicators;
- Assess the sustainability of the RDT quality process going forward both for manufacturer's Product testing (PT) and Lot testing (LT), and the use of recombinant panels;
- Formulate lessons learned and provide realistic and pragmatic recommendations to introduce possible general and specific improvements.

This evaluation was executed remotely, on the basis of a desk review of key documents; and telephone- and skype-based semi-structured interviews with key stakeholders such as Unitaid and FIND staff, staff of the collaborating institutions, and staff of organizations involved in field deployment and within the sample countries.

Key conclusions

The project realized most of its objectives and contributed to Unitaid's overall mission to maximize the effectiveness of the global health response by catalyzing equitable access to better health products.

The grant was implemented successfully and the targets were achieved, except the target of having malaria endemic countries conducting their own LT according to quality standards/practices, which was partly achieved.

The high level of commitment of FIND and the collaborative partners involved, including the country authorities, was identified as the principal positive factor for the success of the project.

National authorities supported the project. Regular stakeholder meetings were held, including

representatives of the national malaria control programmes. Some countries assigned national staff to the project.

Budget realignment proved to be challenging and lengthy, but project management communicated regularly with all stakeholders, hence doing the maximum to avoid further delays.

The evaluation team observed a lack of unified approach among the major partners (WHO, GF, PMI, UNICEF) on the requirements and management responsibility for RDT lot testing going forward. For instance, one of the major procurers of RDTs, the Global Fund, no longer requires pre- or post-shipment lot testing and is not longer interested in continuous sponsoring of the LT effort. There is also a clear need to improve the coordination of mRDT procurement at country level, to avoid the confusion created by coexistence of different malaria products in circulation.

Overall, the project had a positive impact on the market for products used to diagnose malaria by improving quality of diagnostics and significantly reducing the cost of RDT LT and the unit cost of PT per product evaluated. The cost of PT was reduced by more than half compared to the target costs and LT costs reduced from $683 in 2013 to $ 388 in 2015 while using frozen sample and are estimated to fall to $251 when recombinant panels would be used.

Partner countries strengthened their capacity to conduct lot testing of malaria RDTs with support from FIND, especially by improving technical know-how (e.g laboratories), by access to better tools and by reducing costs.

The project also contributed to overcoming market barriers to quality and supply & delivery of mRDTs. Due to product and lot testing, improved quality assured malaria RDTs became available on the market and significantly increased their market share. Only supply & delivery wasn’r fully achieved as the project countries had not begun performing their own lot testing.

The impact of the product evaluation programme on the market was significant. Given that the RDT technology was already available, the project notably improved clinical efficiency, reduced cost and better met the needs of stakeholders (users). The project clearly steered buyers toward high performing products at better costs. Donors have adopted the approach which clearly shifted market share. The strong engagement of all stakeholders involved, including local authorities, is an indicator for the success of the project in this respect.

In the long term, the project will have an important impact on health system strengthening because the project contributes to the long-standing malaria programmes in malaria endemic countries.

Sustainability of the project’s results has been fostered by a satisfactory buy-in by stakeholders, through capacity building, knowledge sharing, bringing technical knowhow, and communication. PT is now partially supported by fees from the manufacturers, however, a fully self-sustaining capacity for PT and LT via sole funding by user fees, was not achieved regardless of the corrective measures undertaken during the project lifespan.

In a sense the project appeared to be a pilot project, and produced a variety of lessons learned, spanning from technical complexity (e.g. recombinant panels), to coordination challenges (many stakeholders in many countries working together), and RDT market and procurement practices.

Recommendations

The recommendations of the evaluation team are based on their findings and conclusions:

R1 We recommend new funding which is required to sustain the achievements of the project.

R2 We recommend Unitaid and its main implementers, FIND and WHO, to initiate discussions on the harmonization of procurement procedures, in particular with NMCP/MoH in the countries, and with the major procurers, especially UNICEF, MSF, PMI, and GF. These discussions should lead to strengthened communication and coordination between NMCP/MoH and the major procurers.

R3 We recommend Unitaid and WHO to continue pursuing consensus on malaria RDT lot testing. In particular, discussions should be held with GF to improve coherence and coordination.

R4 We recommend WHO to share with the project countries the WHO resolutions from the July meeting results and to urge NCMP/MoH to disseminate these resolutions among the relevant actors in the field.

R5 We recommend to adopt a decentralized modality for lot testing and WHO should develop clear guidelines for a country on how to implement this modality, and develop certification standards for the laboratories.

R6 We recommend Unitaid and WHO to support country-based impact studies, and importantly, if possible, to identify averted deaths due to RDT use.

1 EVALUATION MANDATE

1.1 Introduction

Unitaid has mandated ACT for Performance to conduct an end-of-project evaluation of the Foundation for Innovative New Diagnostics (FIND) project on sustainable global and national quality control for malaria rapid diagnostic tests (mRDTs) in order to assess the implementation of the project with a particular focus on the project's overall progress and impact.

Since 2013, Unitaid has provided support to FIND as the lead implementer and to other collaborative partners such as the World Health Organization (WHO), the Hospital for Tropical Diseases (HTD), the Centres for Disease Control and Prevention and the RDT LT labs in the Philippines and Cambodia to implement a project on sustainable global and national quality control for malaria rapid diagnostic tests (grant of $US 9.4 million). The goal of the project was to establish sustainable standards to ensure quality-assured malaria RDTs are increasingly used to support rationale treatment of malaria in endemic countries.

The five-year project terminated December 31, 2017 and the donor agency, Unitaid, expected the evaluation to demonstrate Unitaid's impact, to assess accountability and support direction-setting, and to provide clarity on Unitaid 's role and mandate within the Global Health space.

The evaluation took place between March and May 2018, and was based on a review of the available documentation as well as on consultations with Unitaid, WHO, FIND and associated partners. The report describes the evaluation objectives and scope, the methodology of the evaluation, and presents the evaluation findings, conclusions and recommendations.

The annexes include the evaluation framework, the list of stakeholders interviewed and a bibliography.

1.2 Evaluation objectives and scope

The overarching evaluation question refers to Unitaid's mission: what is the progress made towards the achievement of results at the impact, outcome and output level. The objectives of this evaluation were:

- Assess the programmatic implementation of the project with a particular focus on the project's overall progress and impact the project achieved against its set objectives and where possible against Unitaid 's strategic key performance indicators;
- Assess the sustainability of the RDT quality process going forward both for manufacturer's product and LT, and the use of recombinant panels and;
- Formulate realistic and pragmatic recommendations to introduce possible general and specific improvements.

More specifically, the evaluation assessed the progress made from two perspectives, (i) market impact (intentional and unintentional) of the products/services provided under the project agreements; and (ii) public health impact for the beneficiaries of the medicines, diagnostics and related products/service provided through the project.

The evaluation covered the total five-year project period (2013 – 2017).

2 PROJECT PROFILE

2.1 Project Description

The World Health Organization (WHO) recommends universal parasitological confirmation of all patients suspected of having malaria before administrering treatment, which is dependent on the availability of high quality diagnosis at all levels of the health system. Malaria rapid diagnostic testes (mRDTs) are a key tool for routine diagnosis of malaria. These portable and disposable tests are relatively simple to use, and do not require laboratory infrastructure. The variable quality of RDTs on the market poses a challenge for countries in choosing which product to purchase due to the absence of product and system standards. Poor quality mRDTs may lead to inappropriate treatments and most likely overuse of ACT.

This quality assurance project built on existing programmes that ensured (i) independent RDT product evaluation (product testing, PT), based on data concerning RDT performance against panels of cryo-preserved parasites obtained from febrile patients in endemic countries, and (ii) quality testing of individual RDT lots before distribution (lot testing, LT), through two lot testing laboratories in the Philippines and Cambodia, using the same panels of malaria parasites as in (i) above. The project aimed to transform these into standard and sustainable mechanisms using primarily recombinant antigen panels, but also retain some cultured and patient-derived parasite-positive and parasite-negative blood samples. Recombinant panels are cheaper to produce and do not require freezing for transport and storage, which leads to significant cost reductions. Despite original expectations that recombinant panels would be a one-on-one replacement for wild-type and culture-derived parasite samples, it became clear at the end of second year of the grant, in 2015, that due to the variable reactivity of RDTs with recombinant antigens, they could not replace wild type/culture-derived parasite samples in laboratory-based evaluations, but could. Instead, play an important role for lot verification.

The WHO-FIND Malaria RDT Evaluation Programme[1] has been funded primarily by Unitaid since 2013.

The goal of the project was to establish sustainable standards to ensure quality-assured malaria RDTs are increasingly used to support rational treatment of malaria in endemic countries. The project had four outputs and involved 12 countries: Ethiopia, Uganda, Republic of Tanzania, Kenya, Madagascar, Rwanda, Mozambique, Malawi, Zimbabwe, Myanmar, Cambodia and the Philippines:

- Output 1: Product testing and assessment implemented with manufacturers, and results disseminated;
- Output 2: RDT lot-release and field deployment implemented, based on lot-testing data and performance findings;
- Output 3: An operational malaria recombinant antigen-based RDT product testing programme, funded by manufacturers, introduced; and
- Output 4: Market created for malaria RDT quality control tools, based on recombinant antigen technology.

A set of concurrent activities were implemented over the course of this project to produce the outputs

[1] Unitaid, Malaria Diagnostics Landscape Update, 2015

described above.

Output 1 was expected to be realized through the continuation of product testing based on the current format, and the replenishment of the global specimen bank through field collections of appropriate clinical samples. The availability of samples is a prerequisite to PT.

Output 2 was expected to be realized through the continuation of reference laboratory-based lot-testing services and the replenishment of LT reference laboratory specimen banks.

The finalization of a new sustainable model to incorporate recombinant panels into RDT performance evaluations and the introduction of recombinant antigen panels to partially replace existing parasite-based panels in product testing were the activities leading to Output 3.

Finally, Output 4 was expected to be realized through the following activities: (i) Implementing new lot-testing methods based on recombinant antigen panels in key national laboratories in low-income countries; (ii) Support RDT manufacturers in use of new recombinant materials for internal quality control; (iii) Prepare the required product specifications documentation for a review by the WHO Expert Committee on Biological Standardization (ECBS); (iv) Transfer of responsibilities for recombinant antigen panel quality, storage and distribution to ECBS and affiliated laboratories; and (v) Advertise availability of recombinant antigen panels and monitor uptake. Some of these activities are linked to more than one output.

FIND and WHO/GMP shared technical oversight of the project, and along with the implementing partners CDC, HTD, RITM, IPC and other reference laboratories supported by FIND in India, Nigeria and Peru, ensured the implementation of the project activities. The overall budget was US$9.4 million shared between FIND (US$6.2 million and WHO (US$3.2 million), with the staff budget representing about 45% of the total project budget.

2.2 Project Stakeholders

Seven groups of stakeholders involved in the project were contacted during the evaluation:

- Donor (Unitaid).
- Project lead implementer (FIND).
- Collaborating implementers: WHO/GMP, HTD, CDC.
- Partner countries for RDT LT (IPC Cambodia, RITM Philippines).
- Partner countries for sample collections (UPCH Peru, UOL Nigeria).
- Project beneficiaries for decentralized RDT LT in a sample of countries selected from the 12 project countries: Myanmar for South East Asia; and Uganda for East Africa. The evaluation team initially selected Mozambique for Southern Africa but didn't manage to reach beneficiaries in this country.
- Other partners (countries interested in RDT LT but not formally included in the grant's scope).

3 EVALUATION APPROACH

3.1 Evaluation approach

The methodology was designed to respond to the issues presented in the Terms of Reference (ToR), and to accommodate the short timeframe.

Two methods of data collection were used to collect relevant and useful data with which to address the evaluation questions, as requested in the ToR: the evaluation work was done remotely, on the basis of a desk review of key documents, telephone- and web-based semi-structured interviews with key stakeholders such as Unitaid and FIND staff; staff of the collaborating institutions; and staff of organizations involved in field deployment and within the sample countries. Data was also collected by e-mail to capture the views of the country authorities on the project, especially regarding their involvement in the project design, implementation, and monitoring.

