Mid-Term Evaluation of WHO Diagnostics Prequalification Programme

Draft Evaluation Report

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ABBREVIATIONS

AM	Anti-Malarial
ARV	Anti-Retroviral
BPS	Bulk Procurement Scheme (of WHO)
CDC	(US) Centers for Disease Control
CHAI	Clinton Health Access Initiative (formerly Clinton HIV/AIDS Initiative)
DLT	Diagnostics and Laboratory Department (WHO)
DR TB	Drug-resistant Tuberculosis
EMP	Department of Essential Medicines and Health Products (WHO)
ERP	Expert Review Panel
GF	Global Fund to fight AIDS, TB, and Malaria
GMTA	Global Medical Technology Alliance
IPC	Inter-agency Pharmaceutical Coordination Group
ISO	International Standards Organisation
IVD	In Vitro Diagnostic
KPI	Key Performance Indicator
LLIN	Long-Lasting Insecticide treated Net
MoU	Memorandum of Understanding
MSD	Medical Supplies Department (Tanzania)
NHL-QATC	National Health Laboratories – Quality Assurance Training Center (Tanzania)
NRA	National Regulatory Authority
PEPFAR	(US) President's Emergency Program for AIDS Relief
PMS	Post-Market Surveillance
PMS	Procurement and Supply Management
POC	Point of Care
PQ	Prequalification
PQDx	Prequalification programme for Diagnostics (WHO)
PUDR	Progress Update and Disbursement Request
RDT	Rapid Diagnostic Test
SRA	Stringent Regulatory Authority
TFDA	Tanzania Food and Drug Authority
US FDA	United States Food and Drug Administration
WCC	WHO Collaborating Center
WHO	World Health Organisation

EXECUTIVE SUMMARY

This report details the evaluation of the WHO Prequalification of Diagnostics (PQDx) programme financed by UNITAID. Euro Health Group was selected to conduct this evaluation; the work was undertaken by Jennifer Lissfelt and Julie Pasquier and consisted of 2 days of on-site visits to UNITAID and the programme implementer WHO DLT in Geneva, followed by 30 days of desk review. The desk review entailed analysis of a number of documents and telephone interviews with various stakeholders (authorities of beneficiary countries, international donors and procurement agencies and partner organizations, manufacturers and developers of in-vitro diagnostic technologies, as well as various staff members from UNITAID and the WHO LTD team). The report covers the project period from March 2009 to July 2012. The evaluation team has sought to answer the research questions covering four of the OECD/DAC evaluation areas of relevance, effectiveness, efficiency, and impact in addition to examining: 1) achievements and results, 2) project management and implementation, and 3) the project's integration and collaboration with UNITAID and other related global efforts.

The activities of the PQDx programme are consistent with its plans and objectives. The programme is highly relevant, in that there is widespread belief in the importance of better quality assurance for diagnostics, and a general sense that with the many new technologies and new developers coming along, that importance grows. The need for global prequalification effort is undisputed, and WHO's technical strength and mandate in the field are generally agreed to. However, the results of the PQDx programme to date (16 diagnostic devices prequalified) are generally not meeting expectations as of yet. The programme has however increased the speed at which devices are prequalified.

A main objective of the programme is strengthening of regulatory authorities in five pilot countries and support to these countries to institute post marketing surveillance of diagnostics. This objective has largely been met for Burkina Faso, Tanzania and South Africa and there are indications that this will also be the case for China within the next six months. The activities for Ivory Coast have been put on hold because of unrest in the country.

Although this is not fully justified, the PQDx programme is widely seen as too slow and ineffective (so far), with a relatively negative reputation among partners and suppliers, mainly due to the lengthy process of prequalification, lack of transparency and clarity, lack of leadership and lack of collaboration with other prequalification agencies. The WHO PQDx programme seems to have been too reactive and not able to anticipate or mitigate the risks it faces. WHO has mostly reacted to pressure from the outside to speed up the prequalification process. WHO has not communicated effectively about the value of its rigorous approach to quality, and does not appear to play enough of a role to lead the international discussion on how to effectively ensure quality of diagnostic devices.

Due to the low number of prequalified in-vitro diagnostic tests, the programme has not yet led to significant improvement in the diagnostic landscape. In fact the existing prequalified diagnostics had actually been on the market prior to their prequalification by WHO. International procurement agencies and beneficiary countries cannot rely only on prequalified products for their procurement due to the low numbers available on the market. This is however likely to change in the coming years as the programme is able to increase the overall number of prequalified diagnostics. As soon as procurement agencies are able to fully rely on the WHO prequalified list of diagnostic devices for procurement, the incentive for manufacturers to be on this list will be higher.

The following recommendations are based on the estimations and assessments of the evaluators from their document review and interviews with stakeholders, but are limited by

the fact that less than one day was spent with the PQDx team and UNITAID team in Geneva, and for some of these points much more in-depth analysis may be required. A more comprehensive list of all recommendations including a timeline plan of action can be found in section 7of this report.

Priority no 1: Expedite the Prequalification Process:

Resolve HR challenges:

- Conduct an external analysis to identify HR gaps
- Follow up on recruitment for open positions
- Focus efforts and funding on the PQ process, consider delaying further country activities
- Have discussion with WHO high-level management on how to improve the leadership of the programme
- Become more proactive in quality of diagnostics area, begin regular consultations with stakeholders

Streamline the PQ process without Compromising on Quality:

- Conduct a process analysis to examine the reasons/obstacles that have led to delays for each dossier
- Communicate the results of the analysis widely to stakeholders
- Adopt a strategy to remove non-performing manufacturers from the PQ process
- Through clearer web site instructions, guidance, outreach, enhance incentives/understanding among developers to submit for PQ

Priority no 2: Improve Relations with Stakeholders

Improve Communication about PQ Dx with Stakeholders

- Fill open position of Communications Officer
- Begin regular communications with global community
- Enhance reporting to UNITAID
- Explain and illustrate the rationale behind the PQ Dx methodology for PQ on the website
- Publish on the website more information on the progress of the PQ individual processes
- Clarify expectations and guidance for manufacturers for PQ including a mock dossier
- Specifically address the need for information of the different stakeholders on web site
- Build better relationships with experts in the diagnostics field, and with other PQ agencies

Priority no. 3: Adapt the PQDx programme to the needs of the market

- Adopt a specific strategy and procedure to ensure the quality of new technologies on the market until the developers have sufficient manufacturing data to PQ
- Integrate TB testing into the programme
- Address urgent needs expressed by physicians, countries (e.g. point of care)

1 INTRODUCTION

UNITAID is an international facility for the purchase of drugs and medical supplies used in the global response to HIV/AIDS, malaria and tuberculosis. The institution was founded in September 2006 and is largely financed by new and creative financing mechanisms, with 70% of funding coming from a special fee on airline tickets. Launched initially by the governments of Brazil, Chile, France, Norway, and the UK as a new effort to provide sustainable funding for HIV/AIDS, malaria, and TB efforts, UNITAID works with implementing partners (including WHO, which hosts UNITAID's offices in Geneva) to finance procurement of high-quality medicines and diagnostics for developing countries, "using its market power to expand supply, promote development of new and better products, cut delivery lead times and reduce prices" (*UNITAID web site*). UNITAID works by "leveraging price reductions for quality drugs, diagnostics and essential supplies (such as test kits, ARVs, impregnated bednets and LLINs etc.), by helping to accelerate the pace at which products are made available, by providing a stable, predictable and innovative form of funding, and with multi-year budget commitments." (*UNITAID web site*).

Since 2006, UNITAID has provided support to WHO's Prequalification Programmes "as an investment in the improvement of quality medicines and diagnostics globally". The UNITAID Project Support for Quality Assured Diagnostics (PQDx) programme runs from 2009 through 2013, with $7.5M in funding. The lead implementing partner for the project is the WHO Diagnostics and Laboratory Technology (DLT) Department.

The project's activities complement the existing and on-going activities of the UN/WHO PQDx and expand its efforts focusing on HIV and malaria. Project activities were designed to address the lack of access to quality diagnostics, which significantly affects HIV prevention efforts, slows down treatment, and compromises patient care. The project also attempts to address the problem that affordable and appropriate diagnostics are often not available or are of substandard quality, as found through WHO's experience with variable quality of HIV diagnostics globally and a lack of integrity of malaria tests including their inability to withstand tropical conditions. New technologies are often not properly tested for use in resource-limited locations; rapid tests have shown significant variation in quality from one batch to the next (indicating issues during manufacturing); much manufacturing is now being done in countries with less stringent quality regulations; and many diagnostics are now being rebranded and distributed by a third party (not the manufacturer). Even those products produced in developed countries are often produced only for export, following lower safety/quality standards.

In response to these issues this project is focused on identifying quality HIV and malaria diagnostics that meet international standards and on strengthening national reference laboratories and national regulatory capacity to implement quality assurance (QA) and monitoring systems for diagnostics in five targeted countries (Burkina Faso, China, Ivory Coast, South Africa, and Tanzania). The project coordinates with stakeholders including Center for Disease Control (CDC), the Interagency Pharmaceutical Coordination Group (IPC), UNICEF, the Clinton Foundation Health Access Initiative (CHAI), and others.

The project currently focuses on HIV and malaria rapid tests, and CD4 and Viral Load technologies for HIV diagnosis and monitoring. It is foreseen, however, that the project will be prequalifying TB rapid tests, as well as male circumcision instruments in the future.

2 EVALUATION OBJECTIVES

2.1 UNITAID Project and overall PQDx programme

This evaluation report describes the activities and findings of the mid-term evaluation of the UNITAID Project Support for Quality Assured Diagnostics programme (WHO PQDx), conducted from December 2012 through March 2013. The UNITAID funded Project to support the WHO PQDx programme began in March 2009, with the contract due to end in March 2013. In December 2012, a nine-month extension (with $1M additional funding) of the contract was signed extending the project to December 2013. The project will then be aligned with the yearly cycle common to most other UNITAID-supported projects. It is foreseen that the PQDx support project will in the near future submit a proposal for a five-year continuation of the project.

The evaluation has the main objective of gauging the UNITAID Project's accomplishments and performance to date, the constraints and challenges it has faced, and assessing its relevance, effectiveness, efficiency, and impact. The evaluation team attempted to measure the results of the UNITAID investment in the PQDx programme, by gauging the effects of the UNITAID Project vis-à-vis the objectives it set out to achieve. However, one difficulty is that some results may not be directly attributable to the UNITAID investment as other organizations such as the Gates Foundation contributed to the same activities (until May 2010) as targeted under the UNITAID project. However, some documents, and many respondents (e.g. partner organizations) refer not specifically to the project or UNITAID's role (nor are they necessarily aware of the project at all), but provide information and feedback on the overall PQDx programme and its actions. So, the evaluation focuses on the activities of the Programme since mid-2009, while also specifically measuring performance against specific project objectives and indicators agreed to with UNITAID.

2.2 Stakeholders

The evaluation team sought to obtain perspectives on the project's performance from a variety of stakeholders (including beneficiaries, partners, suppliers/developers) as well as a range of documentation. The primary beneficiaries of the PQDx support Project are the buyers and users of diagnostics PQDx and the pilot countries in which the Project works to strengthen diagnostic regulatory capacity. The manufacturers of diagnostics that have been prequalified are secondary beneficiaries based on potentially increased sales of these products due to their prequalified status.

2.3 Measuring impact

The evaluation looked into the potential impact of the project in increasing the number of high-quality, useful diagnostic technologies for HIV/AIDS and malaria available worldwide. However, since the Project is relatively new (March 2009) and most of the diagnostics in question have only been recently prequalified, sufficient time has not elapsed to measure real impacts of the Project on the market. The Project's Memorandum of Understanding (MoU) states that a desired result of the programme over the long term is to "slow the spread of HIV infection in both children and adults, increase access to ARV and anti-malarial (AM) therapy, and slow the development of HIV drug resistance" by prequalifying products for diagnosis and monitoring of HIV and malaria treatment. (Project MoU document, page 4). It is beyond the scope of this mid-term evaluation to be able to measure and directly attribute any such larger impacts (such as reduced incidence of HIV, increased access to therapy) to this project. However, this evaluation aimed to measure outputs, outcomes, and where possible, impact.

The evaluation team has documented the project's achievements and activities to date, vis-à-vis the objectives and indicators set out for the project in the MoU and planning documents. The team has looked into the reasons for discrepancies between the planned

and realized results, in order to extract lessons learned and recommendations for future implementation.

3 EVALUATION FRAMEWORK AND METHODOLOGY

3.1 Framework

The evaluation team was guided by the project's logical framework, objectives, and indicators. It was also guided by the Terms of Reference (ToR) which laid out the following key research questions related to relevance, effectiveness, efficiency and impact:

Table 1 OECD/DAC Criteria and Relevant Research Questions

Relevance:
- Are the activities and outputs of the project consistent with the objectives and expected outcomes as described in the project plan?
Effectiveness:
- To what extent have the objectives of the project been achieved? - Were they achieved within the timeframe specified in the project plan? If no, to what extent are they likely to be achieved? - What are the main factors influencing the achievement or non-achievement of the objectives? - How is the project addressing potential risks it faces? Are there ways the project should change, to meet risks to its effectiveness?
Efficiency:
- Are the project partners working closely with the relevant national authorities in the project's beneficiary countries? Is there a close connection between the implementers and national authorities? - Has the project reacted efficiently to the donor's requests and changes (logframes, reporting)? Has the project submitted reports, and follow-ups, in a timely way?
Impact:
- Has UNITAID funding contributed to improvements in the landscape for diagnostic tests related to HIV/AIDS and malaria? - Are the activities of the project still relevant to the current environment, market dynamics, and country needs?

These questions are addressed below in the Findings and Analysis sections.

3.2 METHODOLOGY

The EHG evaluation team analysed the objectives and key performance indicators (KPIs) of the project and performance to date vis-à-vis the indicators. The mid-term evaluation has taken into account all the project reports submitted through 2012 (latest document dated Nov 2012). The UNITAID team requested that the evaluation take into account the last report, due Feb 2013, as it would use the new reporting template developed in late 2012; however this report was not received by the evaluation team, therefore not taken into account.

The project's logical framework, objectives, and indicators have evolved somewhat since the project launch in March 2009. The mid-term evaluation has therefore paid particular attention to the last project reports, which follow the most current set of indicators and objectives, defined in the new logframe.
The evaluation team conducted the evaluation through:

- **Meetings and discussions** (Dec 17-18) with UNITAID staff, and WHO project staff in Geneva

- Analysing project **documents**, reviewing web sites, and external documents related to PQDx
- **Interviewing** project stakeholders (partner organizations, country officials, manufacturers, consultants in the field of diagnostics)
- **Documenting findings** – both quantitative and qualitative, recording project accomplishments, activities, timelines, results
- **Charting measurable indicators** to gauge accomplishments vs. targets and plans
- **Analysing the information** through triangulating the information gathered and providing analytical summaries of findings

Achievements of the project, including capacity building efforts in the five pilot countries, were measured relative to project goals, outcomes and outputs as established in contractual agreements and project plans, and the project logical framework (logframe). Performance data was obtained from UNITAID and WHO, through project performance reporting, financial reporting, lists of prequalified suppliers and country activity reports, and other documents. Initial analysis of this data was triangulated with primary information obtained through interviews with key stakeholders and beneficiaries from WHO, UNITAID, pilot country representatives, United States government agencies, representatives from the Gates Foundation and CHAI, MSF and others, as well as several manufacturers/developers who have taken part in the PQ process.

Through this process the evaluation team has sought to answer the research questions in the four OECD/DAC core areas of relevance, effectiveness, efficiency, and impact and examine: 1) achievements and results, 2) project management and implementation, and 3) the project's integration and collaboration with UNITAID and other related global efforts. The evaluation findings are structured in the Detailed Summary of Findings section below in line with the three categories listed above. Further information and documentation is provided in the Documentation of Findings.

4 LIMITATIONS OF THE EVALUATION

The evaluation team would like to note that there were several limitations associated with conducting this evaluation, which should be taken into account when interpreting the findings. These include the following:

- Some contacts of partner organizations, developers, and others were provided by the project team, so there is the possibility of some selection bias.
- Full representation of respondents may not be reflected in this evaluation. Although thee evaluation team attempted to contract all identified respondents many were not available or did not respond within the time available.
- Some documents requested, and some responses to questions posed to the WHO and to the key respondents, were not provided to the evaluation team.
- Some of the in-country responses were provided by WHO country offices, which while valuable, may be somewhat biased in their attitudes toward the programme which is funding the activities implemented.
- Some results may not be directly attributable to the UNITAID investment, e.g. Gates Foundation funding was also used (until May 2010) for activities which the project reported on (and reportedly additional Gates Foundation funding has contributed recently to assist the programme in streamlining its processes). Respondents also provided feedback on the overall WHO PQDx programme, and many were not aware of UNITAID's specific project to support the programme.
- Many documents and contact details were provided to the evaluation team very late in the evaluation process. This required the evaluation team to very rapidly review

numerous documents, re-interpret certain findings already documented from earlier documents; rapidly contact respondents, seek their feedback, and analyse their responses.

5 DETAILED SUMMARY OF FINDINGS

5.1 Evaluation of Project Achievements and Results

In response to the evaluation's key research questions related to the WHO PQDx results and implementation, as agreed with UNITAID, the summary responses to those questions are as follows. (A much more detailed analysis and documentation of findings can be found below, and in the Documentation of Findings section).