Three countries were selected to be interviewed: Myanmar for South East Asia, Uganda for East Africa (with the possible alternative of Kenya and Tanzania) and Mozambique for Southern Africa. The selection was based on a review of available files and reference documents, discussions with Unitaid, and the following four selection criteria: (i) Geographical area (South East Asia, East Africa and Southern Africa countries); (ii) Incidence and prevalence of malaria; population size ; (iii) Countries where lot-tested malaria RDTs were distributed, according to information provided by requesters.

The evaluation framework was organized according to the evaluation criteria and related questions of the ToR (see below and in more detail in Annex A). A questionnaire was developed based on the evaluation framework and customized by group of stakeholders: (i) Donor (Unitaid); (ii) Project implementer (FIND); (iii) Collaborating implementers (WHO/GMP, HTD, CDC); (iv) Partner countries for RDT LT (IPC Cambodia, RITM Philippines); (v) Partner countries for sample collections (UPCH Peru, UOL Nigeria); (vi) Project beneficiaries for decentralized RDT LT (sample); (vii) Other partners (countries interested in RDT LT but not formally included in the grant's scope). All the interviews were conducted except in Mozambique's where the stakeholders couldn't been reached in the short timeframe.

The evaluators conducted an analysis of all reference documents and interviews based on the evaluation framework questions and indicators. Lines of evidence were produced for each evaluation question/indicator and evaluation criteria, to allow for triangulation analysis.

The ToR also required the team to assess the impact of the project on public health, using "severe malaria cases and subsequent death avoided" and "reduced costs of ACT in national malaria programmes" as criteria. However, this turned out not to be possible due to the non-availability of sufficient health facility data, and also because the project impact is difficult to distinguish from other parameters and variables that influence the outcome (treatment) of malaria case management, such as the availability of severe malaria case management, the availability of treatment, and early case detection. Moreover, an assessment of public health impact was not part of the project activities themselves and relevant data were thus not collected by the project team during implementation.

The evaluation team assessed three levels of impact of the project with data collected from a desk review and interviews, i.e., (i) direct impact – the benefits achieved during the project period; (ii) long-term projected impact – the benefits likely to be achieved after the project has ended thanks to the

work of Unitaid; and iii) unexpected impact.

The direct impact was assessed with the updated project logframe impact indicators, such as: number and percentage of malaria endemic countries conducting their own LT according to quality standards/practices; percentage of the global RDT public-sector market reported to WHO that has been lot tested; and the market share of RDTs meeting WHO procurement criteria (from at least the 17 major suppliers).

The resulting health impact has then been assessed according to the contribution to the Unitaid sub-strategic key indicators (increasing public health impact)[2], as indicated in the project logframe: Key Performance indicators (KPI): Area 1: Impact of Unitaid on the market for malaria diagnostic products; KPI Area 1, action 3: Improve quality of medicines, diagnostics and related products.

3.2 Evaluation criteria

The OECD/DAC criteria against which this evaluation was conducted are Relevance, Effectiveness, Efficiency, Impact and Sustainability. Learning was an extra cross-cutting dimension of the evaluation.

The team assessed the relevance of the grant relative to the mission of Unitaid and its strategic objectives. Under the effectiveness dimension, the achievement of outputs was assessed both quantitatively based on the project logframe (desk review) and qualitatively (by interviews). A light Value-for-Money approach was included in the evaluation framework under the criterion Efficiency. As requested in the ToR, a particular focus was put on the impact and the sustainability of the RDT quality system going forward, both for manufacturer's product evaluation and LT, and the use of recombinant panels. The project impact was assessed by providing a plausible story for what would have been the situation without Unitaid support (see sections 4.2 on Effectiveness and 4.4 on Impact).

3.3 Limitations and mitigation factors

Limiting factors and risks for the evaluation were as follows:

- The very short timeline of the evaluation limited the ability to reach a more extensive list of respondants, but the main and most relevant stakeholders were contacted. The beneficiaries in one implementation country, Mozambique, couldn't be reached.
- No field missions were expected for the evaluation, so interviews with stakeholders were done by skype, phone or email, which is less effective than face-to-face discussions.
- A full impact study was not possible to conduct in the short timeframe of this evaluation. As discussed, the estimation of the project impact was done based on a desk review and interviews (perceptions).

[2] In 2017, Unitaid's new strategy report on impact used the following indicators: KPI 1.1 Number of lives saved, number of infections or cases averted; KPI 1.2 Financial savings ($) + health system efficiencies ($) and KPI 1.3 Return on investment = $ benefits / $ costs.

4 EVALUATION FINDINGS

The sections below detail the findings of the evaluation according to the evaluation criteria of Relevance, Effectiveness, Efficiency, Impact, Sustainability and Learning.

4.1 Relevance

This section analyzes to what extent the grant contributed to Unitaid's mission and strategic objectives for 2013-2016 and 2017-2020, and was aligned with global priorities as defined by the WHO Global Malaria Programme.

4.1.1 Alignment with Unitaid's mission and strategic objectives 2013-2016 and 2017-202

Finding #1: The project was aligned with and contributed to the Unitaid's overall mission to maximize the effectiveness of the global health response by catalyzing equitable access to better health products.

The project was implemented across two Unitaid strategies: 2013-2016 and 2017-2020. Unitaid's mission statement in its 2013-2016 strategy aimed to increase access to treatment for HIV/AIDS, Tuberculosis and Malaria for people in developing countries by leveraging price reductions of quality drugs and diagnostics, which currently are unaffordable for most developing countries, and to accelerate the pace at which they are made available.

This strategy had six (6) objectives mainly focused on "increased access", to which the project was perfectly aligned (i.e. Strategic Objective 1: Increase access to simple, point-of-care diagnostics for HIV/AIDS, TB, and malaria)

The Unitaid Strategy 2017-2020 focuses on three strategic objectives: Innovation, Access, and Scalability. There are five access barriers under the three strategic objectives and the project addresses two key barriers i.e. quality, and supply & delivery.

4.1.2 Alignment with the WHO Global Malaria Programme[3]

Finding #2: The project was relevant and in line with the Global Malaria Programme, with National Malaria Control Programme (NMCP) strategic objectives, and with the WHO recommendations highlighted in the World Malaria Report.

This project contributed to establish sustainable standards to ensure use of quality-assured malaria RDTs, and is therefore aligned within the three time-bound milestones to accelerate progress towards malaria control and elimination:

- *WHO Guidelines for the Treatment of Malaria* (2015, Third edition) which comprise updated recommendations based on new evidence and focuses on prompt diagnosis and effective treatment;
- Roll Back Malaria Advocacy Plan, *Action and Investment to Defeat Malaria* (AIM) 2016-2030, which builds the case for investment in malaria;
- Sustainable Development Goals (SDGs), with Target 3.3 focused on AIDS, tuberculosis, malaria and neglected tropical diseases, a set of interconnected global goals agreed by the

[3] The 2017 World Malaria Report presents a comprehensive state of play in global progress in the fight against malaria up to the end of 2016.

United Nations member states as a "plan of action for people, the planet and prosperity" and;

The *WHO Guidelines for the Treatment of Malaria* and the advocacy plan *Action and Investment to defeat Malaria 2016–2030 (AIM)* that builds on the success of the first *Global Malaria Action Plan* for a Malaria free world (2008 - 2015) are aligned with the SDGs, with targets set for 2020, 2025 and 2030 (baseline of 2015). Achieving SDG Target 3.3 by 2030 is interpreted as the attainment of the Global Technical Strategy for Malaria 2016-2030 (GTS) and AIM targets.

The project focused its intervention on the RDT[4] for malaria, in line with WHO recommendations (since 2010); assuming appropriate treatment is provided, the intervention is effective to ensure that a mild case of malaria does not develop into severe disease and probable death. WHO recommends that every suspected malaria case be confirmed by microscopy and/or RDT before treatment. Accurate diagnosis improves the management of febrile illnesses and ensures that antimalarials medicines are only used when necessary. Only in area where parasite-based diagnostic testing is not possible malaria treatment should be initiated on clinical suspicion.

The World Malaria Report 2017 revealed that as many as 312 million rapid diagnostic tests were delivered globally in 2016 and that testing of suspected cases in the public health system increased in most WHO regions since 2010, with the African Region recording the biggest rise, as diagnostic testing in the public health sector increased here from 36% of suspected cases in 2010 to 87% in 2016 (WHO, 2017). This significant rise in RDT utilization points to the importance of procuring good quality RDTs to avoid misdiagnosis, which can have severe consequences in the population.

Box 1: World Health Organization procurement criteria for malaria rapid diagnostic tests

Products should be selected in line with the following set of criteria, based on the results of the assessment of the World Health Organization malaria PT programme:

(i) for the detection of *Plasmodium falciparum* in all transmission settings the panel detection score against *P. falciparum* samples should be at least 75% at 200 parasites/µL.

(ii) for the detection of *Plasmodium vivax* in all transmission settings the panel detection score against *P. vivax* samples should be at least 75% at 200 parasites/µL.

(iii) There should be less than 10% false-positive test results and less than 5% invalid results.

Only products meeting performance criteria outlined above are recommended for procurement.

A review of NMCPs or equivalent in all 12 participating countries of this project also shows the high priority countries give to access quality-controlled RDTs.

In a series of meetings of the RDT Evaluation Programme's Steering Committee, the procedures of RDT PT and LT were re-designed in 2015 and 2016 to build a cheaper system by: (i) partially replacing blood samples with recombinant panels for the country-based LT; (ii) replacing wild-type *P. falciparum* samples by culture-derived samples for the PT; (iii) reducing the overall number of samples required for PT; (iv) limiting heat stability testing to only 1 temperature; and (v) reducing the PT to only 1 phase of testing, instead of 2 phases.

In 2017 and 2018, WHO and CDC Atlanta concluded new contracts for the continuation of the PT activities. Specifically, GMP signed a short "bridging contract" for completion of the Round 8 testing in early 2018, then the WHO Prequalification of Diagnostics team, which is covering this activity, signed a larger contract covering the formal continuation of product evaluation activities at CDC under the WHO prequalification process.

[4] A new method to diagnose malaria – a rapid diagnostic test that uses monoclonal antibodies to detect malaria antigens in a drop of the patient's blood.

4.2 Effectiveness

This section reports on both the implementation and the achievements of the project in relation to the objectives, expected outcomes and outputs as described in the project plan. Table 1 and 2 below provide a detailed analysis of the outcomes and output indicators, as defined on the logframe and as reported in the final report[5].

Finding #3: Overall, the project succeeded as the planned activities produced the expected outcome of improved and affordable quality standards and practices for malaria RDTs to support quality control.

As shown in Table 1 below, most of the outcome targets were reached or exceeded (see final project report[6]). With respect to the second indicator however, the question is whether the countries are really ready to start their lot testing using recombinant panels. The analysis of data collected through interviews with stakeholders revealed that the tools and arrangements to allow LT were only implemented close to the end of the project, due to the delay in decentralising LT to national labs caused by the validation testing required to confirm the dependability of recombinant antigens. The countries received training and performed simulation of LT using recombinant panels, but without having the chance to apply the acquired knowledge on lot testing under a mechanism formally approved by WHO, to validate their procured RDT lots for in-country use.

The benefits of this achievement might be gradually lost as the trained staff may not have the opportunity to practice their skills on LT with recombinant panels if the grant (or another supporting mechanism) doesn't continue.

Table 1: Achievement of the project outcome indicators

Purpose (Outcome): Improved and affordable quality standards and practices for malaria RDTs to support quality control	
Indicators	**Comments**
1. Requested lots for which testing is completed	Fulfillment of 100% of the LT requests has been achieved throughout all the years of the project, thanks to adequate measures put in place to address various risks and difficulties,
2. Malaria endemic countries adopting LT schemes with recombinant panels	All tools and arrangements were satisfactorily completed to allow all the 12/12 project countries and 5/88 non-project countries (target was 3/88) to start their own LT using recombinant panels.
3. Unit cost of RDT LT	Cost estimations were conducted with a health economist, with costs data provided by CDC and the LT laboratories in Cambodia, the Philippines and Nigeria. Costs range from US$214 per lot in Nigeria to $445 per lot in Cambodia, being all well below the target of $609 per lot.