5.1.1 Summary Responses to Research Questions:

Relevance:	**Findings:**
Are the activities and outputs of the project consistent with the objectives and expected outcomes as described in the project plan?	- The activities of the PQDx programme are consistent with its plans and objectives. The programme is highly relevant, in that there is widespread belief in the importance of better QA for diagnostics, and a general sense that with the many new technologies and new developers coming along, the importance grows. The need for a rigorous global PQ effort is undisputed, and WHO's technical strength and mandate in the field are generally agreed to. However, the performance and results of the PQDx programme to date are generally not meeting expectations. The programme has increased the speed at which devices are PQ'd in the last year and reports that many devices are very close to achieving PQ status; the next 2 reports should reflect that.
Effectiveness:	
To what extent have the objectives of the project been achieved?	- Important progress has been made toward end-of-programme targets, but results have been slower than expected. The possibility of the programme prequalifying 34 additional products by the end of the year in order to meet the programme target of 50 prequalified products seems unlikely, given the lead time and the current pipeline of products undergoing prequalification. Objectives for strengthening of regulatory authorities appear to have been met for Burkina Faso, Tanzania and South Africa. There are indications that objectives will be met for China in the next 6 months. The activities for Ivory Coast have been put on hold because of the unrest.
Were they achieved within the timeframe specified in the project plan? If no, to what extent are they likely to be achieved?	- -Generally, there were no benchmarks or timelines set for progress toward the objectives, so it is difficult to gauge how on track the project is toward attaining each objective.
What are the main factors influencing the achievement or non-achievement of the objectives?	- -Achievement of some objectives has been on track due to technical capacity of the project team, inputs from labs and consultants, and work with 4 of the pilot countries. However progress toward some objectives is further behind because of delays due to start-up and setting up of systems initially, the slowness of the PQ process, dossier imperfections, and reported reluctance by some suppliers to enter the PQ process due to the timelines. Human resource limitations may also be a factor. Many respondents also point to a lack of leadership and coordination or collaboration between WHO and other agencies which may hamper more rapid

	progress toward ensuring availability of a wider choice of PQ'd diagnostics.
How is the project addressing potential risks it faces? Are there ways the project should change, to meet risks to its effectiveness?	- Some activities have been conducted to avert risks, but other risks persist, including risks due to the lengthy PQ process timeline, negative perceptions of developers and partners, and limited resources which impede possibilities to expand efforts to more countries and regions. WHO PQDx seems to have been too reactive and not able to anticipate or mitigate risks. It has mostly reacted to pressure from the outside to speed up its process. It has not communicated effectively about the value of its rigorous approach to quality and is not leading an international discussion about how to effectively ensure quality of diagnostic devices. The programme needs to strongly improve its leadership and way of communicating with stakeholders.
Efficiency:	
Are the project partners working closely with the relevant national authorities in the project's beneficiary countries? Is there a close connection between the implementers and national authorities?	- The Programme has reportedly been working closely with officials in Burkina Faso, South Africa and Tanzania, making visits and conducting various capacity building activities. In China the activities have only very recently begun (late 2012), and in Ivory Coast, activities were suspended due to unrest. However most other partners (excluding beneficiary pilot countries) report that their relationship with the WHO PQDx has been disappointing and that the programme does not seem interested in working with other agencies.
Is the programme working efficiently, vis-a-vis time and resources? **(question added by evaluation team)**	- Although this is not fully justified, the programme is widely seen as too slow and ineffective, with a relatively negative reputation among partners and suppliers, mainly due to the long timeline for PQ, lack of transparency and clarity, and lack of collaboration with other PQ agencies to share/streamline the PQ process. The resources of the programme are stretched in terms of HR, and a large share of resources has been devoted to pilot country activities, potentially taking away from the need to improve and expedite core PQ processes.
Has the project reacted efficiently to the donor's requests and changes (logframes, reporting)? Has the project submitted reports and follow-ups, in a timely way?	- Project management and communication have not been ideal, with some reported micro management and communication bottlenecks by top management. In addition, incomplete and delayed communication and reporting, changing formats and reporting requirements by UNITAID, and lack of leadership have been reported as obstacles for the programme's efficient implementation. - The UNITAID project indicators and performance measures have been flawed, at times impossible to measure, and in flux over the 4 years, making performance management and performance based funding extremely difficult. Reporting has been weak (content and clarity) and somewhat delayed.
Impact:	
Has UNITAID funding contributed to improvements in the landscape for diagnostic tests related to HIV/AIDS and malaria?	- There have been positive impacts reported by some countries and developers, in enforcing the need for QA for diagnostics, and for setting high standards. However it appears too early to say the project has improved the landscape for quality assured diagnostics. Diagnostics that

	have been PQ'd by the programme were already on the market, and due to the small number PQ'd, procurement agencies cannot rely on WHO PQ for their procurement decisions. This will change as the number of devices PQ'd increases. Once procurement agencies can fully rely on the WHO PQ list, the incentive for manufacturers to be on this list will be much higher. - Respondents agree on the importance of the PQ process, but impact to date may be reduced due to delays and inefficiency.
Are the activities of the project still relevant to the current environment, market dynamics, and country needs?	- The activities are relevant, and may be even more important in future, with new technologies and new developers coming on to the market. However the programme may need to adapt and streamline operations to ensure positive impact, and be more flexible to ensure quality is addressed for new, much needed technologies (e.g. point of care). - The recent recall of Bioline RDT, which systematically passed WHO batch testing was a strong reminder of the value and necessity of rigorous systems to ensure quality.

5.1.2 Performance vs. Indicators

The goal of the WHO PQDx Programme is to increase access to appropriate diagnostics of assured quality for diagnosis, initiation and/or monitoring of treatment for HIV/AIDS and malaria, by increasing the availability and uptake of WHO PQ'd diagnostics, and by working with pilot countries to help enhance their regulation of diagnostic products. The evaluation team has attempted to measure the PQDx programme's performance and achievement of results vis-à-vis the programme's stated objectives since the 2009 inception of the UNITAID support.

As discussed in the section below on documentation of findings, the PQDx Programme has four main objectives, each with specific indicators and targets. The project's logframe and M&E terminology has changed since the MoU and start-up. Whereas the original logframe in the MoU hinged on four key "Objectives" and a number of "Actions" for the project, the logframe currently consists of one "Goal", two "Purposes", four "Outputs" (which are the original four "Objectives"), 17 indicators under the various outputs and purposes, with 10 main "Activities" to work toward these targets. See list below, taken from the most recent (Oct 2012) project report indicator template.

Table 2: Project Indicators (2012 template)

Key Indicators for the Project (2012 indicator template):
GOAL: IMPACT indicator: Increase access to appropriate diagnostics of assured quality for diagnosis, initiation and/or monitoring of treatment for HIV/AIDS and malaria. Indicator G1.1: Number and % of prequalified diagnostic tests purchased annually by key stakeholders per diagnostic category. **OUTCOME indicators:** **Purpose 1. (Outcome):** Increased uptake of UN/WHO prequalified diagnostics. Indicator P1.1: Number of procurement agencies that commit to procure prequalified diagnostics. • Indicator P1.2: % reduction in actual prices as compared to the market prices for different product categories of UNITAID priority diagnostics. **Purpose 2. (Outcome):** Strengthening of capacity to monitor the quality of diagnostics in beneficiary countries Indicator P.2.1: Number of beneficiary countries with improved regulatory capacity for UNITAID priority diagnostics.

- Indicator P.2.2: Number of beneficiary countries with post market surveillance action plans in place for UNITAID priority diagnostics.

OUTPUT indicators:

Output 1: Prequalified UNITAID priority diagnostics in support of HIV/AIDS and malaria treatment.

- Indicator O1.1: Number of specific UNITAID priority diagnostic product manufacturers incentivised to apply for WHO prequalification.
- Indicator O1.2: Number and % of applications accepted for all product categories.
- Indicator O1.3: Number of dossiers accepted for review for all product categories.
- Indicator O1.4: Number of diagnostic production lines assessed for all product categories.
- Indicator O1.5: Number and % of successful laboratory evaluations of HIV rapid diagnostic tests.
- Indicator O1.6: Number and % of successful laboratory evaluations of CD4 and HIV viral load technologies.
- Indicator O1.7: Number of prequalified diagnostics all product categories.
- Indicator O1.8: Lead time between receipt of a complete dossier and the final overall decision for prequalification of the diagnostic product.

Output 2: Facilitate procurement of appropriate diagnostics of assured quality (i.e. prequalified)

- Indicator O2.1: Number of procurement agencies using WHO procurement guidance

Output 3: Build and/or strengthen regulatory capacity diagnostics in beneficiary countries

- Indicator O3.1: Number of national regulatory authority staff participating in the WHO PQDx process, as a measure of educational learning process.
- Indicator O3.2: % of production lines inspected in which inspectors from low and low-middle income countries participated.

Output 4: Build and/or strengthen capacity for post market surveillance of UNITAID priority diagnostics in beneficiary countries

- Indicator O4.1: Number of beneficiary countries with systems for post market surveillance in place.
- Indicator O4.2: Number of lot testing events and field sampling surveys conducted per beneficiary country.

A review of key performance indicators for **Output 1** (indicators measuring the number of products prequalified and undergoing the PQ process) has found that important progress has been made toward end-of-programme targets, but that results have been slower than expected. The possibility of the programme prequalifying 34 additional products by the end of the year in order to meet the programme target of 50 PQ'd products seems unlikely, given the lead time for PQ and the current pipeline of products undergoing PQ. For **Output 2**, the target is 12 agencies using WHO PQ as a criterion for procurement of diagnostics, but achievement toward this target is unclear from the progress reports and the indicator itself is somewhat unclear in its meaning. Agencies refer to both global procurement agencies (such as UNICEF, IDA, etc) and to national level procurement agencies (usually under the MOH). No global or country procurement agency has yet been able to rely solely on WHO PQ for diagnostics, as not enough products have yet been PQ'd. So although the project reports that 12 agencies are now using WHO PQ for procuring diagnostics, this may overstate the magnitude. The feedback from stakeholders revealed that there is a very strong interest and no controversy in using the WHO PQ programme in their procurement policy. The only thing that is hampering them is the low number of PQ'd devices to date.

For **Output 3 and 4**, relating to support to pilot countries to establish enhanced regulation and Post Market Surveillance (PMS) of diagnostics respectively, as noted in the detailed findings section, significant progress has been made in some of the pilot countries, but the indicators and reporting are inexact and do not adequately reflect the status of these objectives or the progress made. There is not only a strong need but also a high demand for strengthening the national regulatory authorities of beneficiary countries in the field of diagnostics but this might take away resources (mainly human resources) needed to further develop the PQ programme and manage the backlog of products.

Reporting on many indicators in the progress reports has at times been inconsistent and vague. Results for some indicators have not been reported. Interim targets or benchmarks were not set for most indicators so some assertions that an indicator is on track, are sometimes not supported with details. Reporting on the achievement of some benchmarks appears to have assumed that activities that are planned would happen. The indicators for Output 1 (PQ'd diagnostics for HIV and Malaria) are reported very clearly in the Dashboard format, which allows for easy comparison over time, but other indicators are only discussed in the narrative text, and sometimes vaguely, making comparison over time more challenging. Incorporating all indicators in a dashboard format, or enhancing the reports to more clearly show progress against each indicator, is recommended.

The logframe itself and selection of indicators, although revised over the life of the project, may benefit from further improvements and clarification. Some indicators are not particularly useful, relevant, or verifiable. The progress report narratives contain a detailed list of lead time indicators that may be helpful for internal management (e.g., to identify bottlenecks), but are not particularly useful for external or donor evaluation of the programme. Indicator O1.8: the leadtime between receipt of a complete dossier and the final PQ decision has the most relevance for an outside party and incorporates nearly all of the other leadtime indicators. Similarly, while the numbers of dossiers reviewed, inspections undertaken and lab analyses completed are helpful for programme management, they are less relevant for external review than the bottom line Indicator O1.7, the number of prequalified diagnostics. From the workplans and progress report narratives, it appears that the programme is meant to be involved in a wide range of activities to strengthen capacity of target beneficiary countries (Outputs 3 and 4) that are not captured by the four indicators. The four selected indicators, by themselves, as mentioned above, do not provide a good proxy of the progress made.

The chosen indicators focus on the different milestones of the PQ process. Clearly this does not do full justice to the programme, as it gives the impression that the bottlenecks are the sole responsibility of the programme, whereas in many cases the failure of some devices to prequalify is due to critical non conformity (likely to be hazardous or injurious to the user) that needs to be dealt with by the manufacturer. The PQDx programme follows the whole PQ process from when the dossier is in the hands of the manufacturer to the time the dossier is in the hands of WHO. This could serve as a good base for an indicator that would provide a better picture about the efficiency of the programme. Similarly many dossiers get stuck at some stage during the PQ process and often implies that the manufacturers would need to change their system significantly to comply with requirements to pass the particular stage. The manufacturers often do not know how to proceed further and would need support, for which WHO has no resources and/or capacities, especially when there are many suppliers to be processed. An indication of the reasons why different manufacturer dossiers get stuck in the PQ process would also enable a more balanced picture about the performance of the PQDx programme.

Indeed, some manufacturers have been inspected up to 4 different times by the WHO, which drains the resources of the programme. At the same time those manufacturers benefit, free of charge, every time from the advice provided by the WHO inspection team on how to improve their quality management system yet are not demonstrating proper motivation leading to PQ'd diagnostics. Imposing a deadline for taking actions on critical non-conformities and required compliance or removal from the PQ process and need to re-apply could be implemented to increase motivation of the manufacturers and contribute to reallocating resources now used by lower-quality manufacturers toward higher-quality manufacturers.

There might be some confidentiality issues for the programme to report on how well different manufacturers are doing in the process but this should be addressed at least to some degree and be part of the reporting. In the current context where few diagnostic devices have been

PQ'd, some information about where manufacturers are in the PQ process could help international donors and procurement agencies to guide their procurement in beneficiary countries.

5.1.3 Challenges Faced

Since start-up in 2009, the Programme has established procedures and systems with input from various technical working groups and stakeholders. These include systems for dossier review, site inspections, tracking inspections, liaising with laboratories for product analyses, etc. There exists MoUs and other agreements with WHO Collaborating Centers (for lab analysis), with consultants for dossier reviews and site inspections, and with various partner organizations such as PEPFAR. One of the main challenges faced by the programme is grounded in the underestimation of the time and resources required to get the PQ systems up and running; delays that were beyond the control of the project team. The programme has faced other challenges, including reported inaccurate dossiers submitted by developers, staff turnover and open positions, and other management challenges (which are further detailed in section 2 below). The programme has made some changes and adjustments to adapt to challenges faced during implementation including instituting an inspection scheduling and tracking system to make inspections more efficient and easier to track; engaging more consultants to manage the backlog of dossiers to review and sites to inspect; instituting a "fast track" mechanism for some products in great need and with already ascertained PQ from other agencies, etc.

5.2 Evaluation of Project Management and Implementation

5.2.1 Programme Team and Structure

The PQDx programme is composed of a small team of 8 staff members - one programme coordinator and 7 team members who are each responsible for a specific technical area. There are currently 2 open positions which have been vacant for a long time and no support staff. It is unclear why two positions have remained open for such a long time. The bureaucracy and perhaps budgetary constraints for a large organization like WHO to fill positions may be an issue. It seems urgent that at least those two positions be filled as soon as possible. The technical officer in charge of strengthening regulatory authorities only joined the programme in November 2012.

The staffing seems inadequate for the programme to perform its mandate, run the prequalification programme, support the pilot countries, act as the world reference for diagnostics, as well as conduct all other necessary activities such as reporting to donors (upon which the programme is heavily reliant for its resources). An in-depth analysis of the human resource requirements for the prequalification programme vis-à-vis its work load would be useful prior to submission of the next proposal for another support project.

Another point of concern, which is further accentuated by the small size of the team, is the reliance upon strong professional individuals on the team rather than the organization itself. The know-how of the organization seems to be poorly institutionalized, raising issues as to the sustainability of the system when one requires a very high level of in-depth knowledge of the dossiers and critical technical issues in order to lead the manufacturers through the various PQ processes. The organization would certainly benefit by investing more effort in documenting and institutionalizing its know-how.

Table 3: WHO PQDX Team

Name	Position
Gaby Vercauteren	Programme Coordinator, DLT, WHO
Mercedes Peres Gonzales	Technical officer, DLT, WHO (rapid tests)
Irena Prat	Technical officer, DLT, WHO (dossier review; strengthening regulatory support and PMS)
Anita Sand	Technical Officer, DLT, WHO (product testing)
Jeanette Twell	Technical Officer, DLT, WHO (site inspector, manufacturer on-site evaluations)
Dr. Willy Kikoka Urassa	Scientist, DLT, WHO (CD4 count)
Robin Murant	Technical Officer, DLT, WHO (regulatory authorities)
Helena Ardura	Technical officer for review of applications and completeness of dossiers
(vacant post)	2nd inspector
(vacant post)	Communications/Project Officer

The programme relies extensively on contracting of consultants and organizations to perform the work involved in the various stages of PQ: dossier review, on-site inspection, and product testing. In the last year, the WHO PQDx program has extended its pool of consultants to increase the speed of the process. WHO tries to use the same consultants who have performed the dossier review in order to do the on-site inspection, in an effort to better follow up on issues detected in the dossier review as well as to ensure in-depth knowledge of the dossier in preparation for the on-site inspection.

The PQDx also relies on WHO Collaborating Centers (WCCs) for the laboratory evaluation component of the PQ. These WCCs are universities, and various accredited laboratories like the IMT (Institute of Tropical Medicine) in Antwerp or the Muhimbili University of Health and Allied Science in Tanzania for CD4 device testing.

The great expertise of the PQDx technical team is widely acknowledged by partner organizations and to some extent by the manufacturers. This is especially true for the staff involved in on-site inspections (clearly this field of expertise if the most visible to partner organizations and manufacturers). The very technical and specific functions of the various team members requires that manufacturers deal with several team members throughout the PQ process. It might not be feasible all the way through because of the compartmentalization of the technical areas, but the management of the PQ process per dossier might be more customer-friendly.

5.2.2 Leadership of the programme:

The relationship between the programme and UNITAID has been challenging. The quality and timeliness of reporting is regarded as unsatisfactory. Difficult, and at times limited, communication has added to the challenge of the programme-UNITAID relationship. There appears to be insufficient technical understanding from UNITAID about the PQDx programme and the way that it functions possibly due to high turnover of UNITAID portfolio managers in charge of the programme. The PQDx has not clearly explained and communicated its approach to PQ, the challenges it faces, and its needs and constraints.

The general feedback from stakeholders about communications by the programme is also quite critical (with a few exceptions). The PQDx is criticized mainly for its lack of speed, poor communication, lack of transparency and lack of interest in working with stakeholders.

Stakeholders also note that the programme fails to communicate efficiently about the rationale of its approach and methodology. External stakeholders blame the bureaucratic process and lack of flexibility, and seem to have little awareness of WHO's rationale for its rigorous approach to quality. For instance in 9 of 23 manufacturers inspected, WHO inspections reportedly revealed critical non-conformity with the quality management system, despite these companies having received approval from stringent regulatory authorities. There seems to be a lack of constructive debates among stakeholders who think that the WHO PQDx programme only duplicates the efforts of other agencies and therefore wastes resources while preventing products from becoming available on the market where countries can use them with confidence.

The PQDx would benefit from investing more in its communication efforts to the outside world. In addition, strong leadership is required for the programme to advocate and engage in the political debate around the value of the PQDx rigorous approach, which is characterized by more than just bureaucracy, inflexibility and arrogance (contrary to some opinions).

The current level of staffing (number and type of positions), as discussed above, and the need to run the day-to-day activities of the PQDx programme as well as fulfilling other WHO DLT tasks, makes it difficult for the programme to undertake better communication efforts. This is unfortunate, as this would be likely to generate more buy-in and support for PQDx initiatives from other stakeholders, who would be more willing to collaborate if they felt that the programme would be open to such collaboration.

5.2.3 Project Reporting

Several reporting formats have been used by the project since 2009. The original reporting framework provided by UNITAID was not fully developed and did not really enable UNITAID to appropriately follow up on the implementation of the programme. The reporting requirements from UNITAID have now changed several times since the original agreement was signed in 2009. Since 2009 UNITAID has also had several different portfolio managers in charge of the PQDx programme, which has contributed to a slow uptake of the new reporting requirements and frustrations on both sides.

There are three kinds of reporting tools now in use by the project: interim progress reports for the first six months of each year; annual reports which feed-back on the whole year as well as specifically for the second half of the year; and PUDRs (project update and disbursement requests). The report templates do not include clear indications of activities for the period, disbursements and expenditures (let alone broken down by activity). The three reporting tools do not systematically complement each other. The report contents are often vague and lack critical information. The reports mix period-specific actions with cumulative actions, which further adds to the confusion. These factors make it particularly difficult to understand, measure and interpret the results for each reporting period.