[5] FIND, FIND-WHO RDTs Quality Assurance Project Final Project Report (2013-17)
[6] FIND, FIND-WHO RDTs Quality Assurance Project Final Project Report (2013-17)

4. Unit cost of product testing per product evaluated	The cost per product for the year 2017 was US$10,876*, i.e. less than half of the target cost of US$25,000 (baseline of $50,000), and actually not too far from the US$8,678 ** fee paid by the RDT manufacturers for PT. This cost reduction was possible because of increased cost effectiveness towards the end of the project period, e.g. using samples stocks already built up in previous years, and running of the "old system" requiring less staff efforts than before.

Indicator 3. Estimates are based on LT with recombinant panels, as per instructions of the logframe. It should be noted however that the effective use of recombinant panels for future LT will depend on the WHO panels dossier review planned by mid-2018.

Indicator 4. Estimates are based on actual budget spent in 2017 for the PT as per the "old system" using frozen blood samples, as per instructions of the log-frame. If using estimates based on the "new" PT system, then costs are at 8,678 USD per product (more details in section 7. of the narrative above). Of note, both cost estimates do not necessarily reflect future CDC costs.

* Based on 2017 budget spent for frozen blood samples-based testing divided by number of products

** Based on estimated yearly budget for new PT system divided by number of products

Source: Data collected by the Evaluation team from the FIND-WHO RDTs Quality Assurance Project Final Project Report (FIND 2017), other project documents and interviews.

Finding #4: The grant was implemented successfully; all goal level targets were achieved, except that of having malaria endemic countries conducting their own lot testing according to quality standards/practices, which was partly achieved. Overall, the project produced about 75-80% of the four outputs within the planned timeframe and budget, according to the stakeholders interviewed and the team's desk review.

The project fully achieved outputs 1 & 2. Product testing was implemented with manufacturers, and the results disseminated as planned; RDT lot testing was implemented based on LT data and performance findings.

The project experienced delays regarding outputs 3 & 4, in particular rollout of LT decentralization to national laboratories, due to the late signing of the MoU with local laboratories and because of challenges in the development of the antigen-based recombinant panels, which prevented WHO to formally launch a recombinant panel-based LT scheme. All target countries have been provided capacity-building support and established the system to conduct RDT LT with recombinant panels. However, only two of the most experienced laboratories (Cambodia and the Philippines) were conducting lot testing at the end of the grant, and only RITM in the Philippines is currently conducting formal LT under WHO coordination, using frozen blood samples. The other countries would be ready to conduct LT using recombinant panels but this requires formal approval by a group of experts convened by WHO in July 2018.

To assure follow-up of this activity in 2018, Unitaid suggested that WHO use the funds collected from the product test fee (manufacturer fee), to try and cover the cost of about US$ 750,000. At the time of this project evaluation, the team couldn't verify the effective implementation of this additional support, which anyway was too limited to effectively complete the programme.

Notwithstanding the challenge with LT, the implementation of the grant was quite effective as most of the output targets were reached, as reported in the final report, confirmed by the interviews, and summarized in Table 2 below.

Table 2: Summary of the achievement of the project output indicators

Indicators	Comments
Output 1: Product testing and evaluation implemented with manufacturers, and results disseminated	
O1.1: % of met need for usable samples in WHO specimen bank to complete sample sets for fulfilment of Product Testing SOPs	Despite the constraint that samples had to comply with a predefined range of antigen concentrations, it has been possible to always comply with the 100% target of adequate samples available for PT (275/235 or 117%). In 2017, the target even had to be exceeded because the spread of the HRP2 deletion issue obliged to set up a new panel of 40 HRP2 negative Pf samples for Round 8.
Output 2: RDT lot-release and field deployment based on lot-testing data/performance report	
O2.1: Lots evaluated of all lots procured in the public sector in project countries	100% achievement but three countries did not report data in 2017 (Ethiopia, Kenya and Tanzania). After review of the log-frame in 2016, this indicator was reported as the number of lots tested (in-country or in one of the WHO-FIND laboratories) versus the number of lots procured in each country in that particular year, i.e. reflecting the proportion of effectively tested lots among the ones distributed.
O2.2: % of reports issued within 10 calendar days from RDT receipt	The targets of 90% in 2016 and 95% in 2017 were well achieved (Average of the 5 years is 88%). 856/1083 (79%) in 2013<X<747/760 (98,3%) in 2017.
Output 3: An operational malaria recombinant antigen-based RDT PT programme funded by manufacturers	
O3.1: RDTs from eligible manufacturers requested for participation evaluated through the old mechanism and funded through manufacturer payments	The targets of 80% in 2016 and 51% (28/55) of eligible products in 2017 were well achieved and even exceeded (Average of the 5 years 77%). The target was set lower in 2017 because participation in Round 8 in that year also involved mandatory application for the prequalification process, hence implying a much more demanding commitment on behalf of the manufacturers. Not reported in 2013-14-15. 46/55 (83,6%) in 2016 and 35/55 (63,6%) in 2017.
O3.2 RDTs from eligible manufacturers requested for participation evaluated through recombinant panels and funded by manufacturers fees	Targets (80% in 2016 and 51% of eligible products in 2017) and therefore exceeded achievements are the same as for indicator 3.1 above, given that both Rounds 7 and 8 involved testing via the “old system” with frozen blood samples AND included testing with recombinant panels, and both Rounds were of course subjected to payment of fees. Not reported in 2013-24-15. 46/55 (83,6%) in 2016<X<335/55 (63,6%) in 2017.

Output 4: Market created for malaria RDT quality control materials based on recombinant antigens	
O4.1: Target countries conducting their own quality control with recombinant panels	The 2017 target of 100% (12/12) project countries conducting their own LT with recombinant panels was not met. Only 2/12 or 16.7% of project countries (Cambodia and Philippines) and two other non project countries supported by FIND (Nigeria and India) achieved the tasks. Despite having completed all preparatory activities for all 12 countries to start their own LT based on recombinant panels (laboratory assessments, LT workshops, online database etc.), there has been no formal launch of recombinant panel-based testing in none of these, before the end of the grant. The reasons are essentially policy- and funding-related.
O4.2: % of met panel needs from manufacturers	HRP2 recombinant panels were shared with the 25 manufactures who are participating in Round 8, in 2016 already, and pv/pfLDH panels were shared with the same 25 manufacturers during 2017. This resulted in even exceeding the target of 17 manufacturers having received panels (25/17 or 147%).
O4.3: % of met panels need from countries	HRP2 panels were shared with 12 countries (10 project countries, plus Nigeria and Brazil) in 2016. Another set of panels, including HRP2, Pv pLDH and pf pLDH, was then shared in 2017 with a total of 14 countries (11 project countries, plus Nigeria, India, Indonesia, Papua New Page 31 Guinea) during two more LT workshops. The target of 12 countries in 2017 was therefore even exceeded (16/12 or 133%)
O4.4 Manufacturers engaged in WHO PT programme that are procuring panels	According to data provided by Microcoat, only one manufacturer out of the targeted 17 procured recombinant panels via the commercial channel (1/17 or 5,9%). It should be noted that HRP2 panels only became commercially available in September 2017, and Pv and Pf pLDH panels only in January 2018. Moreover, all major manufacturers had already received such panels for free, in 2016 and 2017 (see O4.3 above), so probably had no immediate need (one plate of panels provides material for a large amount of tests).
O4.5: Target countries whose national programmes are budgeting for RDT quality control	The targets of 16.7% in 2016 and 80% in 2017 were achieved and even exceeded: an average in the two years 2016-2017 of 86.5%: 8 out of 11 countries (73%) in 2016; and 9/9 or 100% in 2017.

Source: Data collected by the Evaluation team from the FIND-WHO RDTs Quality Assurance Project Final Project Report (FIND 2017), other project documents and interviews.

Output O1.1 reached the set target according to the project report notwithstanding challenging fluctuations (i.e. decrease) in the incidence of malaria cases in the targeted countries.

The project also successfully achieved output O2.1, which focuses on public sector procurement only. This could have caused a bias because in some countries the private sector has a substantial share of RDT imports, as reported by stakeholders. The project didn't have the capacity to engage effectively with the private sector, for which testing activities (more product flows) could be an incentive to bring better products to the market.

Development of the antigen-based recombinant panels was delayed due to a prolonged search for the ideal candidate recombinant gen to reduce the variable reactivity with RDTs and also due to various factors such as the complications that arose when with the company contracted to develop the panels was bought by another company while the project was ongoing.

The roll out of LT was planned towards the end of the grant, but the countries were not able to implement; this as WHO had not launched the decentralized LT system because of lack of enough funding and the absence of formal approval of the use of the panels by a group of experts. This affected the expected outcomes of the LT initiative at the country level. However, the final report of the project indicates that for LT decentralization, work was conducted since 2016 to sign contracts with LT pilot countries, select reference laboratories, and conduct workshops on LT using recombinant panels. The formal approval and implementation of such recombinant panel-based LT will, however, depend on a dossier review and WHO consultations planned for mid-2018.

Box 2: The Myanmar experience

«Although we tried our best, signing of the MoU was delayed in Myanmar until nearly the end of the project.

Therefore, the outputs cannot fully be obtained in Myanmar within this timeframe.

Fortunately, one staff was able to attend a testing training workshop before the end of the project.»

Source: Testimonial collected from the Evaluation interviews

There are concerns among the stakeholders that the benefits of the LT component of this project may not last long after the end of the project funding as there is no evidence that additional funding has been secured to maintain the LT activities (see section 4.5 on Sustainability).

Assuming that additional funding is secured in the future to support the LT activities at the country level, engagement by laboratory personnel might become an issue if the stringent budgets don't foresee incentives for them, such as performance allowances. More effort to understand local context when implementing such interventions is needed to ensure good level engagement and ownership by local laboratory staff.

Finding #5: The effectiveness of the project was influenced by a series of management and institutional factors. The high level of commitment of FIND and the collaborative partners involved, including the country authorities, was mentioned as the principal positive factor.

Positive factors that contributed to the project's success were:

- Regular communication through emails and teleconferences, and quality of personnel involved;
- Good coordination and working relationship between FIND and its partners;
- The Steering Committee with a range of good scientists was key to help in efficient and well-reasoned decision making;
- Terms of reference with implementing partners were very clear and specific.

Negative factors that hampered timely attainment of intended results:

- Issues with identifying the optimal recombinant candidates and the variable reactivity of recombinant panels with RDT products;

- Delays in signing of the MoU between FIND and project countries towards the end of the project;
- Global Fund did not adhere anymore to the LT programme, towards the end of the project, which makes continuation less likely;
- Interference by some manufacturers against PT, fed by their fear of strict quality control.
- Incidence variation of malaria cases throughout the year influenced the sample collection rate and rapidity.

All stakeholders commended the participative approach of the project with regular communication and prompt feedback by project managers whenever implementing issues arose. The ToR with partners for RDT LT and sample collection where found to be very precise, guiding the partners to conduct their activities successfully. Stakeholders also reported that they had enough budget to perform their work. The reference laboratories had personnel with much expertise, e.g. IPC, having a longstanding expertise with malaria.

As previously stated, technical issues such as antigen-based recombinant panels not reacting as expected and operational issues such as late signing of the MoU, affected the achievement of output 4. Another important factor was the interference by some manufacturers who had been enjoying an open market with little to no quality control standards. In some instances, negative reports about the LT and PT programmes were released by some manufacturers in Uganda, in an effort to discourage people from embracing the project.

Box 3: The Philippines experience

«The achievement of all the expected outputs /outcomes was primarily because of the mutual commitment of FIND and RITM, and regular communication through emails & teleconferences.»

Source: Testimonial collected from the Evaluation interviews

Finding #6: The logframe of the project, last revised in 2016, is well structured with well-defined components, activities, outputs, objectively verifiable indicators, sources of data and assumptions. Notwithstanding the project's logframe, the evaluation team observed the lack of a unified approach among the major partners (WHO, GF, PMI, UNICEF) on the requirements and management responsibility for RDT lot testing.

All changes in the project involved discussions with the Steering Committee; Unitaid attended nearly all meetings as an observer. The committee has to decide on follow-up issues regarding the future use of recombinant protein-based quality control samples.

The logic model of the project flows well from the set objectives/goals to the activities using the resources allocated. The indicators formulated are sound and measureable, with clear targets indicated as well as the data sources and assumptions. The vertical logic model displayed in the logframe responds to international standards and forms the base for the theory-of-change underlying this project.

The hierarchy of objectives reads logically from the bottom to the top, starting with the resources as input up to the goal. If the inputs are sufficient, as it is the case for this project, the activities can be carried out to produce the desired outputs, which will lead to the realisation of the expected outcomes to contribute to the ultimate goal of the project. Overall, the planned activites for this project are found to be consistent with the expected outputs, despite the unexpected complications with the development of the panels and the late roll out of LT in countries. Capacity building of the implementers through LT workshops at the level of the countries were crucial to obtain the benefits generated by the activities.

While there were clear transition plans and targets incorporated into the logframe, the project faced challenges in establishing an unified LT approach amongst the major procurers of RDTs. One of the major procurers, the Global Fund, no longer requires pre or post shipment lot testing and therefore is no longer interested in sponsoring the LT effort. Other stakeholders have serious concerns about decentralization of lot testing due to questions over the capacity to reliably carry out testing with appropriate QC materials. A multi-organizational RDT procurement task force, such as the Roll Back Malaria working groups, has been used as the appropriate 'body' to share all PT- and LT-related activities, throughout the five-year project, and more recently to discuss these differences in approaches and work through the LT transition challenges.

4.3 Efficiency

This section reports on implementation management and the use of resources. Where possible attention is also given to value-for-money of the activites implemented.

Finding #7: National authorities bought in to the project. Regular stakeholder meetings were held, including NCMP representatives. Uganda offered significant incentives to companies that complied with LT when procuring RDTs. Some countries assigned national staff to the project.

The project participants held regular meetings with stakeholders and the steering committee was active throughout the project. Representatives of national authorities were involved in those meetings, an indicator for country engagement with the project. In some countries like in Cambodia, staff from the National Malaria Control Programme was seconded to the local laboratories and assigned to project activities, which allowed them to benefit from the capacity building activities. In Uganda a tax cut was provided to procurers who accepted to go through Lot Testing; they paid 2% duty against 18% for procurers not going through Lot Testing.

Finding #8: Programme management proved to be efficient. All planned activities are implemented within the approved budget, and the overhead rate of 9% is relatively low[7].

The total expenditure of the FIND grant for the duration of the project was US$ 6,059,650 against a planned expenditure of US$ 6,191,375, a slight underspending of 2% which is quite good[8]. Moreover, expenditures were aligned with the planning as shown in table 3 hereafter. All planned activities were realized with the notable exception of country quality control with recombinant panels, an outcome that wasn't achieved.

Funds available at the end of the reporting period were US$ 50,553.84 (which corresponds to the total amount of cash received minus the expenditures).

[7] Standard project overhead is around 15%

[8] FIND, FIND-WHO RDT Quality Assurance Project Final Project Report (2013-17), p.34

Table 3: Summary FIND cumulative 2013-2017 Actual Project Expenses vs Approved Budget

(All costs in US$)	Approved budget	Actual Expenses	Variation	%
Travel & Meetings	421,250	482,784	61,534	115%
Consultancies	2,173,234	1,862,964	-310,269	86%
Commodities	126,000	132,077	6,077	105%
Supplies & Transport	839,500	1,111,553	272,053	132%
Staff costs	2,072,873	1,914,119	-158,754	92%
Operational costs	558,519	556,153	-2,366	100%
TOTAL	6,191,375	6,059,650	- 131,726	98%

Data Source: FIND-WHO RDTs Quality Assurance Project Final Financial Report (2013-17)

Table 4: Summary WHO/GMP cumulative 2013-2017 Actual Project Expenses vs Approved Budget

(All costs in US$)	Approved budget	Actual Expenses	Variation	%
Travel & Meetings	333,750	252,051	-81,699	76%
Consultancies	376,500	240,064	-136,436	64%
Supplies & Transport	107,500	44,844	-62,656	42%
Staff costs	2,152,790	1,576,485	-576,305	73%
Operational costs	279,862	204,943	-74,919	73%
TOTAL	3,250,402	2,318,387	- 932,016	71%

Data Source: FIND-WHO RDTs Quality Assurance Project Final Financial Report (2013-17)

The WHO/GMP portion of the grant's approved budget was US$3,250,402 of which 71% was spent, leaving an unspent balance of about US$ 857,096 at the end of the project. Most of the WHO/GMP budget was intended for staff expenses (66%) and the unexpended amount is mostly coming from that budget line as only 73% of the planned budget for staff was consumed. This was due to an unsuccessful attempt to fill a P3 position for the project in January 2017 and the subsequent decision of WHO/GMP senior management to opt for external consultants to support the project instead. However, no full-time permanent consultant could be hired to replace the P3. Following FIND's exit and Unitaid's refusal of the no cost extension, WHO has very little technical staff to dedicate to resolving outstanding issues and developing a new model of LT.

The project's administrative overhead represents about 9% of the total expenses. According to the

agreement between WHO/Unitaid and FIND[9], the human resources made available for the project comprise 11 FTE distributed among FIND, WHO, CDC and HTD. At FIND, for example, the FTE were distributed among 16 staff positions to various proportions. Only 92% of the allocated budget for staff was spent over the course of the project, which is an indication of efficient project management.

The overall financial analysis of the project combining FIND and WHO/GMP-approved budgets versus actual expenses confirms that the planned budget for output 4 was the most underspent. The budgets allocated to outputs 1, 2, 3 and 5, were fully consumed and the satisfory results observed for those outputs suggest that the project achieved value for money on those activities. Overall, 90% of the total grant budget was expended and the completed activities respected the budgetary limits.

Table 5: Summary FIND-WHO/GMP cumulative 2013-2017 per output

(All costs in US$)	Approved FIND budget	Actual FIND Expenses	Approved WHO budget	Actual WHO Expenses	Total Approved Budget FIND+WHO	Total Actual Expenses FIND+WHO	Variance %
Output 1	1,242,203	1,269,317	115,000	79,606	1,357,203	1,348,923	99%
Output 2	396,267	430,321	152,000	96,813	548,267	527,134	96%
Output 3	938,431	1,053,500	222,750	159,356	1,161,181	1,212,856	104%
Output 4	902,583	740,685	328,000	201,184	1,230,583	941,869	77%
Output 5	80,500	95,555			80,500	95,555	119%
Staff Costs	2,072,873	1,914,119	2,152,790	1,576,485	4,225,663	3,490,604	83%
Operational costs	558,519	556,153	279,862	204,943	838,381	761,096	91%
TOTAL	6,191,376	6,059,650	3,250,402	2,318,387	9,441,778	8,378,037	89%

Data Source: FIND-WHO RDT Quality Assurance Project Final Financial Report (2013-17)

According to various stakeholders, the project's efficiency could have been even better if civil servants assigned to the projects and working in local laboratories could have received financial incentives. The project engaged many consultants for short-term contracts while national staff didn't receive any additional remuneration for their contribution. The same observation goes valid for the training provided. Financial incentives would have fostered the engagement of national staff (civil servants).

Finding #9: Budget realignment proved to be challenging and lengthy. While Unitaid responded to budget realignment requests in a timely fashion, some requests required

[9] Agreement between WHO/Unitaid and FIND - Project plan, p.55

additional information and justifications leading to multiple iterations between the parties.

The difficulties in the development of antigen-based recombinant panels created delays for the rollout of the LT in countries, but on the other hand project management kept good proactive communication with all stakeholders, hence doing the maximum to avoid further delays.

FIND flagged in March 2017 the need to reallocate the budget lines, by submitting a budget realignment request to Unitaid, including a July – December expenditure forecast. It took to December 2017 and multiple discussions with Unitaid to get approval[10]. This may explain the underspending of the "output 4 budget", as the budget spent in 2017 was indeed lower than the previous years.

A total of 4 audits were conducted for the reporting years 2013, 2014, 2015 and 2016, reporting "nothing significant from auditors". A final audit for the year 2017 is currently in process.

4.4 Impact

This section reports on the impact of the project at three levels, (i) impact on the market (as requested by the ToR of this evaluation; (ii) public health impact[11], and (iii) long-term impact on health system strengthening[12].

Finding #10: The project had a significant effect on the global malaria rapid diagnostic tests (RDT) market, but on the other hand supported only a few malaria endemic countries in conducting their own lot testing according to WHO-FIND quality standards (e.g. recommended SOPs). The project increased the market share of RDTs that met WHO procurement criteria, from 80% in 2011 to 91% in 2017, in line with expectations in the project plan. The project also contributed to the improvement of the global RDT public-sector market that was lot-tested, although not up to the expected level, from 30-50% in 2012 to 71% in 2017 (project target was 80%).

Table 6 summarizes the results of the project on three impact indicators, defined by the logframe, and as reported in the final report[13].

4.4.1 Malaria endemic countries conducting their own Lot Testing according to WHO quality standards/practices

In 2017 four malaria endemic countries were conducting their own LT according to WHO quality standards/practices, whether using frozen blood samples or recombinant panels: Cambodia and the Philippines, two of the 12 participating project countries, and two non-project countries, Nigeria (University of Lagos) and India (National Institute of Medical Research). It is important to note that the laboratories in Nigeria and India were supported by other funding sources including technical support

[10] WHO/Unitaid and FIND Disbursement Recommendation Letter 04Dec2017

[11] Note that Unitaid in its new strategy has revised how public health impact is reported.

[12] Impact of Unitaid on the market for products to treat, diagnose and prevent HIV/AIDS, TB and malaria; and Improve quality of medicines, diagnostics and related products (FIND RDT project's logframe : the Unitaid sub-strategic key indicators KPI Area 1)

[13] FIND, FIND-WHO RDTs Quality Assurance Project Final Project Report (2013-17)

and on-site EQA visits (Unitaid grant for RDTs in the private sector for Nigeria, and Caritas funding for India).

Table 6: Achievement of the Goal/Impact FIND Project Indicators

Goal (impact) : Establish sustainable standards to ensure quality malaria RDTs are increasingly used to support rationale treatment of malaria in endemic countries	
Indicators	**Comments**
1: Malaria endemic countries conducting their own LT according to quality standards/practices	Only two countries, Cambodia and Philippines and two other non project countries supported by FIND and WHO, Nigeria and India, are conducting their own LT according to quality standards/practices, i.e. 16,7% and 67% of the project targets. Cambodia and Philipines were already included in the 2012 baseline (targets were 12/12 project countries and 3/88 nonproject countries). Other countries had the capacity set up to do so, but formal launch was not achieved in time. Considers LT according to recommended quality standards and practices, whether using frozen blood samples or recombinant panels. No countries applicable before panel roll-out implemented except Philippines, Cambodia. There is no target for non-project countries but progress has been monitored.
2. Global RDT public-sector market reported to WHO that has been lot tested	The 70 % results is the combined average of the 5 years project (2013-2017) which had a comparative range of 61.5% (2013) <X< 83,4 (2015). 2012 Baseline was approx. 30-50% (during 2012) and project target, 80%.
3. Market share of RDTs meeting WHO procurement criteria (from at least the 17 major suppliers)	The 91 % results is the combined average of the 5 years project (2013-2017) which had a comparative range of 90,8% (2016) <X< 93(2015). 2011 estimated baseline was 83% and target, 90 %. Data gathered by FIND directly from RDT manufacturers via successive RDT sales surveys in 2011, 2014 and 2016 show an impressive decrease of non-complying RDT products from 76.8% in 2007 to only 3.7% on 2016

Source: Data collected by the Evaluation team from the FIND-WHO RDTs Quality Assurance Project Final Project Report (FIND 2017), other project documents and interviews.