Timeliness of reporting from the WHO project team was often-mentioned as a point of frustration by UNITAID. It does appear that, whereas initially reports were submitted more or less on time in 2009-2011, reports in the last year of the project have been submitted late. The reasons for the delays are not always clear (and may be affected by changing formats and reporting requests from UNITAID).

More information on project reporting is provided below in the Documentation of Findings section.

5.3 Evaluation of the Project's Integration with Overall Global PQ Efforts

The PQDx programme is one of many efforts within various organizations to ensure the quality of diagnostic tests. The quality of diagnostics is widely acknowledged as an area of concern for all international stakeholders, especially now, when many new technologies are entering the market.

5.3.1 The WHO PQDx and other WHO Prequalification Programmes

The PQDx Programme has various features that distinguish it from the other WHO PQ programmes (pharmaceuticals and vaccines). There is often a comparison between the three programmes, which reflects poorly on the PQDx although not necessary justified. See below the list of features which distinguish the PQDx from the other WHO PQ programmes.

- The **diverse nature**, technologies and usage involved in in-vitro diagnostics make the devices difficult to compare with each other (RDT, CD4 count machine, reagents, consumables; each test needs appropriate maintenance and device-specific training etc…) and require a very broad technical knowledge, which is not the case in PQ of Pharmaceuticals and PQ of vaccines. A new technology device comes with a new set of issues which needs to be addressed.
- The devices are often produced from **different components** coming from many different locations across the world, with an often complicated chain of companies involved in the manufacturing of the different parts, making the quality control of these devices particularly challenging.
- Diagnostic devices are often presented by the manufacturers and suppliers in **different models or of different quality levels.**
- The field of in vitro-diagnostics is much **less regulated** than that of pharmaceuticals and much work remains to be done to raise awareness on this issue.
- There is little to no literature (at least that the evaluation team could find) about the **hidden costs of faulty diagnostic devices** for health systems, and perhaps inadequate attention to this issue. Diagnostics is the first step in the treatment process, and all care and treatment efforts down the line depend on the quality of the diagnostic device and the administering of the test in order not to be compromised. WHO estimates that the failure to diagnose a TB patient leads to an average of 12 new cases (*WHO TB Report 2011*). The hidden costs of poor quality diagnostics are not always evident to countries or HIV/malaria programmes, but as everything around patient care and prevention begins with testing, if the testing is flawed, the rest of the chain of health care suffers (wasted resources, compromised patient care and negatively impacted programme objectives).

5.3.2 The Value of the PQDx Programme for International Donors and Procurement Agencies

International procurement agencies and international donors in the field of health and development are becoming increasingly sensitized about the quality of diagnostic devices and are seeking to better control their own purchases and the procurement choices for different country programmes. For example, the Global Fund requested the help of WHO DLT in drafting their procurement guidelines and QA policy for Diagnostics (2010). This policy is currently in the process of being renewed (again with the support of WHO DLT).

5.3.3 The Value of the PQDx for National Regulatory Authorities and National Programmes (HIV, Malaria)

In-country regulatory authorities understand the need to ensure the quality of pharmaceuticals, but much less so for diagnostics. The regulatory framework for diagnostics in most countries is lagging behind, which is providing easy entry to non-quality assured diagnostic devices. The work done by WHO in the pilot countries of South Africa, Tanzania

and Burkina Faso (with China also starting in 2012) has begun to make countries aware of this problem.

One important issue is that the hidden cost of poor-quality diagnostic devices is currently not quantified and not sufficiently researched. This overall cost is, however, likely to be significant, as getting the diagnostics right is the first step guiding important investments in treatment (pharmaceuticals, follow up tests, human resources etc…) which can be wasted should the diagnosis be incorrect. Most importantly, the cost of failing to identify cases properly due to faulty diagnostics also comes with a major public health cost for infectious diseases: increased incidence, false negatives leading patients to miss out on treatment and go on to infect others, treatment at a later stage of the disease leading to increased morbidity and mortality, etc.

Countries often lack this kind of critical information in order to take decisions appropriately. WHO can be a great help in this field. Currently the WHO LDT provides support to countries by ensuring quality of the diagnostic devices through the PQ process and by supporting the 4-5 pilot countries to develop their regulatory framework for diagnostics.

With the rise of many new diagnostic technologies, it would be useful for countries to receive support from WHO LDT not only on the quality of different devices, but also on how to choose between different diagnostic technologies according to their comparative cost and the context in which they are to be utilized. This could take into consideration hidden costs and opportunity costs of the different technologies, not only the price and quality of the diagnostic device in itself. For instance point of care (POC) technologies with lower sensitivity/specificity than the standard laboratory technology might nonetheless lead to better health outcomes in some cases, due to the potential reduced occurrence of patients lost to follow-up. Countries having to make the best use of a limited budget might also benefit from guidance on where to integrate the different technologies in the national diagnostic algorithm, and taking into account the context in which health workers are operating.

5.3.4 The Value of the PQDx for Manufacturers and Developers

In a market driven by international donors and national programs conducting international open tenders, the manufacturers are eager to receive international recognition for their products. In the current setting it is difficult for a pharmaceutical manufacturer in the field of HIV, TB and Malaria to reach scale without WHO prequalification. WHO PQ not only represents a quality label but also a significant competitive advantage for manufacturers, as most countries implementing Global Fund grants (and other large health programmes) hardly look beyond the list of pharmaceuticals PQ'd by WHO for their procurement decisions.

However, due to the small number of in-vitro diagnostics devices prequalified so far, this is not yet the case for manufacturers of diagnostics. Most of the PQ'd diagnostics have actually been on the market and in use in many developing countries prior to their PQ. So far the PQDx has not been able to change the dynamics of the market and the manufacturers do not report an increase in market share or turnover that they can attribute to their WHO prequalification. In some product categories, there are only one or two devices prequalified, which leads to a de facto monopolistic situation for countries or agencies that would solely rely on WHO PQ for their purchasing decisions. As a consequence, the poorly regulated diagnostics markets in upper- and lower-income countries continue using non-quality assured technologies.

5.3.5 Controversy among Stakeholders about the Rigorous Methodology of the WHO PQDx programme

When engaging stakeholders in the evaluation, it became apparent that the methodology adopted by WHO for PQDx is currently being challenged internationally. On the one hand, all stakeholders seem to agree about the value of the PQ process to ensure the quality of diagnostic devices (or at least provide a strong guarantee); and they also agree that WHO is the best agency to implement it. On the other hand, since the PQDx has not yet had an impact in the market (simply because too few products have been prequalified so far), it is heavily criticized by the international community. The failure of the PQDx to effectively communicate about its approach and to collaborate more with stakeholders has further aggravated this situation.

5.3.5.1 WHO PQDx versus other Initiatives to Ensure Quality of Diagnostics Globally

The methodology of the WHO PQ programme appears to be widely acknowledged as the most rigorous in the world. However, there are other PQ approaches, some of which are also endorsed and implemented by different departments within WHO; these include:

1 Rapid introduction of the Gene expert diagnostic test for resistant TB - the unique and previously unmet need in the field of resistant TB diagnostics has led to the rapid introduction of the Gene Xpert MTB/RIF device which was supported by WHO. The priority was given to quickly getting the device onto the market, with a plan to resolve any outstanding implementation issues later. Countries that have based part of their TB programmes on this device for the identification of drug resistant TB cases have begun experiencing issues with the device, which is very temperature sensitive and needs frequent calibration (which needs to be performed externally). It would be very beneficial to have this device undergo PQ as soon as possible; however it seems that the manufacturer has not submitted its application to the PQDx yet, and the PQDx donors are focusing their priority for the programme on Malaria and HIV.

2 Endorsement of diagnostic devices - some agencies rely on endorsement in an effort to ensure the quality of diagnostic devices for procurement. This consists of a review of the published literature and clinical trials with no inspection of the quality management system. The PQDx approach is much more comprehensive and relies on the regulatory approach adopted by the Global Harmonization Task Force (GHTF). Clearly procurement agencies do not have all the means necessary to undertake comprehensive assessments such as the PQDx programme, but with the low number of PQ'd products, they have to resort to other approaches to ensure the quality of the devices they agree to purchase.

3 Batch testing - another approach consists of batch-testing products from many different suppliers and publishing the results for the devices that have successfully undergone the tests. For example, the WHO Bulk Procurement Scheme (BPS) programme tests on an annual basis a broad range of malaria rapid tests. Suppliers and products have to undergo a WHO prequalification exercise as a minimum requirement for inclusion in these schemes. This programme is conducted in partnership with other agencies such as UNICEF. BPS does product testing only (they get samples from developers sent to them). It is a much less stringent approach to quality. The PQDx programme re-conducts the tests for the same products during the PQ process.

Batch testing has its limitations: the results of the tests represent results from only one point in time, and the kits tested may not always be very representative of the final product if they are submitted by the manufacturer (they can be made especially for the submission, for instance). If a batch fails the test, the manufacturer can provide a new batch without further checks. The recent recall of the Bioline rapid test for HIV, which was one of the most established tests on the market, was a strong reminder that the batch testing

process only assesses the quality of a device at one point in time, and may not be a sufficient guaranty of quality.

4 WHO PQ of diagnostics vs. approval from a stringent regulatory authority - Many stakeholders consider WHO's methodology for PQ of diagnostics a duplication of the efforts of other stringent regulatory authorities (such as US FDA, and its equivalents in Canada, Japan, Australia and the EU). In fact, the classic WHO PQ process does not take into account marketing approvals from those Stringent Regulatory Authority (SRA) organizations, and requests manufacturers and developers to perform a complete new process that encompasses many of the features required by the SRAs. However the WHO PQDx system goes further than SRAs' process. Below is a list of the main differences between the WHO PQ process and the process for marketing approval from SRAs:

- Stability of under various climates
  The mandate of SRAs is to protect the interest of their own populations, and they do not generally go beyond that. Since most countries with a SRA benefit from a mild climate and good infrastructure, the data that is asked from suppliers in terms of stability of the products does not ensure that the product will be able to perform under more drastic circumstances in terms of temperature, humidity, storage, transport etc.

  WHO PQ'd diagnostics are intended for marketing in a wide variety of countries where the local regulatory authorities are not fully able to ensure the safety and adequacy of the product on the market. A large number of these countries operate in extreme conditions in terms of temperature and humidity. The question whether, for instance, US FDA-approved devices would operate in the same way under more extreme circumstances is therefore very legitimate -- as the infrastructure (buildings, air conditioning, electricity supply, road and distribution network) in many countries may not be able to properly control for the lack of stability of the devices under these conditions.
- User appropriateness
  WHO requirements for the PQDx process take into account that the users in different countries might be very different from those in countries with SRAs, in terms of level of training, culture and languages.
- Post market surveillance
  Post market surveillance in destination countries is often not established as a routine process and therefore the WHO PQ process requires the manufacturers to have addressed the issue at some level and to show that they have made a deliberate effort to create a pathway for complaints about the devices to be fed back to the mother organization.

The above lists the gaps in the SRA process that are addressed by the WHO PQ programme. There are also issues, as reported by WHO, where approvals from SRAs have been found to be unreliable, including:

- Apparent double standards on some systems adopted by SRAs
  As already mentioned above, the mandate of stringent regulatory authorities is to protect the interests of their own populations. In that respect they make a distinction between products intended for marketing on their territories and those that are not. For example, devices produced in the US but not intended for marketing in the US can benefit from an FDA approval but not have to comply with many of the compliance criteria required for a device to be marketed in the US. In this case it can legitimately be argued that the device has not really been approved by SRA authorities although from the outside, this appears to be the case.

- Failure of some SRAs to identify critical non-conformity with the quality system in place (e.g. ISO)
  A reported 9 out of 23 manufacturer inspections performed by WHO revealed critical non-conformity in quality management systems with ISO 15385 certification, although these were for devices already approved by SRAs. A critical non-conformity is the highest level of non-conformity and is defined as likely to result in a hazardous and potentially injurious situation to the user. This raises concerns as to the reliability of the process used by some SRAs to give marketing approval of diagnostic devices.

5.3.5.2 Initiatives to expedite the PQ process

As previously mentioned the WHO has not been able to adequately communicate with other stakeholders about the value of its chosen methodology and the constraints under which it is implementing the PQDx programme. The perception is that WHO is not making an efficient use of the resources because it is duplicating the effort of other agencies, and that the slow process is acting as an obstacle for high-quality products to establish themselves in the markets of beneficiary countries. This vision, although not fully unjustified, is perhaps exaggerated, as often the "devil is in the details" and in such a complex process, one needs to be very specific about what is a duplication and what is not. It would be beneficial for WHO to play a leading role in moderating the discussion about how to go about ensuring the quality of diagnostics.

Taking into account the nature of the WHO PQDx programme, it is critical that it retains the freedom to act in the sole interest of the public. The fact that the WHO PQDx programme is entirely reliant on donor funding for its implementation makes it particularly sensitive to donor relationships and priorities, and in the future may raise concerns about the ability of the programme to take decisions fully independently.

Instead of taking the lead on resolving issues such as the slow PQDx process and its constraints (e.g. the lack of human resources), it seems that the programme has so far only been able to react to pressure from different donors and stakeholders. Below are the different initiatives undertaken by WHO PQDx to speed up the PQ process.

1. Fast-track procedure

The Fast-Track procedure, which began in July 2011, is an abbreviated assessment process for prequalifying products that have been previously assessed by one or more recognized National Regulatory Authorities (which are stringent authorities only). The aim of the fast-track procedure is to avoid duplication of effort and reduce the time to prequalify products. In essence, WHO may accept evidence or assessments undertaken by specific National Regulatory Authorities (NRAs) that are SRAs (see list below) that could fulfil some of the requirements of WHO's prequalification procedures.

The decision by WHO to conduct an abbreviated assessment is based on several factors and is made on a case-by-case basis. WHO will always undertake some level of assessment of the product and its manufacturer to provide assurance relating to unique aspects of quality, safety and performance – e.g., to verify the identity of the product and to ensure its suitability for use in resource-limited settings. Depending on the evidence provided for prior stringent regulatory approval, WHO may expedite the PQ process by:

- Reviewing in-depth only those aspects of the product dossier that are specific to the WHO PQDx, and/or
- Conducting a shortened inspection focused on aspects related to the perspective of WHO end users (e.g. transport/storage stability, customer service networks, etc.).

The SRAs that are recognized by WHO/DLT for the Fast-Track process are:

- Competent Authorities from the 27 Member States of the European Union who are responsible in Europe for the oversight of the Directive 98/79/EC on in-vitro diagnostic medical devices, and the associated Conformity Assessment Bodies (Notified Bodies),
- Food and Drug Administration of the United States of America,
- Health Canada and the associated conformity assessment bodies (CMDCAS Registrars),
- Japanese Ministry of Health, Labour and Welfare, and
- Therapeutic Goods Administration, Australia.

According to the Status of Applications available on the WHO/DLT website, 11 products have or are undergoing a fast-track abbreviated PQ process.

The evaluation team's review of the documents indicates that the average number of days to prequalify 7 products that were not fast-tracked was approximately 350 days, whereas the average number of days to prequalify 8 products that were fast-tracked was approximately 274 days. For this sample, the time used for prequalifying fast-tracked products was reduced by 22% compared to the non fast-track. The length of time for prequalifying varies by product, but the data does support the notion that fast-tracking on average does speed up the PQ process. Respondents, however, including partner organizations and developers, did not share this view – there was widespread negative feedback on the fast-track process and complaints that it appears to be no faster than the regular PQ process.

2. Prioritization of diagnostic devices to be PQ'd

Taking into consideration the length of the process and the resource limitations, the PQDx uses a priority list in order to address the most urgent needs in terms of prequalification. Actions 5.1 and 5.1.3 of the MoU between UNITAID and WHO and activity A1.1 of the project logframe all address prioritization. The MOU and logframe call for the development of formal procedures to prioritize products for PQ, updating the procedures semi-annually and with an annual review of priorities by an IPC interagency working group.

The criteria for prioritization have changed somewhat since the beginning of the project. Initial prioritization criteria were agreed by a group of UN agencies at the Interagency Pharmaceutical Cooperation (IPC) Meeting held in Tunis, November 2008 (including WHO, UNICEF, UNDP, UNFPA, UNOPS, World Bank, African Development Bank, etc.). These criteria are as follows:

- Already listed on the WHO Bulk Procurement Scheme and procured in high quantities by UN agencies
- For HIV or malaria
- Format: Rapid test
- Original manufacturer (i.e. not a re-brander)
- Where there exists few other PQ'd products
- Manufacturer has good commercial and procurement history (i.e. licensed for sale & distribution in a representative sample of countries of intended use).

The text below taken from *Issue 3, Q3 2009 of the Prequalification of Diagnostics Update* on the WHO/DLT website shows that the last criterion ("manufacturer with a good history") was dropped. Criteria were then listed as:

- Diagnostics already listed on the WHO procurement scheme and procured by UN organizations in significant levels
- Products which assist in the diagnosis of infection with HIV-1/HIV-2 and infection with malaria parasites
- Diagnostics in a rapid test format
- Diagnostics that are manufactured by original product manufacturers
- Product categories for which there exists few other prequalified products

A document on the WHO/DLT website intended primarily for manufacturers of diagnostics titled: *Overview of the prequalification of diagnostics assessment process* (*ref* PQDx_007 v4 22 March 2011) provides a slightly different and more general list of priority criteria, as follows:

- the need for diagnostic technologies for a particular disease or disease state
- the appropriateness of the product for use in resource-limited settings; (e.g., Point of care diagnostics)
- the requests from WHO Member States for particular diagnostic products
- the performance capabilities of particular diagnostic technologies, and/or
- the availability of currently prequalified products that are similar or the same.

Through September 2012, 62% of applications received by WHO PQDx were accepted as priority products (i.e., 38% of applications were not accepted). The backlog of products undergoing PQ and time required for PQ confirms the continuing need to prioritize applications.

3. Streamlining of the PQDx process

The Bill and Melinda Gates Foundation has been advocating for the WHO to streamline their PQDx process. It has also reportedly provided the organization with US $1. 4 million to devise a strategy for streamlining and to test it on new CD4 count devices. A proposal for a streamlined process has been submitted to WHO by the Gates Foundation in February 2013. In April 2013 a consultation with a broad range of stakeholders is planned in order to seek feedback on the proposed streamlined process.

4. Conditional approval

The WHO PQ programme for pharmaceuticals has a system in which a product can receive a conditional approval. If the product has previous approval by a stringent regulatory agency, the manufacturer or the buyer can request that the product undergo review by the expert review panel (ERP) of WHO. This process can happen very rapidly. After the product has obtained ERP approval, the manufacturer has one year during which its product can be purchased (such as the other products on the PQ'd list). During this time the manufacturer must undergo the full PQ procedure in order to stay on the list. For the extension period of the PQDx project (March to December 2013) UNITAID has requested WHO to propose a similar system for diagnostics. Feedback from regulatory authorities in beneficiary countries included concern that manufacturers systematically advertise a conditional approval or ERP approval as a WHO prequalification.

The multiplicity of efforts and approaches as described above to expedite the WHO PQ process, while laudable, might result in loss of focus and further inefficiencies. The fact that these initiatives appear to be mostly donor-initiated further highlights the need for the WHO PQDx programme to strengthen its leadership and invest more in discourse and collaboration with the various international stakeholders, and in harmonization across donors. The feedback received from the different stakeholders during this evaluation has revealed that donors have very little awareness about what the others are doing; that they are very interested in learning more about various inputs into the PQDx programme; and that they are very interested in improved collaboration and in harmonizing their approaches for the benefit of the programme.