The FIND QARDT grant aimed to build capacity for in-country LT in all 12 project countries and in three other countries outside the project. Only 17% of the target was achieved for the project countries (2/12) and 67% (2/3) for non-project countries.

Various reasons explain these disappointing LT launching results, in particular technical delays (explained above) and lack of funds post 2017. According to our informants, no funding was available for overall LT coordination and activities related to a full transition, and WHO's request for a no-cost extension from Unitaid towards this end was refused, mostly because RDT procurers couldn't provide sufficient clarity and consensus about their needs for LT (e.g. continued testing or not, every lot or not etc.). To deal with the transition at the end of the Unitaid grant, WHO asked FIND to compile a dossier for a formal review of recombinant panels by a group of experts in order to determine whether these can be safely and accurately used to support lot verification. The dossier was yet not completed by the end of the project.

Actions to address these weaknesses were in progress when the evaluation team undertook the evaluation April 2018, and WHO was planning to make a formal decision on LT continuation in mid-year 2018.

4.4.2 Global RDT public-sector market reported to WHO that has been lot-tested

In 2017, 71% of the global RDT public-sector market reported to WHO was lot-tested, so the 80% project target was not fully achieved. However, we have to take into account the time-lag between the nominator (number of lots tested and lot sizes communicated in the reporting year, in this case 2017) and the denominator (most recent available RDT sale data, usually from the previous year, in this case 2016). As a consequence, if sales increased or decreased in a given year, then the LT coverage will likely be over- or underestimated, respectively.

The coverage of the global RDT market is thus somewhere in the range of 70-80%, with LT most probably covered by all large-size procurements done by the major in the public sector, given that all of them adhere to the WHO recommendations for malaria RDT LT, and some of them even include mandatory LT in their own policies for diagnostics QA.

4.4.3 Market share of RDTs meeting WHO procurement criteria (from at least the 17 major suppliers)

In 2015, 2016 and 2017 respectively, 93%, 90.8% and 90.8% of RDTs (sold by the 17 major suppliers) were meeting WHO procurement criteria. The target of 90% of globally sold RDTs complying with WHO recommendations has been slightly exceeded, demonstrating the success of the programme in shifting the RDT market towards a large majority of high quality products. Data gathered by FIND directly from RDT manufacturers via successive RDT sales surveys in 2011, 2014 and 2016 show an impressive decrease of non-complying RDT products, from 76.8% in 2007 to only 3.7% on 2016.

Finding #11: Unitaid, through this grant, has helped preparing the ground for less costly LT, pending the adoption of LT procedures using recombinant panels. After the official launch of this system, a significant reduction of the the cost of RDT lot testing can be realized, amounting to US$251 per lot, i.e. less than half of the target cost of US$609 per lot[14]. The unit cost of product testing is evaluated at an average US$10,876, i.e. less than half of the target of US$25,000.

Finding #12: The Unitaid grant also significantly contributed to an improved quality of diagnostics. An extensive impact evaluation of the Product Testing programme was done through two large RDT sales and procurement surveys. The sales data show that the market is increasingly dominated by two major manufacturers who produce well-performing products, while the share of others selling substandard ones (e.g. Orchid, ICT) decreased.

The FIND QARDT grant thus helped to overcome market barriers[15], particularly with respect to Quality, and Supply and Delivery. While the RDT technology was already available, the project drastically improved clinical efficacy, reduced costs, and better met the needs of users. The project overcame market barriers in three ways, (i) by improving quality assurance for diagnostics, strengthening and refining PT and by filling a specimen bank at CDC (permitting continuation of PT for many years); (ii) drafting an LT partially based on panels (waiting for approval); and (iii) reducing

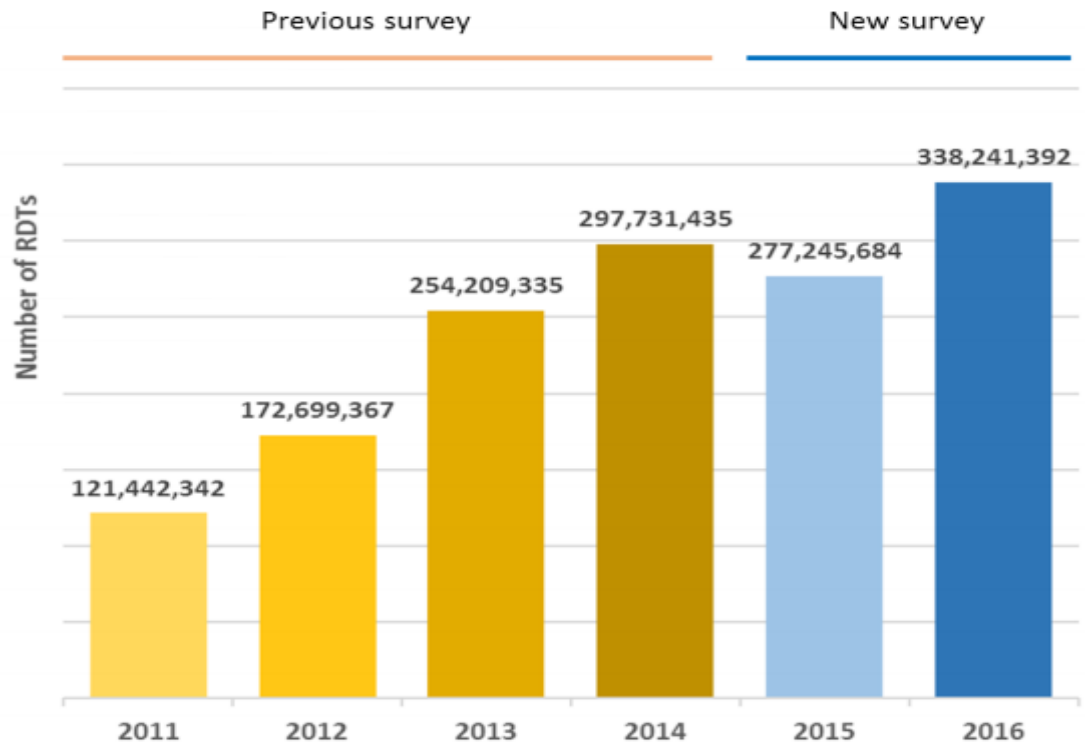
[14] FIND, FIND-WHO RDTs Quality Assurance Project Final Project Report (2013-17), p.20

[15] According to Unitaid strategy 201702021, market barriers are (i) Innovation and availability; (ii) Quality; (iii) Affordability; and iv) Demand and adoption and (v) Supply and delivery.

prices for PT & LT, which is likely to have a trickle-down effect on prices for procurers. RDTs price are now lower and therefore more affordable to all stakeholders.

These positive results were expected as the preceding funding from the Gates Foundation (BMGF) showed that the PT created a good impact on the market (i.e. shifting market share to high performing products). The figure below shows the increase in RDT sales.

Figure 1: Sales data on RDTs between 2011-2016



Source: FIND Malaria RDT Survey (2011-14) and FIND Malaria RDT manufacturers Survey (2015-16)

Surveys conducted by FIND (in 2011 and 2014[16]) produced annual figures on the estimated proportion of high-quality products reaching the market, demonstrating a general shift to better-performing malaria RDTs with the exception of 2015.

Global malaria RDT sales were mainly destined to the public sector, accounting for 78% of the 2015-16 RDT deliveries. This percentage is slightly lower than the average public sector sales estimated for the previous period (2011-14) which fell around 84%.

In the framework of a related Unitaid-funded project on private sector RDTs, FIND also tried to foster private health facilities to use better products and avoid fake devices, but with mitigated success. Whereas the sales of 'non-complying products' in the public health sector have gone down significally, the share of 'non-complying products in the private sector has not diminished at all, and their sales

[16] (1) Malaria RDT Survey (2011-14) *"Impact of the WHO-FIND Malaria RDT Evaluation Programme on the global RDT market"* Report prepared on behalf of the Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland 25th May 2015.
(2) Global survey of malaria rapid diagnostic test (RDT) sales, procurement and lot verification practices (2011-14): *Assessing the use of the WHO–FIND Malaria RDT Evaluation Programme* (2011–2014) Sandra Incardona, Elisa Serra Casas, Nora Champouillon, Christian Nsanzabana, Jane Cunningham, and Iveth J. González.

are even increasing in absolute numbers, probing that increased advocacy and regulatory oversight in that sector are still required.

The proportion of products that did not comply with WHO criteria or had not been evaluated was found to be higher within the private sector (27% for 2015; 26% for 2016) compared to the public sector (6% for 2015; 4% for 2016)[17]. Although private sales accounted only for a minor fraction of the total reported transactions of the 2015-16 survey (~22%), the absolute number of RDTs that did not meet WHO recommendations during this period was still higher in the private sector (36 million RDTs) compared to 'non-compliant' or 'not-tested' sales in the public market segment (25 million RDTs).

Finding #13: The FIND QARDT grant has a positive long term impact on health system strengthening because the project contributes to the long-standing overall malaria programmes in the malaria endemic countries.

The long-term impacts of the project on health system strengthening should not be neglected. In a nut shell those are:

- Guidance and regulations on RDTs, promoting purchase at country level;
- Growth in implementation and performance studies (i.e.HRP2), e.g. in Peru (See Box 5 below[18]);
- Capacity building of national laboratories and of MoH/NCMP;
- Increased knowledge sharing between countries, in particular on procurement and selection of the RDTs;

Box 5: The Peru experience

An important scientific contribution that affected malaria diagnostics, came out of Peru. A large proportion of *Plasmodium falciparum* isolates in the Amazon region of Peru lack pfhrp2 and pfhrp3, which had major implications for malaria rapid diagnostic tests, because this implies that HRP2 detection can not be used.

Globally, almost all RDTs are based on this protein for a diagnostic of *Plasmodium falciparum*. In Peru, however, the Ministry of Health was forced to use RDTs based on for instance molecular diagnostic methods such as LAMP and PCR to diagnose *P. falciparum* and for *P. vivax.*

Source: Testimonial collected from the Evaluation interviews

The FIND QARDT grant aimed to re-shape the RDT business model so that PT becomes sustainable, based on a technology switch from human blood to recombinants. The grant also aimed to develop a more elaborated quality assurance (QA) and quality control (QC) program for RDTs, through LT and positive controls. However, it didn't work out as expected, because the recombinant antigens method appeared to not be usable for comparative product evaluations and as a full replacement of human blood samples. That's a risk that is part of science.

The Bill and Melinda Gates Foundation invested significantly in this area for several years, and the FIND project could thus have foreseen the high risk of using antigens. The original project document didn't however sufficiently address this risk in its "risk assessment" section and foresee mitigating measures in the project design. In particular, the documentation didn't provide enough details on the status of R&D on antigens. Nevertheless the project worked on an alternative, more cost-effective system, in particular redesigned PT to drive costs down via another strategy (i.e. less samples, large stock of specimens built up), and redesigned LT to use panels only as an initial

[17] Source : Annual compliance of products with WHO recommendation - % of sales (A) and number of delivered RDTs (B) in the Public and Private Sector

[18] Gamboa D, Ho MF, Bendezu J, Torres K, Chiodini PL, Barnwell JW, Incardona S, Perkins M, Bell D, McCarthy J, Cheng Q. PLoS One. 2010 Jan 25;5(1):e8091. doi: 10.1371/journal.pone.0008091.

screening tool, equally driving costs down.

In line with GMP (Good Manufactoring Practice) the project transitioned the PT program to prequalification (PQ), which seems to make sense (building synergy with PQ's other activities) and a reasonable plan and budget were put in place.

Round 8 of the testing introduced a hrp2 deleted parasite panel, and also comprised tests that targeted non hrp2 antigens for detection of *Plasmodium falciparum*, which indicates manufacturers innovation.

The project could have readjusted earlier the LT activities, if there had been less delays with the panels development, more buy-in from procurers (especially Global Fund), and solutions to at least fund the coordination part of LT at WHO (costs for the testing itself could have been sustained by user fees for example).

Due to a lack of data, the evaluation team was not able to confirm the key rationale of the FIND project, as described in the project document[19], which is that the vast majority of the deaths due to malaria, particularly the deaths of children in Africa, could have been averted if patients had access to high quality diagnostic testing, as the first step towards effective case management. We couldn't collect evidence supporting this long-term impact in the short timeframe of this study, neither through the desk review nor through interviews. Impact studies in a few selected countries including an indepth assessment at a sample of health facilities, with and without RDTs, such as a study Cochrane Collaboration researchers undertoook in 2014 [20], are needed to prove that impact. If surveys had been incorporated in the grant activities, data would have been available at the end of the project to measure such impact.

Moreover, the pathology nature of Malaria does not provide reliable links between diagnosis, treatment and cure (avoided deaths), and a perfect RDT with a perfect diagnostic cannot avoid a patient's death. Multiple factors beyond the diagnostic component influence a full recovery from Malaria, such as referral time to the health facility, the patient's physical condition, and the timely availability of a correct treatment (including fluids).

4.5 Sustainability

This section assesses the sustainability of the grant and evaluates to what extent the benefits of the project will continue after donor funding ceased.

Finding #14: A self-sustaining capacity of the PT and LT programmes via funding by user fees was not achieved regardless the corrective measures undertaken during the project life.

User fees were only implemented for the PT component to contribute to its sustainability. This was well accepted by the RDT manufacturers, however these fees are not sufficient to cover the PT coordination by WHO PQ staff and other associated costs. With regard to LT, some of the beneficiaries (RDT procurers) didn't seem willing or capable to pay the fees, or contribute via some sort of core funding, needed to reach financial sustainability. Only some but not all country authorities have taken measures to continue LT activities after the end of the grant.

Because of the continued reliance on clinical samples, incomplete analysis of recombinant panel data

[19] Clearly stated in the Agreement between WHO/UNITAID and FIND: Sustainable Global and National Quality Control, p.10

[20] http://www.cochrane.org/CD008998/INFECTN_rapid-diagnostic-tests-versus-clinical-diagnosis-for-managing-fever-in-settings-where-malaria-is-common

and in turn no pilot implementation phase, the LT programme needs continuing donor and/or government support, in order to capitalize on the results of the project at WHO and national reference lab level. Fortunately, FIND was able to support the continuation of lot testing services at RITM during 2018. WHO manufacturers fee funds are insufficient to support the transition as proposed in the no cost extension request to UNITAID. Furthermore, significant investment in coordination of major procurers is required to try and reach a common way forward and the required financing. Discussions are underway between major procurers but it is likely that the LT programme will close December 2018.

The PT programme was transferred to the WHO Prequalification programme, a group well accepted by manufacturers, particularly following new financing arrangements that ensure the financial sustainability and quality of the programme in the coming years[21].

Finding #15: Sustainability of the project's results has been fostered by a strong and satisfactory buy-in by stakeholders, through capacity building, knowledge sharing, bringing technical knowhow, and communication. An adequate level of human and institutional capacity has been built up, permitting in principle to continue delivering benefits.

The project heavily invested in improving local capacity and technical know-how. FIND/WHO's role in the management and the monitoring of the operation was respectful of the leading role of the country partners which helped enhancing their capacities.

One unquestionable project achievement emerged from the data analysis and from information obtained from the National Malaria Country Programmes (NMCPs), and concerns the increased diffusion of and guidance on mRDT procurement among the country-based stakeholders. However, according to the survey respondents, this guidance should target in the future not only the NMCPs, but also Central Medical Stores and National Health Labs (depending on the organizational structure established for mRDT procurement). The inclusion of WHO's regional offices PAHO, SEARO and WPRO should be considered since the procurement of 'bad-performing' products was common among countries of these regions.

After the completion of the Unitaid grant, FIND plans to maintain accessibility of recombinant antigens panels for RDT manufacture, while WHO will maintain a coordinating role, involving the Global Malaria Programme, WHO Biological Standards group, and other mechanisms evolving within WHO around procurement standards and prequalification-related activities.

FIND had a functional agreement with CDC during the entire FIND QARDT project period, based on one year contracts (according to US fiscal years), with an agreed annual work plan, an agreed annual budget with an 80% upfront payment at the beginning of the fiscal year, and a 20% payment upon completion of activities justified by an activity report and a financial report. The work plans covered all project-related activities done at CDC, i.e. the routine PT work done based on the frozen blood samples, but also any testing or validation of recombinant panels, preparation of specimens with locally available cultured Pf samples or negative controls from US blood donors, storage and maintenance of the malaria specimen bank, and characterization of specimens by PCR (later on also by ELISA when handed over from HTD).

[21] New Financial Arrangement to Improve Sustainability, Quality and Global Reach of WHO Prequalification of Medical Products: http://www.who.int/medicines/news/finance-arrangements-prequal-med/en/

At the end of 2017, GMP negotiated contracts with CDC to maintain the WHO Specimen Bank and complete round 8 testing and recombinant LOD determinations for RDTs. In Q1, 2018, CDC and and WHO Prequalification of Diagnostics team developed a contractual agreement for post round 8 product testing.

4.6 Learning

Finding #16: In a sense the project appeared to be a pilot project, and produced a variety of lessons learned, spanning from technical complexity (e.g. recombinant panels), to coordination challenges (many stakeholders in many countries working together), and RDT market and procurement practices.

Probably the biggest lesson learned is the complexity of the recombinant panels' development, outlined as the highest risk factor for the project from the start. During the 1st phase of the project, the difficulty of identifying the best candidates with reactivity to a wide range of RDT products, and selecting a new development partner, seriously affected the project's timeline. During the 2nd phase, their variation in reactivity with different products led to a complete revision of future PT and LT designs. This, in turn, resulted in PT still relying on real parasite samples, and required further experimentation to determine appropriateness for future lot testing. Compilation and data analysis of the latter was not completed before the end of the grant.

Cost reductions were significant, but full sustainability of PT and LT was not achieved. The project proved it possible to reduce the PT and LT testing costs to amounts which could in potential be covered by user fees, and continuation of PT Page 25 is assured under the PQ coordination, with a clear design of procedures and sufficient stocks of samples for the next 5 - 10 years.

The importance of strategic communication to foster a high participation and compliance of all main RDT manufacturers and procurers with the PT and the LT programmes turned out to be a positive lesson. Product submissions to PT remained high notwithstanding the introduction of a fee since 2014 and despite adding the PQ requirement in 2017.

The project demonstrated that strong policies and a government buy-in, adequate programme management, and sensibilisation of stakeholders can turn a "wild market" into a managed one that ensures that patients are tested with good quality products and receive adequate treatment. The shift of the RDT market to high quality products and the fact that the LT covers a large portion of the public sector market, is impressive.

A number of peer-reviewed articles which are directly or indirectly derived from work done within the frame of the RDT-QA project, were published in scientific journals, ensuring wide dissemination of findings and best practices. A non-exhaustive list of such peer-reviewed manuscripts is presented in Annex C. Out of these articles, we commend particularly two that showcase the best practices and learnings from the project:

- Harmonization of malaria rapid diagnostic tests: best practices in labelling including instructions for use. Jacobs J, Barbé B, Gillet P, Aidoo M, Serra-Casas E, Van Erps J, Daviaud J, Incardona S, Cunningham J, Visser T. Malar J. 2014 Dec 17;13:505.
- Global survey of malaria rapid diagnostic test (RDT) sales, procurement and lot verification practices: assessing the use of the WHO-FIND Malaria RDT Evaluation Programme (2011-2014). Incardona S, Serra-Casas E, Champouillon N, Nsanzabana C, Cunningham J, González IJ. Malar J. 2017 May 15;16(1):196. doi: 10.1186/s12936-017-1850-8.

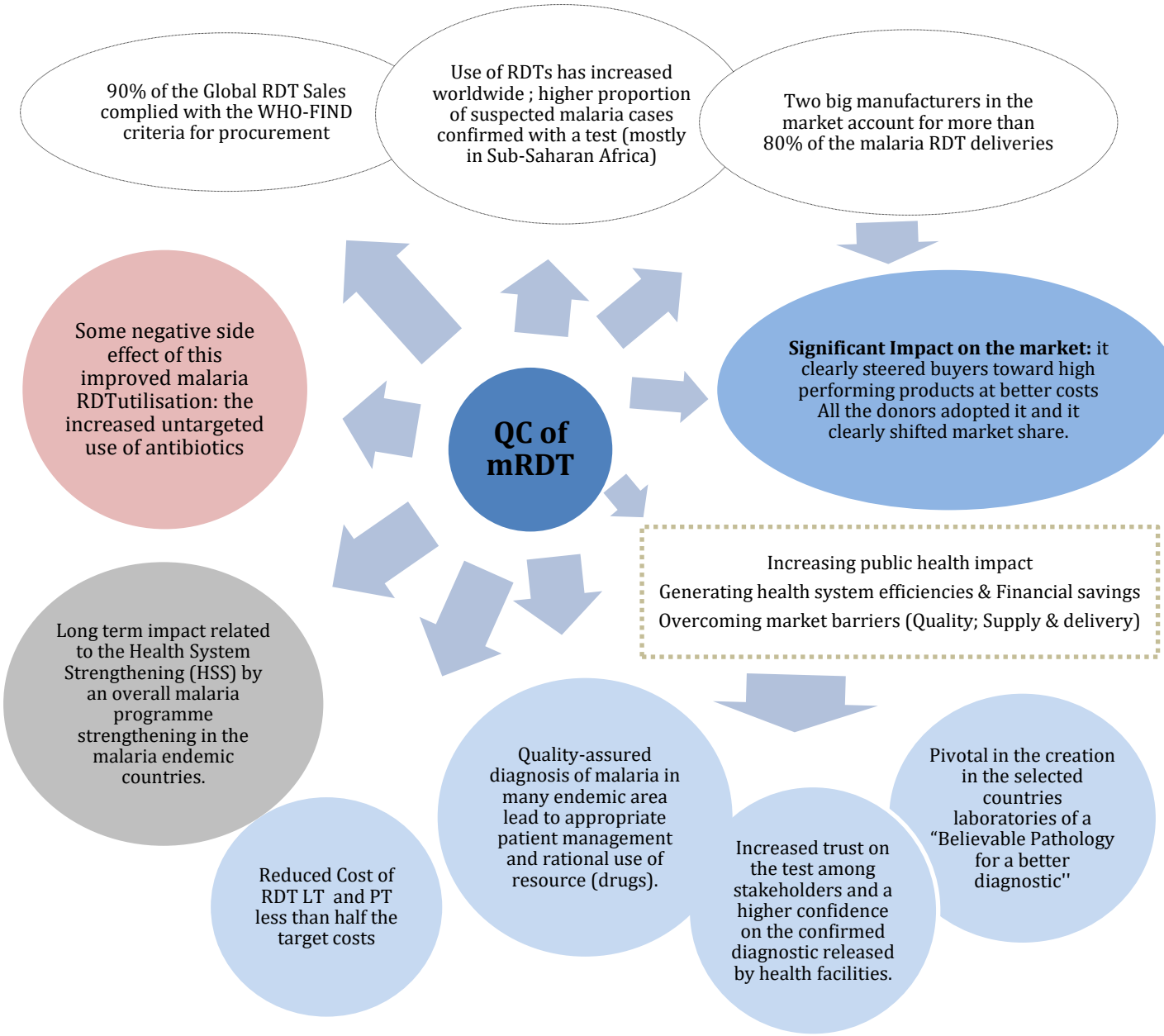
Annex D presents the risk description, assessment and probable response at the outset of the project as well as new risks that occurred and which are reported in the final project report. The annex shows that the risks were tracked over the course of the project. The new significant risks identified are related to the recombinant antigen-based PT and LT. New significant risks include (i) biological complexitiy of the recombinants; (ii) inefficient transition to WHO; (iii) lack of a common vision from all major procurers for continuation of LT; (iv) centralization of core laboratory activities at CDC, and (v) inadequate funding through users fees and other sources.