6 DETAILED DOCUMENTATION OF FINDINGS

As a basis for the findings summarized above in the responses to the research questions and in the three sections (results, management, global integration), the evaluation team documented the following detailed findings, described in the 4 sections below:

6.1 Document Review

a. Country Plans and Reports

Numerous country documents were provided to the evaluation team; findings are summarized below.

Table 4: Findings of Country Activities

Pilot Country	Activities to date (according to project and country reports)	Comments
China	• Information sessions to MoH and Chinese manufacturers organized by WHO China to clarify the objectives and processes of WHO PQ. • In 2011-12 an assessment was conducted by the WHO health system team in China on the motivation and barriers of Chinese manufacturers to achieve WHO PQ standards. • A number of PQ visits – last one in Sept 2012. • A project for PMS of HIV diagnostics is starting. Chinese experts were trained in laboratory techniques for PMS in Feb 2013. These improved techniques will be implemented in 2013 by the China HIV reference laboratory. A review of existing national regulations for PMS is planned for early 2013	The activities with China started in the second half of 2012. The budget for those activities has not yet been disbursed to the Chinese CDC, which is intended as the beneficiary. The activities undergone in China prior to summer 2012 are linked with the PQ of Chinese manufacturers.
Burkina Faso	Action plan drafted in March 2011 MOU between Burkina Faso and the program in Nov 2011 Attendance at Dec 2011 launch meeting/training in Tanzania <u>Objective 1:</u> • Improvement of regulation in the field for diagnostics devices. • Following the training of 15 staff members, the regulatory authority has several team members with expertise in the field of diagnostics regulation. • Designed and is now implementing a regulatory framework for in-vitro diagnostics as a result of the program. <u>Objective 2:</u> • Improvement of quality assurance across the supply chain for priority diagnostics • Training of various supply chain agents • Procurement guideline for diagnostics as well as guidelines for distribution and storage of diagnostics have been drafted and staff trained to implement them. <u>Objective 3:</u> • Strengthening of the post-market surveillance for HIV diagnostics. • Training on post-market surveillance for HIV • Setting-up of a technical committee for HIV tests • Drafting of the guidelines for PMS and design of tools for the management of PMS. • Lot testing on 10 lots for quality control in 10 different sites across the supply chain performed.	The main activities as planned in the Country Action Plan (covering 2 years) have reportedly been performed. The $200,000 budget has been disbursed and utilized.
Ivory Coast	• Mission report done Dec 2009 • Intervention delayed due to instability in the country	On hold. Invitation to participate in Feb 2013 training session being organized by WHO
South Africa	• Representatives attended Dec 2011 launch meeting and training in Tanzania • July 2012 invitation from DOH to WHO requesting participation in SA Ministerial Task Team for procurement of diagnostics in	According to WHO project, communications with SA were difficult

	SA • Aug 2012 mission to SA, assisting DOH to interpret WHO PQ standards, using quality standards for their programme • SA DOH inspectors participated in 2 inspections (China, Korea), of HIV RDT manufacturers • WHO reviewed SA regulations, provided input • Support from WHO (at request of DOH) in 2012 on HIV RDT quality assurance through PMS, and through improving technical specifications for tendering	initially, but improved with new WHO WR in country. Activities ramped up in 2012. Potential for SA to spearhead regional collaboration in diagnostics.
Tanzania	Objective 1 – building/strengthening regulatory capacity: • Situation Analysis (Nov 2009) • National Action Plan to strengthen regulatory and post-market surveillance of diagnostics developed (approved by MOH Dec 2010) • Dec 2011 launch of program in Tanzania, combined with training meeting including others from Africa region • 4 missions to Tanzania • TFDA produced and finalized guidelines on evaluation of diagnostics applications; evaluation of dossiers; for registration of diagnostics; and for PMS of diagnostics. • TFDA proposed amendments to TFDC Act of 2003 to include regulation of diagnostics • Furniture, computers, equipment procured for TFDA. • Funding provided, process begun to recruit 2 new staff for TFDA • Improve the HR capacity of diagnostics through trainings ((14 staff from TFDA, NHLQA&TC, MSD and PHLB were trained for two days form 12-14 December 2011); study tours to stringent regulatory authorities (e.g. 3 people from NHLQA&TC to Germany Feb 2013; 2 people from TFDA visit WHO HQ to study dossier assessment method). • Ensure adequate human resources: 4 staff have been recruited to implement regulation of diagnostics including PMS activities at TFDA (2), NHLQA&TC(1) and MSD(1) Objective 2: PMS quality Improvements: • SOPs for storage and transportation of medical products have been developed by MSD and reviewed by WHO • 50 Log Tag temperature monitors were donated to MSD in Dec 2011 by WHO to monitor temperature change during distribution of diagnostics • Objective 3: Improve QA training and PMS: • Ensure the quality of HIV and malaria diagnostics: Protocol and tools for monitoring the quality of HIV assays by end users developed; QC samples prepared and given to HIV testing sites • Develop plan and procedure for sampling of priority diagnostics from end users at all levels for PMS and conduct pre-market batch testing at NHLQA&TC of HIV rapid assays sampled by MSD and TFDA • 288 inspections done on diagnostics coming into Tanzania Jan-July 2012 • Process for accreditation of NHL-QATC Lab for post-market surveillance of diagnostics begun, and application sent to SADCAS Board	Apparent progress since Dec 2011 launch. $20,000 disbursed to Tanzania by Oct 2010 (of $200,000 total action plan budget). Remainder of $200 000 budgeted was likely disbursed, but not clear from reporting.

Note: a budget of $200,000 per pilot country was made available to the pilot countries

From the review of country documents, it is evident that there has been significant communication and work with in Burkina Faso and Tanzania. China, Ivory Coast and South Africa are lagging somewhat, due to various circumstances including unrest and instability in

Ivory Coast putting activities there on hold, limited communications and slow start-up with South Africa, and slow start-up with China.

The project's reporting on country activities is somewhat buried in the interim and annual reports, making it difficult to discern on-going activities, expenditures, completed actions, results in the countries. The evaluators attempted to gauge activities in each country through progress reports, feedback from the countries, and Country Action Plans.

b. Interim and Annual Project Reporting

The original reporting framework provided by UNITAID was not fully developed and did not really enable UNITAID to appropriately follow up on the implementation of the program. UNITAID was eager to move to the new reporting framework while the PQDx preferred to keep to the legal agreement. Since 2009 UNITAID also underwent successive changes in the portfolio manager in charge of the PQDx programme, which also lead to a very slow uptake of the new reporting requirements and frustrations on both sides. UNITAID and WHO have agreed on a new reporting format around September 2012. This new format was not used by WHO in the last interim report submitted in October 2012. The PQDx programme communicated they would use the new format for the final annual report due in February 2013.

The reports submitted by the PQDx require a substantial investment in time for a reader who is not involved on a daily basis with the routine of the programme in order to extract key information and track the progress of the programme. Their content is often vague and lacks critical information. The activity and indicator table refer to the narrative part and requires prior knowledge from the reader in order to be understood, or refer to additional external documentation which is not readily available or provided. The high staff turnover within UNITAID further decreased the organization's institutional knowledge about the PQDx and ability to make sense of the reports.

The reports mix period-specific actions with cumulative actions, which further adds to the confusion. The different formats presented also make it particularly challenging to compare and compile the information in successive reports. The cumulation of all these factors make it difficult to understand, measure and interpret the results for the time period in question.

Timeliness of disbursements: UNITAID self-reported significant delays in its disbursements to the PQDx programme. These delays are however not possible to track through the reports. It seems however that the delays did not impact the Programme's implementation, as PQDx was able to access bridge funding from WHO (and other sources, including Gates Foundation) until the funds from UNITAID were disbursed.

According to the project MOU, reporting and disbursements were to take place at the approximate timing and under the conditions noted below. The actual report and disbursement dates are from the analysis of the data in financial and M&E reports submitted from 2009 to 2012 (with reporting dates taken from the dates on the reports themselves – assuming these are accurate submission dates). Some reports appear to have been submitted on time, some had extensive delays between original submission and final, other reports appear to have been submitted two or more months late. Disbursements also did not follow the forecasted timeline, reportedly due to use of Gates funding that was ending May 2010, and some (self-reported) disbursement delays from the UNITAID side. It is unclear how or whether any disbursement delays may have affected project activities.

Table 5: Disbursement Dates and Conditions

From MOU: Estimated Disbursement or Reporting Date	Planned Payment Amount	Conditions	Actual report date	Actual disbursement and date
On signature of MOU	$1,000,000	N/A	N/A	$1,000,000 (April 2009?)
1 Oct 2009	N/A	Submission of 1st interim progress report	On time: Oct 1, 2009	None
20 Oct 2009	$1,250,000	Approval of first progress report by UNITAID		None
15 March 2010	N/A	Submission of 1st annual report	2 months late: May 15, 2010 – 1st annual report (March 23, 2009-March 15, 2010)	N/A
1 June 2010	$2,200,000	Approval of 1st annual report by UNITAID		None
1 Oct 2010	N/A	Submission of 2nd interim progress report	1 month late: Oct 30, 2010 -- 2nd interim report (15 March-1 Oct 2010)	N/A
15 March 2011	N/A	Submission of 2nd annual report	On time: March 15, 2011 -- 2nd annual report (Jan-Dec 2010)	N/A
1 June 2011	$2,500,000	Approval of 2nd annual report by UNITAID		
1 Oct 2011	N/A	Submission of 3rd interim progress report	On time: Oct 1, 2011 -- 3rd interim report (Jan-Sept 2011)	N/A
15 March 2012	N/A	Submission of 3rd annual report	3-5 months late: June 2012 (final Aug 31, 2012) -- 3rd Annual report (Jan-Dec 2011)	$2,850,000 (Dec 2011)
1 June 2012	$550,000	Approval of 3rd annual report by UNITAID		$2,000,000 (Aug 2012)
1 Oct 2012	N/A	Submission of 4th interim progress report	2 months late: Nov 26, 2012 -- 4th interim report (Jan-Aug 2012)	N/A
Total to date				**$5,850,000**
After settlement of all obligations (target date June 2013)		Submission of final project and financial report		
Total	**$7,500,000**			

c. Logframe and Indicators -- Achievements and Results against targets

This evaluation focused primarily on the current list of indicators in the most recent logframe and progress report dated 28 Oct 2012. It should be noted that the current list of indicators varies in content as well as format from the agreed indicators in the original MoU with UNITAID. Some indicators from the original MOU are not included in the most recent reports, while new indicators have been added (Indicator P1.1.). In addition, some indicators in the original MoU were meant to measure "actions" that have been completed so there is

no reason to track them any further. Progress reports are organized by the "actions" originally agreed in the MoU, where indicators in the logframe are numbered differently and are organized by "goal, purpose and outputs" making comparison of the two cumbersome. A review of the indicators follows.

Goal (Impact): Increase access to appropriate diagnostics of assured quality for diagnosis, initiation and/or monitoring of treatment for HIV/AIDS and malaria				
Indicator Number	**Indicator Measure**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**	**MOU Indicator**
G1.1	Number and % of prequalified diagnostic tests purchased annually by key stakeholders per diagnostic category.	50 million units	Not reported to date. According to the logframe, the indicator is to be based on market analysis reports. Baseline market analysis reports have been completed, but more recent market analysis reports that would include sales of prequalified diagnostics have not been completed.	5.8.1.

Progress toward achieving this overarching goal of the programme is ostensibly measured by Indicator G1.1. However, to date, no progress reports have included data for this indicator. Progress is rather measured through performance on the objectives and indicators that fall under this overarching goal. This is a long-term goal of the programme (with a target of 50M PQ'd tests per diagnostic category per year procured), so it is not really measurable on its own until the end of the programme.

According to the MoU, summary reports are to be prepared annually, beginning in Q1 2010. Progress reports state that "reporting milestones have been met" and "data regarding diagnostics procured through WHO, UN agencies and the Global Fund were collected in 2009" and that "procurement data from Global Fund, SCMS, UNICEF, UNITAID and WHO/CPS records for 2011 and 2012 were collected and analysed for establishing a baseline for diagnostic procurement practices before prequalification (volumes, prices, product types, geographic trends, etc.) and for comparison with the market after prequalification." Further, the most recent progress report states that a comprehensive market analysis for 2012 was expected to be completed in January 2013.

Purpose 1. (Outcome): Increased uptake of UN/WHO prequalified diagnostics				
Indicator Number	**Indicator Measure**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**	**MOU Indicator**
P1.1	Number of procurement agencies that commit to procure prequalified diagnostics.	5	Not reported to date. According to the logframe, the indicator is to be based on market analysis reports. Baseline market analysis reports have been completed, but more recent market analysis reports that would include sales of prequalified diagnostics have not been completed.	None
P1.2	% reduction in actual prices as compared to the market prices for different product categories of UNITAID priority diagnostics.	25%	Not reported to date. According to logframe, indicator is to be based on market analysis reports. Baseline market analysis reports have been completed, but more recent market analysis reports that would include sales of prequalified diagnostics have not been completed.	5.8.3

Similar to indicator G1.1 above, progress reports have not included data for indicators P1.1 and P1.2. The indicators are also intended to be monitored through market reports which are reportedly submitted directly to UNITAID. The name of indicator P1.1 is not entirely consistent with the definition in the logframe. The name suggests that the number refers to agencies "*that commit to procure*…" which could imply that the countries counted have a long-term commitment to buy prequalified diagnostics. The logframe definition, however, states that the number refers to countries that have actually procured prequalified diagnostics: no long-term commitment is implied.

Purpose 2. (Outcome): Strengthening capacity to monitor the quality of diagnostics in beneficiary countries				
Indicator Number	**Indicator Measure**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**	**MOU Indicator**
P2.1	Number of beneficiary countries with improved regulatory capacity for UNITAID priority diagnostics.	5	4 reported. Improved regulatory capacity is not defined.	5.9.3
P2.2	Number of beneficiary countries with post market surveillance action plans in place for UNITAID priority diagnostics.	5	4 reported. Indicator is a weak proxy for the outcome.	5.10

The two indicators listed in the log frame for this outcome are not particularly helpful in measuring the desired outcome. Indicator P.2.1 does not specify how "improved regulatory capacity" is determined. From progress reports, one may infer that the indicator may report the number of the five target countries that have received any technical support from the programme. However, the level of assistance varies significantly by country. Burkina Faso received technical assistance that included training on regulation of medical devices for 15 participants; support in developing registration guidelines and procedures; and inspection of local IVD distributors. In contrast, support to China is described primarily as re-establishing contacts. Both countries however are reported as having improved regulatory capacity.

Ivory Coast is the only country that is not reported as having improved regulatory capacity due to assistance being suspended. This description of this indicator is slightly different from the corresponding indicator in the MoU. MoU Indicator 5.9.3 was defined as the number of beneficiary countries with *action plans for strengthening national capacity* for regulation of diagnostics). Indicator 5.9.3 is more objectively measurable, but also is not a particularly strong proxy for measuring strengthened capacity.

Similarly, the second Indicator for this outcome, P.2.2 is not particularly helpful as it also only reports the number of target countries that are deemed to have post-market surveillance action plans in place. The indicator does not provide any indication of whether the action plans have been implemented and as such is not a very strong proxy for strengthened capacity.
Indicator 5.10.2 in the original MOU, which was intended to track the number of beneficiary staff trained in post-market surveillance of diagnostics, would be a better proxy for strengthened capacity. A target of 100 staff members trained was established in the original MoU, but it appears that progress of this indicator has not been tracked or reported.

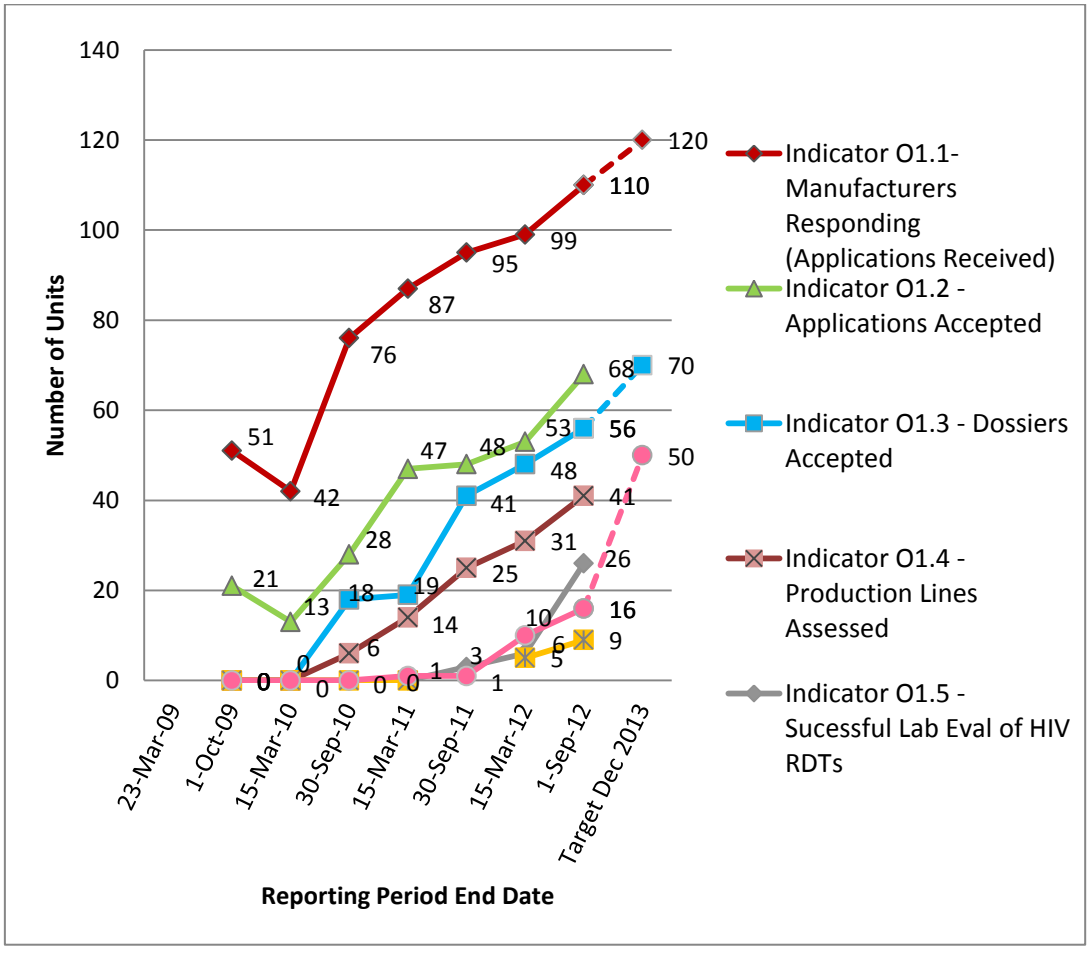
When compared to the pharmaceutical field, the area of diagnostics is very loosely regulated especially in upper and lower income countries. Additionally the sheer variety of entirely different devices and technology makes it particularly challenging to regulate. Most regulatory authorities in middle and lower income countries lack sufficient funds and technical capacities to regulate; a WHO prequalified device is a very valuable recognition for them. However in the current situation they cannot only rely on this taking into consideration the small number of diagnostic tests which are prequalified.