5 CONCLUSIONS

Conclusion #1: The project was a success despite the challenges with the recombinant panels that in itself offered an opportunity to learn.

The diagram below highlights the key results of the project.

Figure 2: Impact of the FIND Project – Key highlights



Conclusion #2: The project had a potentially positive impact on the market for products to diagnose malaria by improving quality of diagnostics and significantly reducing the cost of RDT LT and the unit cost of PT per product evaluated.

The project generated financial savings and health system efficiencies. In this respect the project

exceeded its objectives as the cost of the LT was reduced by more than half compared to the target costs (US$251 per lot; US$609 was the target cost), and the cost of the PT was also reduced by more than half compared to the target costs (US$10,876 per product; US$25,000 was the target cost).

The FIND Project also made a great contribution in overcoming market barriers, specifically on Quality and on Supply & delivery: i) the improvement in the process of PT and on LT panels refining improved quality assurance for Diagnostics (Quality); and ii) reduced prices for PT & LT, with a likely trickle-down effect on prices for procurers. RDTs prices are now lower and therefore more affordable with an increased access to all stakeholders.

Conclusion #3: The impact of the product evaluation program on the market was significant. Given that the RDTs technology was already available, the FIND project drastically improved the clinical efficiency, reduced cost and better met the needs of stakeholders (users).

Although private sales accounted for a smaller fraction of the total reported transactions in 2015-16 (~22%), the absolute number of RDT deliveries that did not meet WHO standards during this period was higher in the private sector market segment (36 million RDTs) than in the public sector (25 million RDTs).

The FIND Project clearly steered buyers toward high performing products and at better costs. All the donors adopted it and it clearly shifted market share. The strong engagement of all stakeholders involved, including local authorities, is an indicator for the success of the project in this respect.

The malaria RDT market share is currently concentrated around two main manufacturers which account for more than 80% of the malaria RDT deliveries. Manufacturers' estimations on their RDT deliveries to the public sector indicated an approximate 78% / 22 % public/private market ratio for the 2015- 16 period. Nevertheless, considering that several manufacturers were not included in our survey, namely companies not involved in the public sector (i.e. not participating in PT rounds), the current estimate of the private sector weight in the whole market is most probably underrated.

The private sector presents a higher percentage of products that do not comply with WHO criteria or have not been submitted for evaluation, and is more diversified, i.e. higher number of manufacturers delivering RDTs and less market share covered by the two 'major' suppliers (SD+AB) compared to public sector.

Conclusions #4: In the long term, the FIND Project will probably have an important impact on Health System Strenghtening. For instance, during the past two years, the percentage of global RDT sales that complied with the WHO-FIND criteria for procurement ranged around 90%.

The project fostered for instance a *"Believable Pathology for a better diagnostic"* in the selected countries' laboratories, which generated an increased trust in the test among stakeholders and a higher confidence in the confirmed diagnosis released by health facilities. Quality-assured diagnosis of malaria in endemic areas leads to appropriate patient management and a rational use of resource (drugs).

However, as reported by various studies, some negative side effect of this increased use of RDTs, improving malaria drugs utilisation has resulted in an increased untargeted use of antibiotics: *"The introduction of rapid diagnostic tests for malaria to reduce unnecessary use of antimalarials could*

drive up untargeted use of antibiotics.That 69% of patients were prescribed antibiotics when test results were negative probably represents overprescription. This included antibiotics from several classes, including those like metronidazole that are seldom appropriate for febrile illness, across varied clinical, health system, and epidemiological settings[22]". It is often assumed that better disease specific diagnostics will reduce antimicrobial overuse, but they might simply shift it from one antimicrobial class to another. Current global implementation of malaria testing might increase untargeted antibiotic use and must be examined.

The World Malaria Reports for 2015, 2016 and 2017 show clearly that malaria RDT use increased worldwide and that the proportion of suspected malaria cases confirmed with a test (mostly RDTs in sub-Saharan Africa) rose dramatically. The total volume of RDTs released in the market during the 2011-16 period was 1,461 million. In the past six years the quantity of sold RDTs has increased 2.8 times (from 121 million in 2011, to 338 million in 2016). This upwards trend was only interrupted in 2015, when a temporary stagnant period was observed.

Conclusions #5: Partner countries strengthened their malaria testing capacity with support from the FIND project, especially in improving technical know-how (e.g laboratories), in access to better tools and in reducing costs.

However, financial sustainability of the program is a challenge in spite of the reduced costs. The project envisioned that a large part of the PT and all of the LT activities would be based on recombinant panels, hereby drastically reducing the programme costs and allowing for sustainability via RDT manufacturers fees for PT and the endemic countries funding sources for LT[23]. The benefits of this grant may not last long after the end of the project funding as there is no evidence so far that additional funding has been secured to maintain the LT-activities.

The evidence base to support recombinant panels for lot testing was not fully compiled and analyzed prior to the end of the grant. WHO and FIND are taking this work forward independent of donor support ie. UNITAID.

Commitment by laboratory personnel came up as an issue in our interviews, due to the absence of incentives such as performance allowances. Understanding local context and adapting the project's design to it, is crucial.

Coming at the end of the grant, and due to the challenges with the recombinant panels, both PT and LT processes still fully rely on whole parasite samples (even if redesigned to reduce costs by other means). For LT, the review of available data by a group of experts is required to decide about transition

[22] Impact of introduction of rapid diagnostic tests for malaria on antibiotic prescribing: analysis of observational and randomised studies in public and private healthcare settings Heidi Hopkins,1 Katia J Bruxvoort,1 Matthew E Cairns,1 Clare I R Chandler,1 Baptiste Leurent,1 Evelyn K Ansah,2 Frank Baiden,3 Kimberly A Baltzell,4 Anders Björkman,5 Helen E D Burchett,1 Siân E Clarke,1 Deborah D DiLiberto,1 Kristina Elfving,6 Catherine Goodman,1 Kristian S Hansen, 1,7 S Patrick Kachur,8 Sham Lal,1 David G Lalloo,9 Toby Leslie,1,10 Pascal Magnussen,11 Lindsay Mangham Jefferies,1 Andreas Mårtensson,12 Ismail Mayan,10 Anthony K Mbonye,13,14 Mwinyi I Msellem,15 Obinna E Onwujekwe,16 Seth Owusu-Agyei,1,17 Hugh Reyburn,1 Mark W Rowland,1 Delér Shakely,18 Lasse S Vestergaard,11,19 Jayne Webster,1 Virginia L Wiseman,1,20 Shunmay Yeung,1 David Schellenberg,1 Sarah G Staedke,1 Christopher J M Whitty1

[23] FIND project proposal

to a system partially based on recombinant quality control samples.

PT and LT programmes were also re-designed to reduce their costs through a series of modifications, which resulted into a cost reduction for PT by nearly 10 times, and if recombinant panels are confirmed by the WHO July 2018 recombinant panels dossier review to be adequate for the initial LT, then costs for LT plus confirmatory testing would be reduced by nearly 30%.

The estimated costs per product evaluated are about US$8,700. Estimated costs per lot tested vary from US$214 to US$445 depending on the testing country, and confirmatory testing costs are estimated at US US$533 per lot at CDC[24]. For full, long-term, sustainability, a funding gap of at least US$500,000 to US$600,000 per year remains[25]. It should be noted that various components were eliminated – during the project life - to reduce complexity and thus costs, such as the annual on-site EQA assessments of the LT laboratories. All procurers, except the Global Fund, preferred a centralized LT service with easier monitoring of quality.

As clearly stated in the FIND-WHO Final Report[26] 2018, "*full sustainability* of *the PT and LT programmes via funding by user fees only has not been achieved",* mainly due to the recombinant panels technical limitations[27]. However, it is important to note that the initial objective of the project was not to introduce user fees but to develop and support market availability of recombinant antigens.

WHO coordination required substantial transaction costs. During the implementation of the grant the primary 'links' between WHO/GMP and WHO/PQ were the sharing of PT data with the PQ team. These data were used to prioritize applications for assessment. The WHO PQ team was also invited to the meetings of the Steering Group where the PT results were discussed. WHO/GMP and WHO/PQ collaborated to agree on changes to the WHO recommended malaria RDT procurement requirements and to investigate suspected product defects which were identified through the WHO-FIND LT programme (e.g. products containing single use buffer vials and false negative RDTs in Eritrea).

The project gave particular attention to enhancing stakeholder's capacity (MoHs, manufacturers, and laboratories). Constant exchange and intensive communication between the main actors and implementers during the five years project life span contributed to "learning on the spot". Alliances were established.

FIND and WHO organized and facilitated consultations with all main RDTs manufacturers28 as well as annual and bi-annual meetings of the malaria RDT procurement task force[29]. In addition consultations were held with the Malaria Harmonization Task Force (HarT) and more importantly with the in-country relevant institutions such as MoH/NCMPs, and private sector players such as

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[24]These estimations are only applicable if recombinant panels can be used for initial LT, pending formal review of data at the WHO by mid-2018, by a group of experts.

[25] FIND/WHO RDTs quality Assurance Project - Final Report (2013-2017)

[26] FIND, FIND-WHO RDTs Quality Assurance Project Final Project Report (2013-17), March 30th 2018, p.25

[27] For PT, these are covered by the funds of the PQ programme, but they are currently still needed for continuation of the LT. A big unknown for LT is what countries will charge themselves through a decentralized lot testing model.

[28] In 2013, 2014 and 2016, specifically for the RDT-QA project

[29] Which includes all major RDT procurers as GFATM, USA/PMI, UNICEF,MSF, WB, CHAIetc.

distributors, pharmacists and clinicians associations. FIND/WHO also attended and presented RDT-QA related work at annual Post-marketing surveillance workshops organized by the WHO PQ programme.

This intensive networking increased the sustainability of the project's results because of a buy-in by the following stakeholders:

- **RDT manufacturers**: Positive response to the PT and LT programmes with high interest in the evolution and transition phase to WHO-PQ. Shared updated background knowledge.
- **RDT procurers**: Adhered to the guiding principles of the program and bought in to the operational and technical aspects of the programme. However, according to the project's final report (p.15): "*procurers started expressing divergent opinions about if and how the LT effort should continue, in the context of funding shortage beyond 2018. USAID/PMI for example definitely looks for continuation but maybe with less frequent LT (e.g. only a fraction of lots), and has a strong preference for centralized LT at CDC. Global Fund has changed their policy and no longer recommends pre or post shipment LT. They favour decentralized testing post deployment. Opinions are currently being documented and compiled to feed into WHO's decision for LT continuation by mid-2018*".
- **RDT HarT**: All outcomes of the RDT Harmonization Task Force (HarT) have been incorporated in the PT.
- **Private sector**: Showed great interest in the programme, especially in relation to the QA and QC mechanism in place.
- **MoHs/NCMPs**: Positive opinions and interests from all levels of the different MoHs /NMPCs; well informed and knowing which RDT to buy.

Conclusion #6: Nothwithstanding the positive sustainability promoting elements discussed herebefore transition and sustainability plans didn't perform as planned, and hence the Evaluation Team is not entirely sure that the catalytic Unitaid investment will actually have a long lasting sustainability.

The technical risk appeared to be high, and was not wholly foreseen and properly addressed/acknowledged in the original proposal documents (risk assessment section) and subsequently in the project design.

Additionally, mRDT products that are not in line with the WHO procurement are mostly drained to the private sector where strict standards of quality are not always present. MoHs demonstrated limited knowledge about the alternative mRDT distribution channels at national level; on the other hand, National Regulatory Authorities could be a good ally to face this challenge.

There is thus a clear need to improve the coordination of mRDT procurement at country level, in order to avoid risks of confusion created by coexistence of different malaria products in circulation. Coordination in-country could be enhanced at different levels:

- Increase communication between different procurers acting simultaneously in the same country. Our observation based on survey was that procurement practices of UNICEF, MSF and GF-Principal Recipients presented several specific organizational particularities that might contribute to the in-country divergences;
- Increase communication between MoHs and procurers i.e. NMCP/MoHs should be always

informed about planned transactions, and able to centralize and approve all orders destined to public sector. This would often imply an empowerment of NMCP/MoHs' role in mRDT procurement, since the underlying perception from conversations with country contacts was that they were usually by-passed.[30]

6 RECOMMENDATIONS

The recommendations of the evaluation team are based on their findings and conclusions.