Output 1: Prequalified UNITAID priority diagnostics in support of HIV/AIDS and malaria treatment.				
Indicator Number	**Indicator Measure**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**	**MOU Indicator**
O1.1	Number of specific UNITAID priority diagnostic product manufacturers incentivised to apply for WHO prequalification.	120	The Logframe says this indicator is “on target”, but progress reports do not provide any details.	5.1.2
O1.2	Number and % of applications accepted for all product categories.	100 63%	68 applications accepted, 62% of applications accepted. % of apps accepted is not a useful indicator of programme performance	5.2.1
O1.3	Number of dossiers accepted for review for all product categories.	70	56 dossiers “received”. Logframe says “on target”. Description differs from previous MOU indicators: 5.2.3 – number of dossiers reviewed; 5.2.7- number of dossiers accepted.	5.2.3 or 5.2.7
O1.4	Number of diagnostic production lines assessed for all product categories.	70	41 lines assessed	5.3.6
O1.5	Number and % of successful laboratory evaluations of HIV rapid diagnostic tests.	40 87%	26 successful evaluations / 93% of all evaluations. % of successful lab evals is not a valid indicator of programme performance.	5.4.1 (%)
O1.6	Number and % of successful laboratory evaluations of CD4 and HIV viral load technologies.	17 40%	9 successful evaluations/ 100% of all evaluations. % of successful lab evals is not a valid indicator of programme performance.	5.5.1 and 5.5.2

O1.7	Number of prequalified diagnostics all product categories.	50	16 diagnostics prequalified	5.6.2 and 5.8.2
O1.8	Lead time between receipt of a complete dossier and the final overall decision for prequalification of the diagnostic product.	270 days	167 days Original target was set too high (i.e.. easy to achieve)	5.6.1

For the most part, the indicators for Output 1 were established at the beginning of the programme and have been tracked consistently. Most of these output indicators are measurable and verifiable and have been presented in a clear format in annual and interim reports. The "dashboards" that summarize these indicators provide a fairly good snapshot of the programme's progress toward achievement of what could be described as the bottom line output of the programme- Prequalification of UNITAID priority diagnostics. Below is a depiction of the programme's progress toward this output[1].

Figure 1: Output 1: PQ'd UNITAID Priority Diagnostics in support of HIV/AIDS & malaria



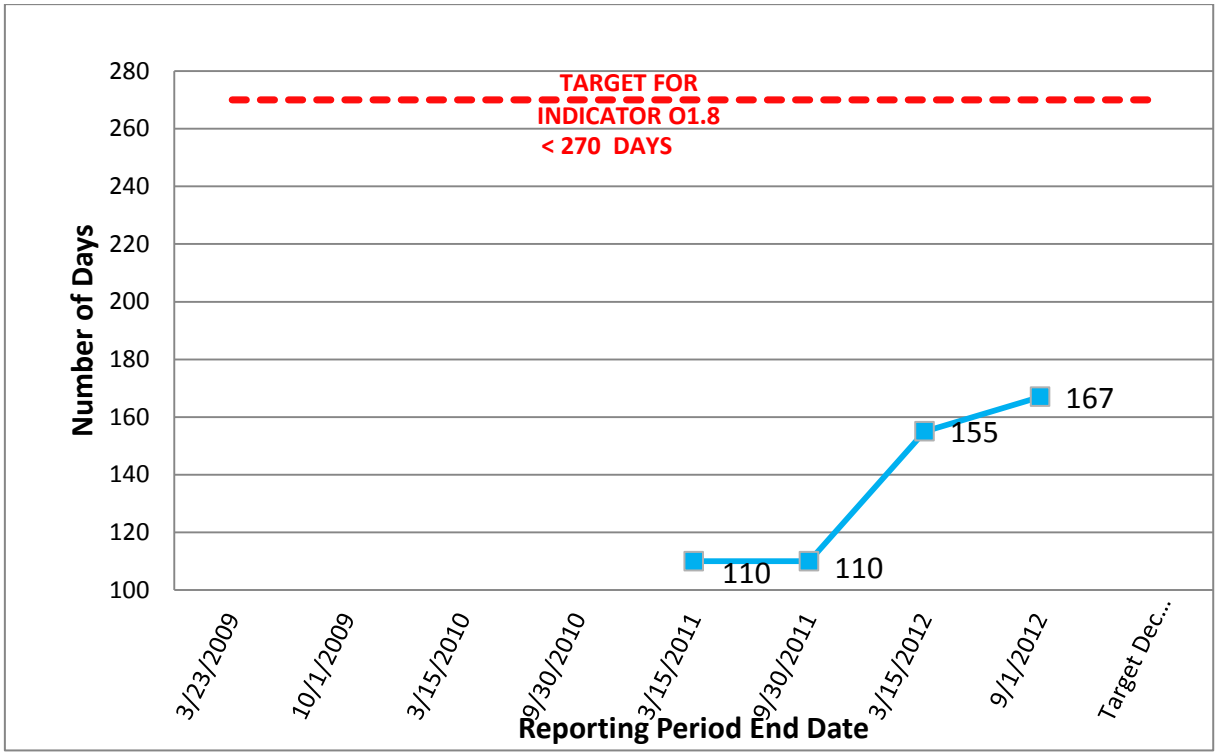
The indicators reflect what the narrative sections of progress reports have explained—that project start-up was slower than expected, but that progress toward end-of-project targets is being made. The number of production line inspections undertaken is 41, leaving an

[1] The chart also highlights a discrepancy in reporting. The first report states that 51 applications were received, 21 of which were accepted, where the second report lists lower cumulative figures for these indicators.

additional 29 inspections that must be completed over the remaining 14 months to reach the project target of 70. Perhaps, most importantly, the number of diagnostics actually prequalified as of September 1, 2012 is 16, leaving 34 additional products that must be prequalified over the remaining 14 months to reach the project target of 50. According to the DLT webpage, 22 additional diagnostics are in various stages of the prequalification process. Given the time required to receive dossiers and complete the prequalification process, it is not likely that this key target will be met. As explained in the progress reports, some of the delays in Output 1 are due to slower than expected project start-up (e.g, getting systems, procedures and processes in place).

As depicted in the graph of Indicator O1.8 below, the lead time between receipt of a complete dossier and the final overall decision for prequalification of the diagnostic product is well below (better than) the MOU target of 270 days. The large difference between the actual and the target is consistent with the observation that the original target was set too high (too easy).

Figure 2: Indicator O1.8 - Lead time between Receipt of a Complete Dossier and the Final Overall Decision for Prequalification of the Diagnostic Product



On a more general note, some of the indicators are also presented as ratios and absolute numbers. The absolute numbers are reasonable indictors of the programme's outputs and achievements. The ratios of successful lab evaluations (e.g., ratio of successful lab evaluations/all lab evaluations undertaken), however is more indicative of the quality of diagnostics submitted than of the programme's contribution. Similarly, the ratio of applications accepted to applications received is more indicative of the quality of the applications submitted than of the programme's contribution. It should also be noted that output targets were set for the end of the programme: no interim targets have been established. Without interim targets, there is a lot of flexibility for programme management to assert whether interim results are on track or not, which undermines the usefulness of the indicators.

Output 2: Facilitate procurement of appropriate diagnostics of assured quality (i.e. prequalified)				
Indicator Number	**Indicator Measure**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**	**MOU Indicator**
O2.1	Number of procurement agencies using WHO procurement guidance	12 agencies or countries	Reported in logframe that: "GF, UNICEF.UNPD; MSF, WHO, Crown agents, *and a number of Member States use WHO guidance*", but details are not provided in logframe or narrative.	5.7.2

The description of indicator O2.1 is not entirely specific (e.g., does this indicator refer to *all* WHO procurement guidance *all* of the time?) and is not directly tied to the desired output. The results are not discussed in the narrative of the accompanying progress report, so actual progress against this target and output is not entirely clear.

Output 3: Build and/or strengthen regulatory capacity for diagnostics in beneficiary countries				
Indicator Number	**Indicator Measure**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**	**MOU Indicator**
O3.1	Number of national regulatory authority staff that have participated in prequalification process.	20	16	5.9.1
O3.2	% of inspections in which inspectors in low income and low-middle income countries participate.	50%	Report say "approximately 20%", but details not provided. The original MOU target has been deemed unrealistic by PQDx	5.9.2

These two indicators, while sufficiently measurable process indicators, are by themselves not particularly strong indicators of achievement of the stated objective: strengthened regulatory capacity. These two indicators do not reflect the full range of activities that the programme undertakes to support strengthened regulatory capacity. For instance, participation in training events and related conferences, and technical assistance to develop and implement action plans contribute to the objective, but are not reflected in the indicators.

Output 4: Build and/or strengthen capacity for post market surveillance of UNITAID priority diagnostics in beneficiary countries				
Indicator Number	**Indicator Measure**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**	**MOU Indicator**
O4.1	Number of beneficiary countries with post market surveillance systems in place	5	4	5.10.1
O4.2	Number of lot testing events and field sampling surveys conducted per beneficiary country	7	Reports say SOPs implemented for lot testing at NRLs by Q2 2012.	5.10.4

The new logframe for the project includes two of the four indicators originally included in the MOU with UNITAID. Progress of Indicator O4.1 has been slower than expected, due in part to slow start-up in target countries. Also, political unrest in one of the five target countries, Ivory Coast, has suspended work there and prompted consideration of whether Ivory Coast should be removed as a target country. More generally, the indicator is a weak indicator of the expected output and wording provides significant flexibility in determining achievement.

Progress of indicator O4.2 has also been slower than anticipated. MOU milestone of having SOP's for field sampling implemented by Q2 2010, was only reached in Q2 2012.

Lead time Indicators of Programme Efficiency

Seven indicators from the original MOU that are intended to track lead time for programme activities are not included in the current logframe. These indicators have been discussed in regular progress reports, but the reporting has not been consistent and the usefulness of the indicators for evaluative purposes is open to discussion. Some of these indicators might be helpful in providing internal feedback to programme management, such as identifying bottlenecks, but most are less relevant for an external evaluation. Indicator O1.8 which tracks the lead time between receipt of a complete dossier and the prequalification (discussed in the section on Output 1 above) is a sufficient indicator of overall programme efficiency for an external evaluation. Specific comments on each of the lead time indicators follow.

Lead Time Indicators from MOU			
Indicator Number	**Indicator Definition**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**
5.2.1.	Lead time between receipt of an application and priority decision made.	15 days	Target met in last four reporting periods. Improved since first two reporting periods in which the lead times were described in progress reports as "over 3 months" and "approximately 3 months". The slow turnaround at the beginning of the programme can likely be attributed to getting systems and procedures in place.
5.2.4	Lead time between receipt of a complete dossier and the start of an assessment.	30 days	Target consistently met from three most recent progress reports
5.2.6	Lead time between receipt of a complete dossier and the end of an assessment.	120 days	Not reported in recent progress report. Inconsistently reported in previous progress report - 132 days and 83 days were both reported for 2011.
5.3.1	Lead time between receipt of a complete dossier and first inspection at manufacturing site	150 days	Reports say "target consistently met" by large amount. However, this indicator can be both misleading and not a particularly relevant indicator of efficiency. As mentioned in several progress reports, inspections can be conducted in parallel with full dossier assessment (e.g. before a dossier is considered complete). In addition, lead times vary considerably by product, so the average is not a helpful indicator of efficiency. Two progress reports list the average lead time of 4 days. The most recent progress report states only that the average lead time is "much shorter" than the target.
5.3.3	Lead time between end of inspection and issuing of final inspection report	120 days	Reports say "target was met", but no details are provided. Previous progress reports do not provide any details on whether target was met. The reports correctly state that the lead time is highly dependent on follow-up by the manufacturer to resolve any issues identified during the inspection (before issuance of final report). As such, the usefulness of this indicator as a measure of the programme's efficiency is not certain.
5.3.4	Percentage of inspection reports sent to manufactures within 1 month of inspection.	75%	Reports say "target was not met" for last three progress reports. Two of the reports do not provide the percentage number, the third report states that 35% of initial inspection reports were sent within the 1 month

			target.
5.4.2	Lead time between the start of lab evaluation and final lab report.	120 days	Reports say "target was met", but no details are provided. Lead time for the previous reporting period was listed as 51 days, which is much better than the target.
5.4.3	Percentage of lab evaluation reports sent to manufacturers within 1 month.	75%	Reports say "67% - target not met". Target was met (83%) during previous reporting period. No other progress reports include information on this indicator.

Other Indicators from MOU			
Indicator Number	**Indicator Definition**	**Target Dec 2013**	**Results as of 1 Sept 2012/Comments**
3.1.2	Percentage of budget allocated to LIC, LMIC, UMIC as % of total budget.	>85% LIC; <10% LMIC; <5% UMIC	Not reported in Progress Reports.
5.1.1.	Formal prioritization procedures developed and approved by interagency group at IPC meeting	Q2 2009 - on website by Q3 2009	Report states "Targets met".
5.1.3.	List of priority diagnostics reviewed and updated annually by inter agency group (IPC)	Publish list Q1 2010 and annually thereafter	Report states "Target met. List updated regularly on website"
5.1.4	Complete Business plan for prequalification of diagnostics	By Q3 2009 and revised BP by Q4 2011	Submitted Business Plan late with Annual Progress Report on 15 May 2010. Revised business plan not completed. "Update of the business plan was postponed to Q3-Q4 2012"
5.3.5	Number of manufacturing sites and diagnostic production lines re-assessed	<10	One site was re-inspected during the recent reporting period. Not a relevant indicator: by saying target is LESS THAN 10, project want to AVOID re-inspections? What is this meant to measure?
5.7.1	Guidance Document on procurement tendering processes for diagnostics and lab items finalized.	Q1 2010	Reporting is inconsistent. Narrative states "the guidance document on procurement and tendering process is available on the web pages" where a table in the same report states "Guidelines in finalization stages." Document could not be found on WHO/DLT web site. Evaluation team was provided a draft version of this document dated July 2012.
5.10.2	Number of beneficiary countries staff trained in post-market surveillance	100	This indicator has not been tracked in progress reports. Progress report narratives discuss training plans in general terms, but the specific number of participants has been mentioned only once (15 participants from Burkina Faso, in recent progress report).

6.2 Interviews/Feedback from Stakeholder Respondents

The evaluation team ensured total confidentiality to all respondents, whether in phone interviews, meetings, or by email (responding to questions sent by the evaluators). As such, this report does not attribute any comments to any particular individual, organization, or country. Rather, the evaluation team has taken the responses and summarized them in sections according to the type of respondent and the main theme of the comment.

The evaluation team struggled initially to obtain contact details for key stakeholders, but after some delays and after some research produced some key people to interview, the evaluators spoke with and got feedback from a broad set of respondents. Some names were provided by the WHO project team whereas others came from UNITAID programme staff and finally others came from other respondents who suggested additional people to interview.

The PQDx program interacts with a wide range of different stakeholders and beneficiaries. The evaluation sought to gather feedback from different groups. These were identified as beneficiaries: patients, practitioners, national regulatory authorities, procurement agencies, donors, manufacturers and developers. This evaluation did not seek feedback from patients and practitioners because of feasibility constraints. The below comments list feedback provided by respondents as they were asked to identify what they consider the two most critical weaknesses and two most critical strengths of the programme, what they feel are the results of the programme and their suggestions for the future. The list is not exhaustive and does not repeat when different respondents identified similar issues. The comments have been extracted from the respondents' feedback and kept as close as possible to actual comments/quotes, in an effort to document the concerns of the different stakeholders. Overall findings from different groups of respondents are found on the following pages.

Partner Organizations - Respondents from Clinton Health Access Initiative (CHAI), Bill and Melinda Gates Foundation (BMGF), the Global Fund, MSF, USAID/PEPFAR, US CDC, UNICEF, and independent consultants in the field of diagnostics were interviewed for this evaluation.

Partner Organizations: Identified Weaknesses
▪ The WHO PQDx is slow and cannot keep pace with the rapidly changing field of diagnostics. This becomes worrisome as more and more technologies and developers come on the market. There are still not enough RDTs PQed, after several years of the programme. (Almost all respondents identified the slowness of the program in getting diagnostics devices prequalified as the main weakness). ▪ WHO makes the PQ process cumbersome and not transparent, even for products that have FDA approval and a long history on the market. ▪ The WHO PQDx programme duplicates the efforts of other agencies ▪ The PQDx programme communicates poorly with other stakeholders. ▪ The WHO PQ programme has not improved product access, price or quality. It has been too slow, and the information is not publicly accessible (not transparent). ▪ Due to a lack of transparency, it is not clear whether PQ delays are mainly from the WHO side or whether they arise from the manufacturers. It is therefore difficult to identify the main factors as we don't know where the bottlenecks are. ▪ There should be more publically available information on the PQ process on their web site. ▪ The Programme seems disinterested in communicating with companies about the PQ process, and has a general unwillingness to cooperate with other international and national efforts to harmonize diagnostic QA efforts. ▪ Attitude has been a big problem. There has been a view that the WHO PQ process is the only true measure of quality in the world….. The WHO PQ staff has shown no interest in or willingness to cooperate with other regulators and partners around the world to streamline and harmonize PQ for diagnostics. ▪ Leadership (of the programme) has been weak, and the results reflect that. The leadership of the organization is largely responsible for its lack of flexibility and its ineffectiveness. ▪ The Programme performs informal prioritisation of products (e.g. Alere PIMA CD4 test before the BD flow cytometer) and the decision-making for this prioritisation is not transparent. ▪ The fast-tracking of already widely approved products should be possible, but it requires WHO to be more flexible about process and requirements…. WHO has not shown any willingness to be flexible in this regard – e.g., accept independent laboratory evaluations of the products and not conduct its own laboratory evaluations, which historically has added close to a year to the overall process. The "fast track" process is no different, time-wise, from normal PQ. ▪ UN and WHO procurement does not always follow the conclusions/ recommendations of the PQ teams. ▪ Given the risk of creating a de-facto monopoly, it is concerning when PQ is only given to one diagnostic product out of a much larger group of products e.g., for malaria RDTs, SD Bioline. ▪ The PQ programme is completely lacking the willingness and maybe the ability to communicate with other partners. ▪ The small size of the PQDx team cannot possibly deal with the workload, hence the delays. ▪ The web site is not user friendly and one really has to look to find useful information. ▪ It is currently difficult for procurers (whether donors or ministries of health etc) to insist on WHO PQ given that the PQ process takes quite a long time and may therefore block the use of much needed diagnostic tests.

Partner Organizations: Identified Strengths / Need for PQDx
▪ There is a great need for this QA before procurement as most countries have almost no post-market surveillance of diagnostics, and quality problems do occur on the ground, impacting public health. ▪ PQ of diagnostics is very important (increasingly so), and necessary. If the system worked better, many more manufacturers would want to apply for PQ. ▪ The endorsement by the WHO provided by the PQDx program is the highest recognition in terms of quality. ▪ The PQDx provides timely advice when requested. It is great as a reference organization. They have been very responsive to our needs. ▪ The PQDx process takes into account the local requirements in terms of stability, logistics and user friendliness which stringent authorities from developed countries do not. ▪ WHO PQ perform a thorough and effective job of providing quality assurance, especially for products used in resource limited settings. ▪ WHO had issued a warning on the Bioline RDT prior to the recall. This is also a good example of the need for much better post-market surveillance (PMS) of diagnostics in countries……..The PMS system is not well structured or working in most countries, and there is no data collection or surveillance/reporting. This is a gap in countries, with a potential important role for WHO to work more on this. ▪ WHO has a unique place in the international health community in that it is considered to be the ultimate authority on diagnostics. But, in the last 6 years, very few diagnostic products have been PQed, and other organizations have stepped in to fill the void. ▪ We are on the brink of many new diagnostic technologies, with many new companies doing RDTs, point-of-care instruments, etc. So there will be an increasing need for better QA of these new products and suppliers. ▪ The incentives (to apply for WHO PQ) are still there for manufacturers. But, if the WHO continues to operate at its current pace, this won't last forever. ▪ It is good to set a high standard like the one set by the PQDx programme. After a while manufacturers know that they have no other way but to comply. This is what happened in the PQ programmes for pharmaceuticals and for vaccines, and now nobody questions the high standards -- they just comply. ▪ Over the last year the programme has improved and is now handling the work faster and communicating better than previously. ▪ The WHO PQ recommendations are an integral part of Global Fund's procurement policy due to the fact that the GF policy is based on the outcomes of the WHO prequalification of diagnostics ▪

Partner Organizations: Impact
▪ Warnings issued on products that have undergone PMS have been useful e.g. the SD Bioline serological HIV RDT. In November 2011, WHO issued a Field Safety Notice based on PQDx findings. However, this warning made people switch to other RDTs that weren't good quality either. This is a direct result of insufficient alternatives PQ'd. So, yes, it triggered a change, and the manufacturer improved the quality of their RDT, but many countries have switched to a worse solution in the meantime without even realising it. ▪ The small amount of prequalified diagnostic devices on the list gives an unfair advantage to those in comparison to similar products which are not yet prequalified. ▪ Impact will only be there when a critical mass of prequalified diagnostics can be chosen from. Countries and agencies were purchasing the PQ'd devices prior to their prequalification and have no other option but to continue to purchase non- PQ'd devices until those get PQ'd. ▪ Many organisations perform quality assessment of diagnostic devices at least to some extent, as they cannot rely on the PQDx programme for this, because too few products are prequalified. It is too bad that information is not shared between the different actors.

Partner Organizations: Suggestions for the Future

- Maybe it is time for the PQDx programme to "get philosophical" and figure out what role it should be playing. It is trying to do everything, but not coping well with the current volume and need, let alone as more technologies come along.
- Perhaps WHO could give guidance to developers on the kind of pre-market evaluations it wants to see and the best sources of those evaluations – i.e., the evaluations that would carry the most weight with WHO. They can suggest protocols, sample sizes, independence of the evaluations, etc. This would be immensely helpful to developers.
- There is a need for some standardization of protocols to test the quality of new diagnostic products. Some are doing this (e.g. London School) now. WHO tried to do this previously, but did not manage. But WHO should accept these standard protocols once other experts have agreed, and should get behind them, as there is a real need for this.
- The greatest need is timely PQ of new, point-of-care (POC) diagnostics that are either in the market or will enter the market in the next few years. It is for these diagnostics, with little or no history in the marketplace, that WHO guidance is most needed and would be most valued. I think novel POC diagnostics for HIV need to be prioritized.
- In the future it would be good if WHO could give additional information to countries about PQ'd products: where does a diagnostics device fit in the diagnostic algorithm, how to do post-market surveillance for those devices, what are the risks and benefits when compared to different technologies, etc.
- A healthy suspicion of companies and their profit motive is good, but that attitude can be taken too far sometimes. WHO should show more openness to new ideas, and to problem solving.
- WHO should look at the problems with the submission process, why companies are not submitting many dossiers, why there are paperwork problems, etc. They should figure out WHY this is happening (cumbersome process, lack of clarity, etc), and find solutions.
- WHO PQDx should be the "arbiter to assess quality of data", not do all the data gathering themselves.
- The value add of the Programme is definitely in the PQ requirements for resource limited settings. Thus CE and FDA etc can never fully replace the need for WHO PQ, although harmonisation and synergy is still possible (i.e. WHO PQ would not necessarily have to repeat testing performed by other strict regulatory authorities). It is also important to note that, more and more (and the FDA seems to have taken the lead on this), products are not only approved based on technical accuracy and good manufacturing alone, but on a risk-benefit analysis. An example is the FDA approval of the OraQuick oral fluid test for HIV, which has a lower sensitivity than blood-based tests but increases testing uptake at community level.
- It would be useful for WHO PQ to prioritise tests that are likely to be adopted early or where gaps in quality assurance exist for any one disease.
- For the PQ process to happen faster, there is a need for testing panels.
- It would also be useful to provide more information on why products have not yet been PQ'd (not just "in process") - if possible it would be useful to have a timeline of dates as to when the dossier is with the manufacturer and when it is back with WHO. That would also ensure accountability. It would be useful to show the expected dates of the evaluation for each product, the study protocol for evaluation, the list of partners involved in the evaluation of each product, and additional info on the products (catalogue number, manufacturing site etc).
- It would be useful to have an interagency committee to share issues related to the PQ of in vitro diagnostic tests; this could perhaps be chaired by WHO.
- The WHO PQDx programme is dependent upon donor financing and therefore donors' agenda, and this can be detrimental when the donor agenda becomes WHO's agenda. Even though they say they are not a regulatory agency, they act as one and are accepted as such in the world community. They should be able to take a position according to the sole interest of the public and not donor organizations.
- There should be a more streamlined way of reporting adverse events relating to diagnostic tests - facilitated using a standard form (not yet devised).
- Additional information should be added to the web site, to make the process more transparent: (expected dates of evaluation for each product group; study protocol for evaluation; list of partners involved for evaluation of each product group; additional information on products: catalogue number, manufacturing site; dates of submission of dossier from manufacturer and dates of requested and received responses from manufacturer and PQDx, etc).
- If possible, add other, more neglected, diseases to the PQ programme. It would be particularly useful for PQ to incorporate diseases that are considered low risk in developed countries (with, as a consequence, less rigorous quality requirements to get FDA/CE -- e.g. quality data for malaria tests can be self-reported) but high risk in developing countries. These include diseases like dengue, Chagas, leptospirosis, brucellosis, tuberculosis, sleeping sickness and Kala Azar, and also blood grouping devices, biochemistry reagents, handheld analysers and point of care biochemistry, etc.
- The web site should give a lot more information. It would be great to know at what stage of the PQ process the organization has arrived at. In the absence of full prequalification this could help the countries have some indication about the quality of the products.
- PQDx does not seem to respond to constructive input into the process. The process needs to be overhauled to be effective.

Country Stakeholders - Under the UNITAID grant, the PQDx programme has been working in 5 pilot countries to strengthen the regulatory authorities and QA activities. The countries received a budget of $200,000 each to perform, in collaboration with local WHO agencies and the DLT team, the activities in a proposed action plan. Respondents from Burkina Faso, China, South Africa, and Tanzania were interviewed and/or communicated with in writing. Their comments/feedback are as follows:

Country Stakeholders: Impact / Results
▪ Before this project, we were not aware of the critical need for regulating diagnostics just as we do for medicines. ▪ Thanks to the programme, (our country) has a more comprehensive regulatory basis for evaluation of applications for market approval for diagnostic tests, and for inspection of suppliers and users of reagents/tests. We now have resource people with knowledge of regulation of diagnostics. ▪ Before this project, we were not aware of the critical need for regulating diagnostics just as we do for medicines. ▪ Quality concerns around diagnostics and medical devices have led (our country) to recognize the weaknesses in their own QA around these products, and to try to rapidly build PMS systems. The country would like more support from WHO. ▪ Missing guidelines for registration of diagnostic products, post-market surveillance and other critical documents are now in use in our country. ▪ WHO support to the country's capacity has been very helpful in providing parameters for regulations, in helping build capacities for local inspectors (by inviting them along on inspection trips), and by helping build PMS in the country. ▪ There is better quality of diagnostics (in the country now) due to awareness of the manufacturers that all the HIV assays are being batch tested before being released to the laboratories. ▪ The government awareness has been increased and there is more support for regulation of diagnostics which was very weak before. ▪ A product that receives approval from the WHO is a safe and effective product. The WHO through the PQDx programme have highlighted to manufacturers the need to always consider how the product performs & is used by the end-user.

Country Stakeholders: Suggestions for the Future
▪ WHO will need to build capacity within WHO to oversee diagnostics quality, and more capacity will have to be built across countries (and whole regions), not just these few pilot countries. ▪ WHO should increase the dedicated personnel available at WHO HQ, if possible. ▪ Improve synergies and coordination with other teams in WHO country offices in charge of PQ of medicines and vaccines. Knowledge, experiences and lessons learned should be better shared in the future. ▪ There is a need to harmonise this with the planned Pan African Harmonization activities for regulation of diagnostics where WHO can play a critical role in technical support. ▪ Involve the manufacturers and suppliers to share post market data which is not the case presently. ▪ It would be good if the WHO would do training on how to go about manufacturer inspections. ▪ If in the future the budget could be disbursed faster a lot of time will be gained in the implementation of the activities. ▪ It would be great if the WHO would have a set of international guidelines and standards in the field of diagnostics for regulatory authorities to adapt to their local context. ▪ The funding for strengthening regulatory authorities in countries should be continued as there are still many gaps to address. ▪ The funding should be extended to other beneficiary countries which could use the knowledge, tools and documents developed in the pilot countries to develop their own. ▪ The government awareness has been increased and there is more support for regulation of diagnostics which was very weak before. ▪ A product that receives approval from the WHO is a safe and effective product. The WHO through the PQDx programme have highlighted to manufacturers the need to always consider how the product performs & is used by the end-user.

Developers and Manufacturers - Interviews as well as feedback from a written questionnaire have been received from different groups of developers and manufacturers; some having undergone prequalification (for at least one product) and others still in the process. In addition some developers of new technologies not yet on the market but hoping to gain WHO prequalification in the near future were also interviewed. A very rigorous prequalification process is often not in line with the interest of the manufacturers, which may explain some of the critical views of manufacturers on the PQDx Programme.

Developers and Manufacturers: Identified Weaknesses
▪ Slow turnaround, lack of flexibility with regard to different test outcomes ▪ They should not duplicate regulatory processes that already exist but work within those systems and fill the gaps. ▪ We have not been through the program, but all we hear about is how long it takes which is a major disincentive to investment in test development. ▪ Test developers will not enter the field for much-needed tests if this system results in a significant delay between final manufacture of a clinically valuable test, and the ability to sell it. ▪ The strength is the idea of having a global prequalification process. However, the weaknesses of this particular program outweigh its benefits. The weakness is that the program duplicates efforts, and does not have the capacity to evaluate diagnostics on a timely basis. WHO wastes time, effort and money on recertifying things that already have proven track records. They also audit sites that already go through ISO and FDA audits. ▪ The one size fit all approach of the PQDx programme is not fair. It cannot be that a well established company which is selling its products everywhere in the world for many years is treated the same way as a company with new products on the market. ▪ I think they have, if anything, delayed progress to market without significantly improving quality. Because they have delayed some products and caused the companies to do duplicate regulatory efforts, this in essence has increased company costs and therefore potentially the prices to the users. ▪ The fast-track procedure lasts just as long as the normal one. ▪ Pricing is a major factor. Bigger companies drive competition out of the market by their financial strengths. Smaller companies can't compete.

Developers and Manufacturers: Strengths / Need for PQDx
▪ Strengths – independence of the validations, reputation of WHO ▪ Program is very effective and should continue to keep quality products on the market. ▪ The WHO submission and audit encourages quality improvements through the action of a rigorous and highly professional audit. ▪ WHO's auditors are very high level and world experts in diagnostics tests. ▪ The PQDx programme is a high-quality programme that facilitates the manufacture of safe and effective devices for the diagnosis of HIV. ▪ The main strengths of the programme are the highly skilled individuals (both quality and technical) involved and also the extremely well constructed checklist provided to us during the evaluation.

Developers and Manufacturers: Impact / Results
▪ Most countries bypass this (PQ) process for most diagnostics with the exception of rapid tests…I do not think (the PQDx programme) is providing the QA that was intended. ▪ There was no incentive for our company to seek PQ…..The products were on the market and were being sold effectively without PQ. ▪ After prequalification of our product no increase in turnover has been seen, but it might be too early to say. ▪ Lesser quality products have been kept out of the market. ▪ The current procurements are too price sensitive, and do not consider overall PQ status or results of the manufacturers/products. So the company which does not meet WHO PQ standard but sells the products at low price can still get awarded the tender.

Developers and Manufacturers: Suggestions for the Future

- The project MUST evaluate products in a timely manner and should have a 2 tiered system so that products that are already certified by another Stringent Regulatory Authority do not have to go through the entire process.
- The WHO wastes time in a case by case approach in the way they communicate with the manufacturing companies. They should better concentrate on communicating very clearly to all about what their requirements are, so that everybody can prepare accordingly and not have bad surprises along the way because new requests are suddenly raised during the process.
- There is no information coming from WHO on how developers of new technologies can prepare for prequalification. It would be very useful in order to build in the quality from the development stage.
- The PQDx should allow for conditional approval just as the WHO prequalification of medicines programme does.
- There needs to be a much faster turnaround – no more than 3-4 months should be sufficient for studies to validate the performance of tests, with CE and appropriate ISO being a prerequisite (and this aspect of manufacturing quality and consistency not needing to be re-assessed by WHO). This may be better achieved by coordinating the efforts of other bodies (such as PATH, the central lab in South Africa, etc) rather than WHO trying to do the studies centrally.
- Recommend greater reliance on long-established industry standards for the actual manufacturing steps (CE, ISO); greater utilization of academic partners in concentrating on performance studies (PATH, FIND, etc), and a focus on turnaround times.
- WHO should focus on the gaps in FDA and CS standards instead of redoing it all.
- There is also some trouble in reaching broad agreement on what may be acceptable performance for some tests – for example, CD4 tests where measuring CD4 T-cell levels against an imperfect gold standard (flow cytometry) and a numerical cutoff (eg 350/µl) cannot be reduced to simple specificity and sensitivity. The accuracy of new tests (or perceived lack thereof) must be balanced against their ability to provide greatly improved access to testing.
- The program should be focused on ensuring that products achieve the sensitivity/specificity or performance THAT THEY CLAIM, rather than "qualification" against a given standard….There is not "one size fits all" for diagnostics, and public health programmes should be able to use tests with assurance that they perform as the manufacturer claims, but with flexibility to choose tests with different performance criteria depending on their own circumstances (cost, volume, remote settings, stability, etc)
- Both the manufacturers and academic groups that develop tests against the criteria of "unmet need" are not helped by an inflexible and slow system that focuses entirely on "gold standard" performance, rather than operational performance on the balance of sensitivity, specificity, reliability, loss to follow-up, power requirements, stability, etc.
- There is a need for independent quality (performance) studies in the diagnostics devices area, but it is not clear that this is best achieved by a centralized system due to the diversity of clinical samples required for different diseases. The well-established CE mark system and various ISO standards are probably sufficient for ensuring consistency/quality of manufacture, so the focus of WHO (through PQ or another mechanism) should be on performance.
- WHO methodology is very stringent. Lack of proper guidelines affected preparedness on our part. WHO should enhance guidelines for developers/manufacturers. Manufacturers need more time to prepare the required documents.

Overall Highlights of Respondent Comments
• WHO PQDx does offer some unique, major, acknowledged strengths • Devices that have been PQ'd do get a high level of recognition • WHO PQ is seen as a quality guaranty • Unanimity about the need for a global PQ programme • Unanimity about WHO as the logical agency to be running the global PQ programme • Main weaknesses of the program widely recognized as slow pace, inflexibility, lack of clarity and transparency, lack of collaboration with other stakeholders • Poor communication from the program and inability of the program to defend its chosen approach • Poor and inflexible leadership

6.3 Financial Review

The WHO PQDx Programme's operations are funded almost entirely by the UNITAID funding. The Programme had start-up funding from the Gates Foundation from 2006 to 2010 ($2.4M?), and some minor funding ($100,000?) from the Global Fund (e.g. to assist with GF's new Quality Assurance Policy for Diagnostics), and also minor funds from dossier applications ($12,000 per application). (Note the "?" is included as the records are not clear on this funding, and the evaluators did not receive details). According to the project staff, there are also some contributions in-kind of staff time, facilities, and equipment; and there is some support from the US CDC to compliment WHO PQDx activities such as EQAs and assisting with a training event in the NICD lab in South Africa.

According to one WHO respondent interviewed, the relative lack of core WHO funding is in line with much of WHO's work currently, with much of its operation funded externally (22% of WHO's overall budget is from "self contribution"; .i.e.. their core funding from member state contributions); whereas 78% of funding now comes from voluntary/partner/external support.

According to the 4th Interim Progress report, the project's Disbursement Schedule from UNITAID was to be as follows:

1 October 2009	Submission of first interim progress report. No funds requested
1 June 2010	Upon approval of first annual report by UNITAID Secretariat
1 October 2011	To be discussed on the basis of financial information submitted with this report
1 August 2012	To be discussed on the basis of financial information submitted with this report

As of the 4th interim report (Nov 2012), three disbursements had been made to the project: $1,000,000 (April 2009); $2,850,000 (Dec 2011); and $2,000,000 (Aug 2012) totalling $5,850,000 (remaining undisbursed funds $1,650,000).

Funding for the PQDx programme from the Bill and Melinda Gates Foundation ended in May 2010, and is given as the reason for the lack of requests for disbursements between the UNITAID project start (and initial disbursement of $1,000,000) in 2009 and the two subsequent disbursements in 2011 and 2012. The Gates funding apparently had to be expended before more could be received. There has been one disbursement per year (with exception of 2010); one more disbursement is expected before project end.