R1 We recommend donors to continue the grant with new funding to sustain the achievements of the project.

Short term support is particularly needed to enable the pilot countries and their laboratories to roll out the Lot testing, if approval of the new system by a group of experts can be achieved by mid-2018, and according to their recommendations about how to use the recombinant panels (most likey only as a tool for the initial screening, with confirmatory testing based on real parasite samples). Medium term support is needed to scale up the pilot to additional countries. In the design of a new phase financial sustainability should be one of the key objectives and mechanisms should be developed (budget lines in national budget; cost recovery) to guarantee this.

R2 We recommend UNITAID and its main implementers FIND and WHO to initiate discussions on the harmonization of procurement procedures, in particular with NMCP/MoH in the countries, and with the major procurers, especially UNICEF, Doctors Without Borders (MSF), US President's Malaria Initiative (PMI), and Global Fund (GF). These discussions should lead to strengthened communication and coordination between NMCP/MoH and the major procurers.

The procurement practices of UNICEF, MSF and GF-Principal Recipients comprise specific rules and regulations that might contribute to in-country divergences.

NMCP/MoHs are currently regularly by-passed in the purchase of malaria testing and treatment equipment and goods, and their role in mRDT should thus be empowered. At a minimum NMCP/MoH should always be informed about planned transactions, and able to sign off on the purchases destined to public sector.

R3 We recommend UNITAID and WHO to continue pursuing consensus on malaria RDT Lot testing. In particular discussions should be held with GFATM (Global Fund) to improve coherence and coordination.

To date, we still don't have a consensus on a scenario for Lot-testing of malaria RDTs, notwithstanding consultations led by WHO with the four major procurers PMI, UNICEF, MSF and GFATM. It is urgent to move forward and reach a consensus on the continuation of the malaria RDT lot testing. The malaria RDT procurement task force of mid July 2018 has this topic on its agenda.

R4 We recommend WHO to share with the project's countries the WHO resolutions from the

[30] Some data is already published: http://www.who.int/bulletin/volumes/93/12/14-151167.pdf https://www.ghdonline.org/uploads/Unitaid-Malaria-Dx-Tech-Mkt-Landscape-3rd-Ed-April-2016.pdf, pp.13-14

July meeting results and to urge NCMP/MoH to disseminate these resolutions among the relevant actors in the field.

Implementation stakeholders actors at the local level are not always well informed as information remains at the central level (MoH/Malaria Programme).

R5 We recommend to adopt a decentralized modality for Lot testing and WHO should develop clear guidelines for a country how to implement this modality, and develop certification standards for the laboratories.

If the evidence supports the safe and accurate use of recombinant antigen panels, a decentralized model responds better to the specific institutional, policy and legal context, health system organization, and technical skills and knowledge of a country; fosters ownership and engagement; reinforces country capacity (transfer of technology, training); and may be cheaper for a country than a centralized model. WHO could set up a global system of two or three reference laboratories that support the country laboratories to comply with the certification (quality) standards. To re-assure all the major RDT procurers (who currently prefer a centralized system) and manufacturers (who ultimately would have to replace failed lots), it would require a good system of certification and regular on-site EQA.

The idea of a decentralized system should be discussed with relevant stakeholders (i.e. procurers) and alternatively a more stepwise approach could be introduced, starting with a central lab and progressively decentralizing to regional and country laboratories.

***R6 We recommend Unitaid and WHO to support country-based impact studies, to identify averted deaths due to RDT use*.**

Impact studies, using averted death as indicator, are meant to demonstrate that quality RDTs are life saving devices, lead to better malaria management and will help to build political support for the RDTs (e.g. Uganda study *"Impact of rapid diagnostic tests for the diagnosis and treatment of malaria at a peripheral health facility in Western Uganda: an interrupted time series analysis"*).

Unitaid should also support evidence-based country-level studies on side effects of RDT introduction such as increased use or misuse of antibiotics by health staffs.

Annex A Evaluation Framework

Evaluation criteria/Questions		Indicators	Data collection method	Responsible
What is the progress made towards the achievement of results at the impact, outcome and output level from two perspectives: i. Market impact (intentional and unintentional) for the products/services provided under the project agreements; and ii. Public health impact for the beneficiaries of the medicines, diagnostics and products/service provided through the project.				
1	**Relevance**	**The extent to which Unitaid support is suited to the priorities and policies of the target group, recipient and donor.**		
1.1	Are the **outcomes and impact** aligned with Unitaid's mission for 2017-2021 is to maximize the effectiveness of the global health response by catalyzing equitable access to better health products.	• Adequacy of i. the outcomes/impact of the grant with the Unitaid's overall mission	• Literature review	• Rodrigue Deubeue (RD Lead of the Desk review and reporting on Relevance)
1.2	Was the grant relevant to contribute to one or more of **Unitaid's strategic objectives**?	• Adequacy of i. the outcomes/impact of the grant with the Unitaid's KPIs as the following: o Adding value to the global response KPI 1.1 Increasing public health impact **(according to the results under Effectiveness)**	• Literature review	• RD
2	**Effectiveness**	• **The extent to which Unitaid support attains its objectives**		
2.1	Are the **outputs of the grant consistent with the objectives and expected outcomes** as described in the project plan? If changes have been made, **has the Unitaid Secretariat been involved** in discussions and decision making on the changes?	• Coherence of the planned initiatives with the objectives and expected results as described in the project plan • Estistence of amendements to the contracts, or other relevant documents. • Views on whether the project has been modified and if the Secretariat have been involved in the decision-making	• Literature review (Work plans and project document) • Telephone interviews	• RD (co-lead) • Eric Donelli (ED co-lead)
2.2	Were the outputs of the project for the evaluation period fully achieved within the timeframe and budget specified in the initial project plan?	• Extent to which the outputs are achieved : o Output 1: Product testing and evaluation implemented with manufacturers, and results disseminated;	• Document review	• RD

Evaluation criteria/Questions		Indicators	Data collection method	Responsible
		○ Output 2: RDT lot-release and field deployment implemented based on lot-testing data and performance findings; ○ Output 3: An operational malaria recombinant antigen-based RDT product testing programme funded by manufacturers introduces; and ○ Output 4: Market created for malaria RDT quality control materials based on recombinant antigens technology.		
2.3	What are the main factors influencing the achievement or non-achievement of the outputs or overall outcomes across all countries and within each beneficiary country?	• **Views** on the main factors influencing the achievement or non-achievement of the outputs or overall outcomes	• Telephone interviews	• ED
3	**Efficiency**	• **Extent to which the project use least costly resources possible to attain the planned results**		
3.1	Have the grant implementer and co-implementers ensured project planning, implementation and assessment **in collaboration with the national authorities**? Can the grant implementers and their partners demonstrate that national authorities were aware and participating in grant activities at the national level?	• Views on whether the national authorities were involved adequately in the program planning, implementation and monitoring, using **participatory approaches** that were **inclusive of primary stakeholders' needs** • **Views of the performance of the projects accoding to the national authorities**	• Telephone interviews • Emails and/or interviews with the selected countries	• ED
3.2	How **cost efficient and cost effective** was grant implementation? Cost-efficiency: Extent to which the program has converted its resources/inputs (such as funds, expertise, time, etc.) economically into results What factors have been considered to ensure that **value for money** has been achieved?	<u>Economy:</u> • **Table of Project's costs** in total and broad categories (%staff / %consultants/%material/%travel/etc.) <u>Efficiency:</u> • Actual expenditures on Planned budget (**Disbursement rate**) • Gap between the activities planned and the activities realized (Work plan versus budget) • Proportion of costs attributable to **administrative overhead**	• Content analysis • Document review • Telephone interviews	• RD with MG • ED

Evaluation criteria/Questions		Indicators	Data collection method	Responsible
		• Number **# of Human Resource and capacities** Value for money: • **Views** on whether critical factors have been considered to achieve value for money		
3.3	Were **challenges** raised with the Unitaid Secretariat in a timely manner and did the Secretariat participate in resolving these challenges?	• Views on whether the **challenges** were raised and resolved in a timely manner with the Unitaid Secretariat	• Telephone interviews	• ED
3.4	Were there any concerns or reported instances related to **potential diversion of products, counterfeit products or poor quality products**?	• Views on whether reported potential diversion of products, counterfeit products or poor quality products have been identified by stakeholders	• Telephone interviews	• ED
4	**Impact**	• **The extent to which the project produced impact**		
4.1	Has the grantee been able to report on impact as originally framed in the project plan and Log-Frame? If not, has the grant impact been measured in another way?	• Extent to which the impact have been reported and in which way ○ # & % of malaria endemic countries conducting their own LT according to quality standards/practices ○ % of the global RDT public-sector market reported to WHO that has been lot tested ○ Market share of RDTs meeting WHO procurement criteria (from at least the 17 major suppliers)	• Literature review • Telephone interviews • Emails and/or interviews with the selected countries	• RD • ED
4.2	Where relevant, can the grantee attribute Unitaid's financial support for medicines, diagnostics or preventive products purchased to patients tested or treated in each beneficiary country?	• Views on whether Unitaid's financial support can be attributed for the output	• Telephone interviews • Emails and/or interviews with the selected countries	• ED
4.3	Estimation of the resulting public health impact	• KPI Performance indicators: Area 1 : Impact of Unitaid on the market for products to treat, diagnose and prevent HIV/AIDS, TB and malaria	• Desk review • Telephone interviews	• RD • ED

Evaluation criteria/Questions		Indicators	Data collection method	Responsible

		• KPI Performance indicators Area 1 Action 3: Improve quality of medicines, diagnostics and related products
		• Costs of inappropriate treatment due to presumptive misdiagnosis and the subsequent reduction in Artemisinin Combination Therapies ACT costs to national malaria programmes.
		  ○ Public health impact estimated by number of deaths averted and severe malaria cases avoided
		  ○ Costs of inappropriate treatment due to presumptive misdiagnosis and the subsequent reduction in ACT costs to national malaria programmes.
			• Desk review
			• Telephone interviews
				• RD
				• ED

5 Sustainability				
5.1	To what extent did the benefits of a programme or project continue after donor funding ceased?	• Existence of a sustainability strategy • Views on whether benefits of a programme or project continue after donor funding ceased	• Literature review • Telephone interviews	• RD • ED
6 Learning and Risks Mitigation				
6.1	Have lessons learnt been documented and widely disseminated by grantees and Unitaid?	• Existence of lessons learnt documented • Extent to which lessons learnt were widely disseminated by grantees and Unitaid	• Literature review • Telephone interviews	• RD • ED
6.2	Have the findings and recommendations of audits (where relevant) been used to improve grant performance?	• Existence of findings and recommendations of audits • … and have been used to improve grant performance)	• Literature review • Telephone interviews	• RD • ED
6.3	Have programmatic and financial risks been identified and tracked over the course of grant implementation?	• Existence of programmatic and financial risks dentified …and tracked	• Literature review and Telephone interviews	• RD

Annex B List of documentation used

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9) https://wwwnc.cdc.gov/eid/article/24/3/17-1723_article
10) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5951549/
11) https://academic.oup.com/jid/article/215/7/1156/3058211
12) https://www.nature.com/articles/s41598-017-15031-2
13) Terms of Reference for the evaluation of the project
14) FIND RDT Logical Framework
15) FIND RDT Update power point presentation
16) Project Communications
17) Agreement between WHO/Unitaid and FIND - Project plan
18) World Malaria Report 2017
19) FIND-WHO RDTs Quality Assurance Project Final Project Report (2013-17)
20) FIND-WHO RDTs Quality Assurance Project Final Financial Report (2013-17) – FIND
21) FIND-WHO RDTs Quality Assurance Project Final Financial Report (2013-17) – WHO/GMP
22) WHO Guidelines for the treatment of malaria, third edition, published in April 2015