Table 6: Disbursements and Key Accomplishments Per Reporting Period

Date submitted	Project report period	Disbursement, and cumulative disbursement to date	Cumulative number of applications received (Project Target: 120)	Inspections conducted (cumulative)	Cumulative number of dossiers prioritized and accepted for review	Cumulative number of products PQ'd
Nov 26, 2012	4th interim report (Jan-Aug 2012)	$2,000,000 ($5,850,000 cumulative)	110	41	68	16
June 2012 (final Aug 31, 2012)	3rd Annual report (Jan-Dec 2011)	$2,850,000 ($3,850,000 cumulative)	99	31	53	10
Oct 1, 2011	3rd interim report (Jan-Sept 2011)	0 ($1,000,000 cumulative)	95	25(7)	48	1
March 15, 2011	2nd annual report (Jan-Dec 2010)	0 ($1,000,000 cumulative)	87	14	47	1
Oct 30, 2010	2nd interim report (15 March-1 Oct 2010)					
May 15, 2010	1st annual report (March 23, 2009-March 15, 2010)	$1,000,000	17			

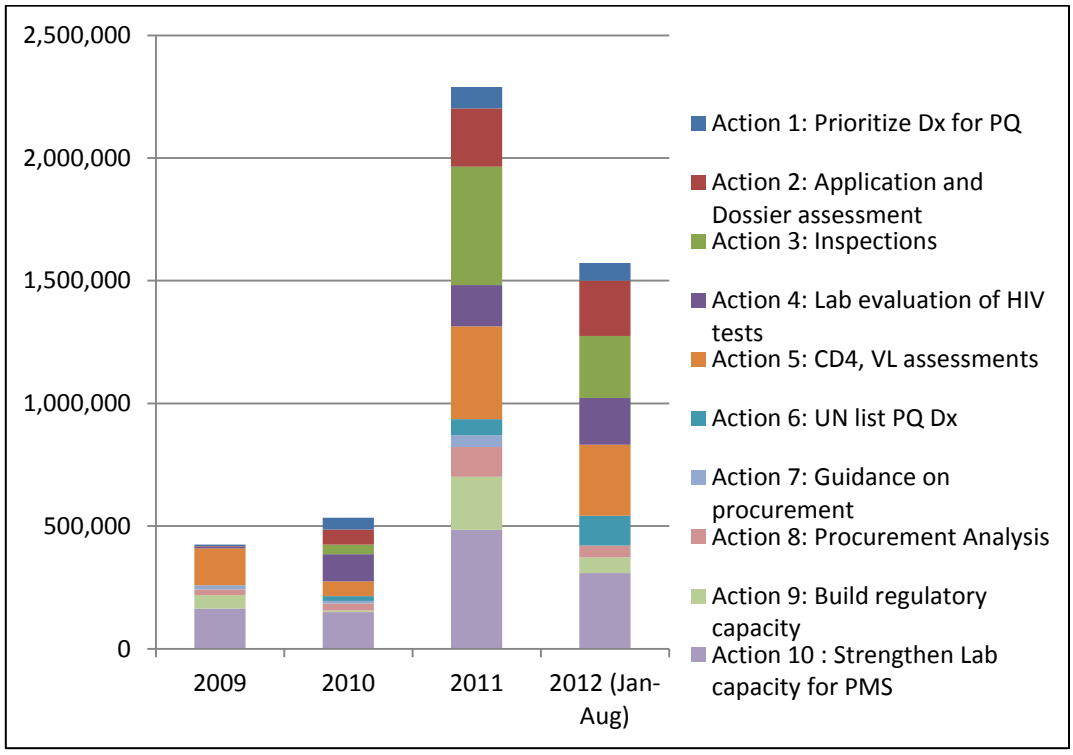
A major challenge for the evaluation was that disbursements were not tied to achievement of objectives or performance. There does not appear to be a performance-based funding model in use for this project. It is extremely difficult to measure progress when each objective did not have a timeline of expected results against which to gauge progress. Most objectives are merely meant to occur by project end, so one can only track progress toward reaching these objectives (as the evaluation has done, see chart and description above). The project reports attempt to show progress using a "% completed" measure for various actions, but for many, this percentage is rather meaningless, e.g. when saying that "capacity has been built" in 80% (4 of the 5) of target countries, without any measure for actual improved capacity, with a focus rather on meetings or trainings held.

Project Spending by Objectives - The charts below depict the project's spending across the various objectives and activities. The first chart, as the title suggests, depicts PQDx spending by action by year. One thing that is evident from the chart is that relatively little spending happened in 2009 and 2010. Spending in 2011 was more than four times that in 2010. This could reflect that WHO/DLT was still relying on other fund or that activities really did not get going until 2011. This chart also allows for a quick comparison of spending by action by year.

The relative amount spent on strengthening lab capacity for post market surveillance in the first two years is striking. The documents indicate that this activity was strengthening the beneficiary countries, but most country contact did not happen until later. Looking more closely at the detailed budget shows that most of this spending was for "Coordination" (a note in parentheses

says salary), so this might be salary of staff working to begin implementation of country activities.

Figure 3: PQDx Spending by Action

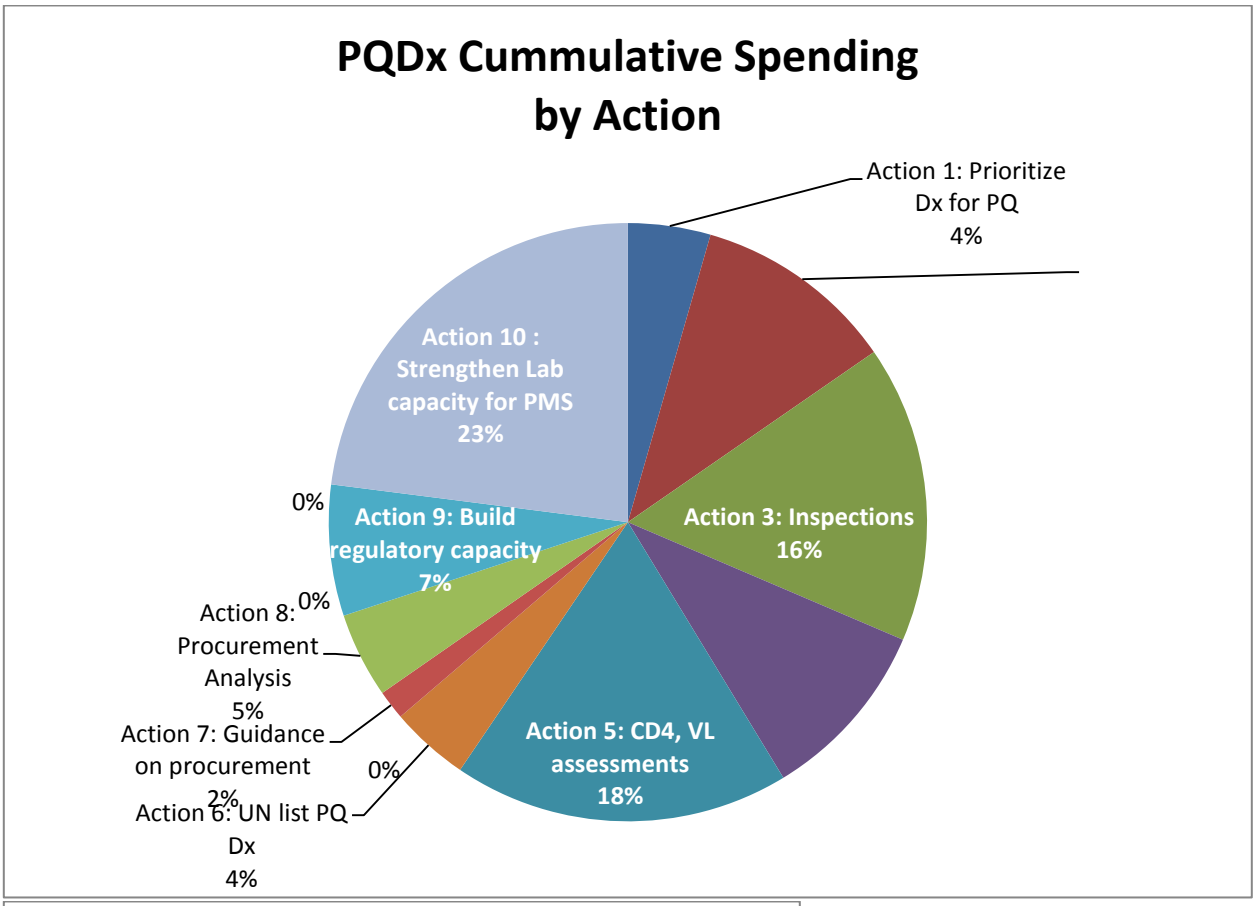


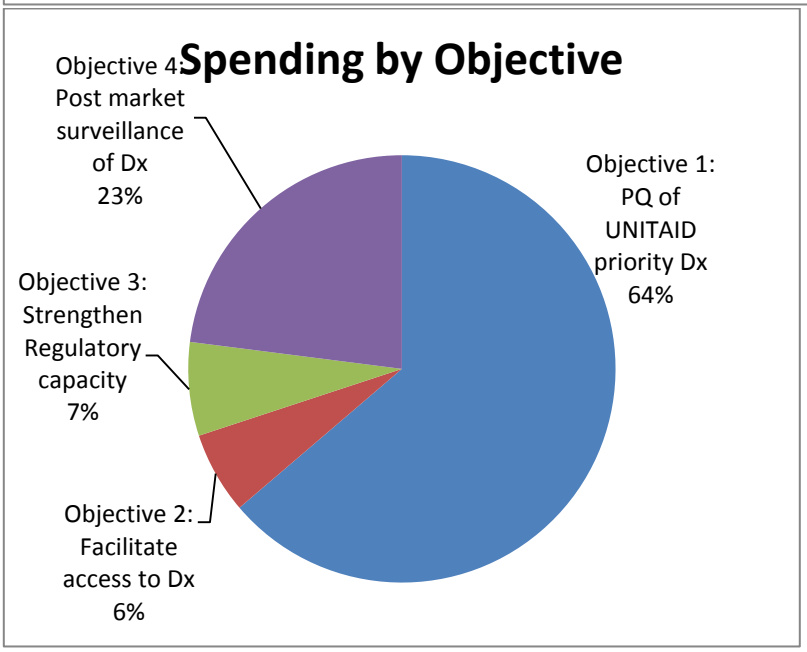
The second chart (below) shows cumulative spending by action including the percentage of overall spending for each activity. Again, here, spending on PMS appears to be the single action with the most overall expenditure.

The third chart shows cumulative spending by objective. The chart confirms that the largest percentage of total expenditure was for Objective 1: prequalification of diagnostics. Expenditures for this objective include the main activities of dossier collection, review, inspection and lab analysis. Second was the spending on PMS mentioned above. The chart indicates that spending on this category may be too high vis-à-vis other activities. Given the delays in prequalification, one might suggest prioritizing/reallocating resources toward Objective 1.

As mentioned, the budget reporting in the progress reports was inconsistent and difficult to reconcile. Expenditure summaries in progress reports overlapped. Reports inconsistently showed expenditures for the reporting period or cumulative expenditures through the reporting period. Expenditures from progress reports do not match up with figures in the budget spreadsheets for the most recent report.

Figure 4: PQDx Cumulative Spending by Action and Objective





6.4 Review of Management of Risks and Constraints:

Through reviewing project and external documentation, and interviewing a broad range of stakeholders, the evaluation has analysed the project's risks and challenges, and efforts made to date to address them. In the current Logframe (Oct 2012) document, the project identifies a number of potential risks that it faces, and actions it proposes to overcome or mitigate these risks. These are listed below, in the first 2 columns. The 3rd and 4th columns are the evaluation team's findings on actions taken to date (according to the project reports), and comments. The evaluation team added one additional perceived risk at the end of the list.

Table 7: Risks and Mitigating Actions

Identified Risk (from Logframe)	Project's Proposed Actions to Mitigate this Risk (from Logframe)	Project's Activities to Date (from project reports)	Comments of evaluators
Poor understanding of PQ; limited awareness of added value of PQ; lack of commitment from procurement agents to procure PQ'd diagnostics	Communication strategy to create awareness of added value of WHO PQ among manufacturers, donors, procurement agents, and national authorities. **Specifics:** PQ newsletter, stakeholder meetings. Have PQ beneficiaries advocate on behalf of PQ.	Newsletters ("Updates"), Stakeholder meetings, Direct outreach to manufacturers and manufacturer association, regular Interagency Pharmaceutical Coordination group meetings, coordination with regulatory authorities, presentations to key audiences. (Specific numbers of each are not available from reports) Prequalification of Diagnostics information session scheduled for 2010 was cancelled.	Remains a strong risk. Implementation of communication strategy has been very mixed. Information on PQDx programme, application process, and list of PQed diagnostics are available on the WHO/DLT web site. But the website is hard to navigate and has not been updated recently. (No newsletter updates beyond Q3/4 2011). Feedback from interviewees is that guidance and communication are not clear.
Lack of government engagement; time to implement policy changes; lack of political stability (elections, conflict).	Advocacy at the government level, using competition between countries and regional regulatory networks as leverage to ensure government commitment. Establishment of regional regulatory networks to drive regulation forward and ensure support to neighbouring countries in case of political instability, thus decreasing sole dependence on national capacity and expertise. **Specifics:** advocacy within NRAs; establish regulatory networks through regional meetings.	Dec 2011 launch of program in Tanzania, combined with training meeting including others from Africa region (Burkina Faso, South Africa, Kenya, Uganda, Zanzibar). Preliminary discussions with countries on establishing regional cooperation.	Efforts toward regional networks and collaboration among countries are only nascent. Countries report desire for more support in this area.
Manufacturers do not apply for PQ; lack of commitment from procurement agents to procure PQed diagnostics	Advocate and obtain commitment from procurement agents and countries to establish and implement a quality policy which gives preference to PQed products. Highlight risk involved in procuring poor quality products. **Specifics**: advocacy at supplier level by communicating and showing market potential; information sessions for manufacturers and FAQs posted on project web site.	Invitations to apply for PQ sent to manufacturers. Presentations were made to manufacturers and to procurement agents. (details are not specified in progress reports).	Remains a strong risk. Advocacy efforts among manufacturers and procurement agents have been weak and more importantly undermined by poor performance (e.g., slow PQ, poor communication). Greater outreach and work with developers and manufacturers is recommended.
Prequalification is delayed, with a full list not available for procurement agents; factors hampering fair procurement e.g.	The current list of products eligible for WHO procurement (based on previous acceptable results in the WHO Test Kit Evaluation programme) remains valid. As products are PQ'd they are added to this list. Advocate use of adequate procurement specifications to major procurement agencies. **Specifics:** ensure	List of PQ'd products is posted on the website. Procurement guidelines are not yet available on the website.	Remains a strong risk. Critical mass of PQ'd diagnostics are needed to get commitment from procurement agents. Advocacy efforts are undermined by poor performance.

inadequate procurement specifications.	comprehensive list of PQ'd products for procurement agents.		
Lack of country engagement: limited awareness of the need for improved **regulatory capacity**, lack of skills or resources in-country; turnover of key staff.	WHO support to countries for changes in legislation and implementing or improving regulation of diagnostics. Setting up regional regulatory networks will facilitate progress and create a sustainable environment. **Specifics:** lobby for legislative changes to include diagnostics. Engage stringent NRAs in trainings, promote global guidance (through Global Harmonization Task Force, International Medical Devices Regulatory Forum, etc).	Support for action plans, some training and advocacy efforts have been undertaken in Burkina Faso, Tanzania and to a lesser extent South Africa. Engagement with China is beginning. Minor involvement (e.g. meeting/training event in Tanzania) of other countries so far.	Some programme efforts to address this risk appear to have been successful, but risk of budget priority shifts and staff turnover remains. Interviewees beneficiary countries have acknowledged improved awareness of the need for regulatory efforts and other benefits from programme support.
Lack of country engagement: limited awareness of the need to do **PMS activities** ; lack of skills or resources in-country; turnover of key staff; information of insufficient quality to report product failure or avoid stock out (e.g., information sharing is delayed or incomplete; end users do not have adequate means to report adverse events or log complaints)	Provision of standard form and adequate training with Standard operating procedures and protocols will go a long way. **Specifics:** establish or improve post-market surveillance practices. Engage WHO collaborating centres for trainings.	Limited trainings have been held to date. Assistance with development of workplans and procedures and protocols.	Some programme efforts to address risk appear successful, but risk remains, especially outside the pilot countries. Interviewees from pilot countries have acknowledged the need for PMS, and improvements made with support of the programme. Three countries are implementing various aspects of PMS.
Additional potential risks:			
Slow prequalification could impede introduction of new POC technologies to needed countries.	Programme and stakeholders might consider outreach to developers and provisional approval process for high priority new technologies needed in countries. Programme should interact with manufacturers during development stage of new products.		Prequalification should "incentivize" manufacturers to develop new products, but that has not been the case. Slow or burdensome PQ process actually works against the overall goal of increased access to quality diagnostics.

In the table below, the evaluation team lists the perceived strengths, weaknesses, opportunities and threats to the PQDx programme based on findings.

Table 8: SWOT Analysis

Strengths	**Weaknesses**
• Base at WHO, with other PQ programs, expertise and strong international mandate and reputation of organization housing the project • Technical capacity, expertise, credibility • In-depth quality checks (inspections) not done by other organizations • Programme has demonstrated in numerous cases its ability to identify critical non-conformities where other SRAs have failed.	• Long timelines required (bottlenecks?) for PQ • The very diverse nature of diagnostic devices makes the PQDx particularly technical and challenging which is not the case in other PQ programs (pharmaceuticals, vaccine). • Growing pains, adjusting objectives • Difficult relationships & communication between implementer and donor • Small staff, relatively low funding level, lack of core funding from WHO • Dependent on donor financing and therefore donor's agenda • Poor leadership and communication to the outside world
Opportunities	**Threats**
• Growing realization of importance of QA for diagnostics worldwide (especially since the recall of Bioline) • Potential to partner with FDA/PEPFAR, EU, others to maximize use of limited resources • Potential to strengthen in-country capacity by focused TA and on-the-job training with country officials • Opportunities to branch into PQ of more priority products (circumcision devices, TB tests, etc) • Poor capacity for post-market surveillance in countries, lack of attention to ongoing QA creates opportunity for centralized PQ programme to have impact	• Poor understanding (among many) of importance of PQ for diagnostics • Appearance of redundancy or irrelevance (given other organizations' PQ activities) • Delays in PQ; risk of becoming a major bottleneck (as happened with ARV medicines PQ project in early days) if WHO PQ is required for all RDTs • Risk of manufacturers lack of incentive to get products PQ'd • Countries are used to procuring non PQed devices and may become increasingly reliant on non-quality assured devices in their health systems. • Risk of country unrest, lack of action, incapacity, lack of interest or follow-through • Threat (in future) of WHO PQ'd product facing quality crisis or recall – would be devastating to programme's reputation?

7 RECOMMENDATIONS & ACTION PLAN

The following is a prioritised list of all recommendations. Brief explanations are given below each heading whereas full explanations must be found in the evaluation report.

Priority number 1: Expedite the Prequalification Process:

Identified Issues	Recommendations	Proposed Timeline
Resolving HR challenges		
1. Inadequate manpower to process suppliers through PQ, given demand and workload	1.1. **Conduct an external analysis to identify gaps in the human resources** *(quality and quantity) with the work to be completed for timely process of suppliers through PQ.* *1.2.* **Follow up on recruitment.** *Some positions are still vacant. Taken into consideration the difficult and lengthy process of recruitment within WHO, UNITAID might want to follow up with a log frame indicator on the recruitment. Alternative methods for recruitment (e.g. medium term contractor) might alleviate the cost and difficult process of recruitment.* 1.3. **Focus efforts and funding on the PQ process,** *consider delaying more country activities until in-house PQ issues resolved (resume the country activities when the backlog in the PQ pipeline has been resolved).*	**Immediately** (March-April 2013) After completion of the above (April 2013) **March 2013**. Some on-going commitments might have to be fulfilled, e.g. China
2. Lack of leadership of the PQ programme	**2.1 Have discussion with WHO high-level management on how to improve the leadership of the programme.** *Heavy criticism from other stakeholders about leadership, bottleneck created by director, need to decentralize some functions. Consider Operations Manager position?* **2.2 Become more proactive in quality of diagnostics area, begin regular consultations with other stakeholders in diagnostics field** *(and UNITAID staff should take part) - The program should lead the debate on ensuring quality of diagnostics. Several initiatives are run in parallel, and coordination and harmonisation are needed. (E.g. consider organizing a symposium, taking the lead on developing a standard protocol for testing of diagnostics, convening regular meetings with key experts, etc). Re-establish credibility in the field, which has suffered.*	**Immediately** (and in concert with 1.1) Before end of 2013

Streamlining the PQ process without compromising on quality		
3. Long delays, confusion about reasons for this	**3.1 Conduct a <u>process analysis</u> to examine the reasons/obstacles that have led to delays for each dossier** *WHO is not responsible for all the delays, many can be attributed to the manufacturers.* **3.2. <u>Communicate the results of the analysis</u> widely to stakeholders.** *Explain the responsibility and reasons for the delays (e.g. PQDx finding critical non-conformities). In the absence of PQ this would help stakeholders to make procurement decisions. This may require amendment of confidentiality policy signed between PQDx and manufacturers.*	In parallel with 1.1 (by June 2013) As soon as process analysis is complete (June-July 2013)
4. Non-performing or sub-standard manufacturers	**4.1 Adopt a strategy to <u>remove non-performing manufacturers</u> from the PQ process,** *Non-performers drain the time/resources of the program and reflect badly on performance. (E.g. a deadline to comply or a fee if process is to be extended beyond a given deadline).*	Decide and adopt methodology by July 2013 Manufacturers to comply before end of 2013.
5. Confusion, lack of interest among developers	**5.1 Enhance incentives/ understanding among developers to submit for PQ** *Improve guidance, outreach through clearer web site instructions and templates*	June 2013

Priority number 2: Improve Relations with Stakeholders:

Identified Issues	Recommendations	Proposed Timeline
Improve Communication about PQ Dx with Stakeholders		
1. Lack of Communications Person on program team	**1.1. Fill the open position of Communication Officer** *Communicate (through communiqués, on web site, etc) with global stakeholders about program constraints and rationale behind the PQ methodology. Become proactive in leading the debate on how to best ensure the quality of in vitro diagnostic tests.* **1.2. Improve regular reporting to UNITAID** *consider revisions to indicators, enhanced reporting formats to more clearly report on programme accomplishments vs. objectives*	**Immediately** By June 2013
2. Needed enhancements of PQ Dx website as main portal to the	**2.1 Explain and illustrate the rationale behind the PQ Dx methodology for PQ on the website**. *Publish more information on the progress of the PQ individual processes.* *Fully clarify expectations and guidance for*	Posting on website by August 2013. Full completion

world	*manufacturers for PQ (consider posting a mock PQ dossier)* *Specifically address the need for information of the different stakeholders on web site (NRAs, developers, procurement agencies etc.)*	and improvement of site during the next phase of implementation
3. Inadequate relationships and cooperation with international stakeholders	3.1 **Begin high-level communications with top experts in diagnostics field.** *Leadership of the program to specifically concentrate on this task, with WHO top technical leads. (Related to HR2.2 above). A better understanding of the program is needed to obtain buy-in and support of international stakeholders.* 3.2 **Consider enhanced partnerships with FDA, EU, other agencies** *to coordinate, streamline PQ, share data, etc*	April 2013 By end 2013

Priority Number 3: Adapt the PQDx Programme to the Needs of the Market:

Identified Issues	Recommendations	Proposed Timeline
1. No procedure in place to ensure quality of new technologies on the market	**Adopt a specific strategy and procedure to ensure the quality of new technologies on the market until the developers have sufficient manufacturing data to PQ.** *Currently, developers cannot apply for PQ until they have undergone commercial manufacturing for some time. A process is required to ensure the quality of the devices upon entry to the market, and to facilitate PQ later when sufficient data have been generated.*	**Immediately** and in consultation with other key stakeholders
2. Urgent need for QA of TB testing devices	**Integrate TB testing into the program** *New technologies in that field have entered the market and in-country programmes are already reporting quality issues impacting their programmes. (supplier need to submit application and device added to the priority list)*	Immediately if possible
3. Increased focus required on priority technologies	**Address urgent needs expressed by physicians, countries** *e.g. for Point of Care technologies – prioritize these for PQ*	June 2013

WHO PQ DX ACTION PLAN		2013										2014	
		March	April	May	June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb
HR	**Conduct an external analysis** to identify gaps in the human resources												
	Follow up on recruitment for positions on the PQ team that are still vacant												
	Focus staff efforts and funding on the PQ process, consider delaying more country activities until in-house PQ issues resolved												
	Have discussion with WHO high-level management on how to improve the leadership of the programme												
	Improve leadership, become more proactive in quality of diagnostics area, **begin regular consultations with other stakeholders in diagnostics field**												
Streamline PQ	Conduct a **process analysis to examine the reasons/obstacles that have led to delays** for each dossier												
	Communicate the results of the analysis widely to stakeholders												
	Adopt a strategy to **remove non-performing manufacturers from the PQ process**												
	Improve communcations and guidance to developers												
Improve Relations with Stakeholders	**Fill the open position of Communication Officer**												
	Begin c**ommunications with global stakeholders** to explain rationale and methodology												
	Improve **reporting to UNITAID** (format, contents)												
	Enhance **programme web site**, include instructions and templates												
	High-level **communications with top experts in diagnostics field**												
	Consider **enhanced partnerships with FDA, EU, other agencies**												
Adapt to Market Needs	Adopt **strategy and procedure to ensure quality of new technologies** not yet ready for full PQ												
	Integrate TB testing into the program												
	Address urgent needs expressed by physicians and countries (e.g. POC)												

8 ANNEXES

8.1 Evaluation Terms of Reference

Technical Terms of Reference for a Request for proposals for A consultancy to carry out a Mid-term Evaluation of the WHO diagnostics Prequalification Programme

1. INTRODUCTION

1.1 Objective of the ITB (Invitation to Bid)

Mid-term evaluations are a tool that the UNITAID M&E Team uses to strengthen project management and ensure that UNITAID funded projects achieve optimal results.

The objective of the proposed consultancy is to assess the progress made towards the final objectives of UNITAID support to the WHO Prequalification programme for diagnostic tests for HIV/AIDS and malaria. The review should include recommendations on how project management can be improved to help the project achieve its objectives more effectively and efficiently.

UNITAID/WHO is an organization whose activities are supported by public funding and is hosted by the World Health Organization (WHO) UNITAID is supported by public funding and is hosted by the World Health Organization ("WHO"), whose financial, procurement and HR rules it follows. Therefore, it is important that non health-related items that provide infrastructure support for the delivery of health services be cost-effective. For this reason, bidders are requested to propose the best and most cost-effective solution to meet UNITAID/WHO requirements, while ensuring a high level of service.

1.2 About UNITAID

UNITAID Mission

Statement

UNITAID is a global health initiative, established to provide sustainable, predictable and additional funding to significantly impact on market dynamics to reduce prices and increase the availability and supply of high quality medicines, diagnostics and related commodities for the treatment of HIV/AIDS, malaria and tuberculosis, primarily for populations in low-income and lower-middle income countries. For further information on UNITAID's mission, guiding principles, legal framework, procurement policies (including quality assurance standards) and current types of projects, please refer to the UNITAID web-site (www.unitaid.eu).

UNITAID was established in 2006 and its mission is to contribute to the scale up of access to treatment for HIV/AIDS, malaria and tuberculosis by leveraging price reductions of quality medicines, diagnostics and related products, which are currently unaffordable or unavailable for low and middle income countries. UNITAID concentrates funding support for projects which can demonstrate an impact on the markets for medicines and diagnostics either through a reduction in the cost of medicines and diagnostics, an improvement in availability of quality formulations and suppliers or an increase in timely delivery of the required products to low and middle- income countries. UNITAID aims to support national and international efforts and complement the role of existing international institutions.

UNITAID projects are implemented through partner organizations that provide treatments, diagnostics and related products to beneficiary countries in three disease areas, HIV/AIDS, TB and malaria.The principal functions of the Secretariat are to carry out and manage the day-to- day operations of UNITAID, including implementing UNITAID’s strategy, the work plan of UNITAID as approved by the Board, managing and coordinating relationships with Partners, and coordinating and facilitating technical support and advice to the Board.

2. DESCRIPTION OF SUBJECT / PRESENT ACTIVITIES

2.1 Introduction

The service provider is expected to provide an assessment of the likelihood of the project achieving the objectives that were initially set by UNITAID and its implementing partner and of the progress of the project under mid-term review.

In addition, the service provider should provide recommendations on how to improve the effectiveness and efficiency of project management, including partner reporting on project activities and finance. The reviewers are also asked to consider the process of Prequalification of Diagnostic tests in a broader context, including the types of organizations, processes and procedures that could facilitate the work of quality assurance of diagnostic tests.

The review should take no more than 2 months to complete and the budget submitted to UNITAID should take into consideration the short expected duration of the project, that it is a desk review and that UNITAID expects concrete recommendations that are related to the project and that can be implemented within its life-span.

The selected provider(s) will be expected to work closely with the UNITAID Secretariat to undertake reviews of the projects using official documents, evaluation checklists, questionnaires and other associated tools that may be used to evaluate UNITAID-funded projects. UNITAID requires that the consultant(s) consider the following information:

- the legal agreements between UNITAID and its implementing partners for each project;
- the progress reports and the follow-up performed by UNITAID Portfolio Managers with regards to semi-annual and annual reports from implementing partners; and
- the financial reports from implementing partners in order to assess the relationship between the financial information provided in each progress report and the information provided on activities, results and for the associated M&E indicators.

Assessment of the above-mentioned documentation will facilitate the identification of the project's strengths, weaknesses, opportunities and threats and contribute to improving the chances that a project's end outcomes are achieved. Details of the project requiring review are listed by disease/project area in Annex 1 of this document. Service providers will be provided with project plans, legal agreements, project reports, including financial reports, from Implementing Partners as well as any other information deemed necessary to perform a thorough review of the project.

2.2 Characteristics of the provider

2.2.1 Status

The service provider shall be a public institution, a private or individual company, an international consulting group or individual, or other organization with proven expertise in:global health, public health financing or development area;

- procurement, purchasing and supply chain of health products (specifically diagnostics) to diagnose and prevent HIV/AIDS, TB and malaria; and
- the regulatory environment for health products in low and middle income countries, particularly Africa.

In addition, the ability to communicate (written and verbal) in both English and French would be an advantage.

2.3 Work to be performed

2.3.1 Key requirements

The proposed project design, method and analysis should be adequately developed, well-integrated, well-reasoned, and appropriate to the aims of the project.

2.3.2 Keydeliverables/reporting requirements

The project requiring mid-term review is UNITAID support to the WHO Prequalification Programme for diagnostic tools for HIV/AIDS and malaria. The review is restricted to a desk review of available documentation as well as consultation with a wide range of stakeholders including the UNITAID Secretariat, the Prequalification of diagnostics Programme, manufacturers of diagnostic tests for HIV/AIDS and malaria and other stakeholders that may be added over the course of the review. The evaluation questions cover the areas of relevance, effectiveness, efficiency and impact. For these reviews the questions are:

Relevance:

1. Are the activities and expected outputs of the project consistent with the objectives and expected outcomes as described in the project plan?

Effectiveness:

2. To what extent were the objectives of the project achieved
3. To what extent are they likely to be achieved?
4. What are the main factors influencing the achievement or non-achievement of the objectives?

Efficiency:

5. Are the project partners working closely with the relevant national authorities in the project's beneficiary countries?

Impact:

6. Can the partner organization attribute UNITAID funding to improvements in the landscape for diagnostic tests related to HIV/AIDS and malaria?

The tasks and responsibilities for the review will include meeting with UNITAID Secretariat members and other stakeholders to:

1. review the project documentation, including project specific monitoring indicators and financial reports; project appraisal, project evaluation and/or project impact assessment in th
2. review the current reporting templates for both project activity and project financial reporting and suggest improvements to routine project reports and modify, if necessary, the frequency and timing of reporting;including strengths, weaknesses, opportunities and threats;
4. advise on other organizations, processes and procedures that could be put into place to facilitate the quality assurance of diagnostic tests; and
5. advise and assist in the development of an action plan to incorporate the lessons learnt from internal project management of specific projects and partners over the course of UNITAID's operational activities.

The service provider is expected to produce a final written assessment of the project under review including recommendations to the UNITAID Secretariat on how to improve the effectiveness and efficiency of partner reporting on project activities and finance,.

Bidders should submit a financial proposal (preferably in US dollars) for the work to be carried out.

2.3.3 Duration and timelines

This consultancy is for a period of 2 months. The work should start on 03 December 2012 or as soon as possible thereafter and will end on 04 February 2013.

8.2 EVALUATION FRAMEWORK

		Evaluation Methodologies			
		Document Review	Progress against Indicators	Survey	Key Informant Interviews
Primary Evaluation Questions and Research Tasks	Relevance - Activities/outcomes vs. project plan - Contribution to UNITAID's goals - Appropriate for the current environment, market dynamics, and country needs? - Coordination or follow-on from other WHO programs in diagnostics?	- PQDx Programme support Project Reports - UNITAID Reports	- Progress against stated objectives	- Review of Manufacturers Survey conducted by WHO (note: this survey has not been by WHO. However the evaluators obtained feedback from a broad range of manufacturers and developers).	- UNITAID Staff - WHO PQDx staff - Target Country Representatives - Partner organizations - Developers and manufacturers
	Effectiveness - Objectives achieved? - Suggest Improvements to reporting templates and timing - Ways to make the project more effective in meeting goals - Mechanisms to encourage supplier participation - Incorporate lessons learned in Action Plan from evaluation.	- PQDx Project Reports - Manufacturers' Survey Report - Country documents	- Progress against stated objectives by reporting period - Identify obstacles to expected progress	- Review of Manufacturers Survey conducted by WHO (see note above)	- WHO PQDx staff - Suppliers - Target Country Representatives - Partner organizations - Developers and manufacturers
	Efficiency - Working relationship with target country authorities - Assess project management including S.W.O.T. analysis	- PQDx Programme Reports - Country documents	- Progress reports & Timelines - Progress against indicators - Country reports	- Review of Manufacturers Survey conducted by WHO in 2012 (see note above)	- Target Country Representatives - WHO PQDx staff
	Impact - Link between project actions and improvements/outcomes - Scaling up of access to appropriate diagnostics for HIV/AIDS and malaria in the targeted countries	- Country Action Plans (baseline & benchmark data?)	- Review of logframe - Progress toward main Impact indicator	- Survey of target country representatives on changes from baseline data	- Target country representatives - WHO PQ staff - Partner Organizations

8.3 Persons ContactED/interviewED

UNITAID TEAM		
Dr. Kate Strong	Monitoring and Evaluation officer, UNITAID	Met Dec 17
Kvetoslava Dzackova	Financial department, UNITAID	Met Dec 17
Robert H. Matiru	Portfolio manager, UNITAID	Met Dec 17
Raquel Child	Technical program coordinator, UNITAID	Met Dec 17
BAN, Hyun Hee	Monitoring and Evaluation department, UNITAID	Met Dec 17
Gauri KHANNA	Monitoring and Evaluation department, UNITAID	Met Dec 17
Dr. Greg Martin	Former Portfolio Manager	
Carmen Perez	Formerly with GF PMS team, now UNITAID	
Emma Hannay	UNITAID Market Dynamics Team	
WHO DLT team members		
Gaby Vercauteren	Coordinator, DLT, WHO	Met Dec 17
Mercedes Peres Gonzales	Technical officer, DLT, WHO	Met Dec 17
Irena Prat	Technical officer, DLT, WHO (technical documentation analysis; Strengthening regulatory support and PMS)	Met Dec 17
Anita Sand	Technical Officer, DLT, WHO (laboratory analysis)	Met Dec 17
Jeanette Twell	Technical Officer, DLT, WHO (manufacturer on-site visit)	Met Dec 17
Dr. Willy Kikoka Urassa	Scientist, DLT, WHO (CD4 count)	Met Dec 17
Robin Murant	Technical Officer, DLT, WHO (regulatory authorities)	Met Dec 17
Helena Ardura	Technical officer for review of applications and completeness of dossiers	
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Elena Trajkovska - Contracts Manager (etrajkovska@unicef.org) **Helene Moller** - Chief, Health	United Nations Children's Fund (UNICEF) Supply Division, Copenhagen

Technologies (hmoller@unicef.org) **Ludo Scheerlink** - Technical Officer (lscheerlinck@unicef.org)	
Maurine Murtagh Maurinemurtagh@sbcglobal.net	Former head of CHAI labs area Now independent consultant, based in California
MANUFACTURERS/DEVELOPERS	
Avi Pelossof VP of Infectious Diseases Area Avi.Pelossof@alere.com	Alere (makers of Pima point-of-care CD4 machine, also makers of components for many RDTs)
Duncan Blair Duncan.blair@alere.com Director, Health Development Initiatives Alere Inc. 9th Floor, 11 Narathiwat Soi 7, Khet Sathorn, Thungmahamek Bangkok 10120 Thailand Phone: +66 (0)2 105 6305	Former CHAI, now with Alere PQ in process for several products?
David Anderson Anderson@burnet.edu.au	Burnet – CD4 maker submitting dossier for PQ
Joanna Sickler (jsickler@zyomyx.com)	Zyomyx - CD4 maker submitting dossier for PQ
William Rodriguez, MD wrodriguez@daktaridx.com CEO, Daktari Diagnostics, Inc. Office + 1 617.336.3299	Daktari - CD4 maker submitting dossier for PQ
Mike Lochhead Mike.lochhead@mbiodx.com Vice President MBio Diagnostics, Inc. 5603 Arapahoe Ave, Suite 1 Boulder, CO 80303 Direct: 303 952 2810	Mbio CD4 maker submitting dossier for PQ (not yet begun the process)
Steve D. La Ryan (I. J. Kim) Taylor (Tae Young Hor) Taylor Hor sales@standardia.com taylor@standardia.com, Kenny Lee kenny@standardia.com	Standard Diagnostics
Thierry PAPER , CEO PAPER@biosynex.com	Biosynex (PQ'd)
See Gloria Young, below	Becton Dickinson
Fabrice GERARD Market Access Director Emerging Markets Abbott Molecular Division Cellphone:+33618234815 **Dr Anke Coblenz** (US based) (leading the PQ process for Molecular division for HIV Realtime assays.	Abbott

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Thomas Ippolito, Chembio Diagnostic Systems Inc. tippolito@chembio.com	Chembio Prequalified and still in the process for other products
Neil Mehta, Premier Medical Corporation Ltd. nmehta353@optonline.net	Premier Medical PQ in the process for several products
Michel Bonnier, BioMèrieux michel.bonnier@eu.biomerieux.com	Biomerieux PQ'd and still in the process for another product
OTHER STAKEHOLDERS:	
Rosanna Peeling – LSHTM (Rosanna.Peeling@lshtm.ac.uk)	Consultants who have conducted other reviews and evaluations of PQDx in recent years
Gloria Young gloriayoung2011@gmail.com (based in California)	HIV diagnostics consultant for the MD team, the ex-head of HIV diagnostics for BD before her retirement. (She led most of the process for getting PQ'ed)
Jean Francois Delavision jfdelavison@ahimsa-partners.com.	Ahimsa Partners (Consultant, engaged by WHO previously to evaluate the PQ process and give recommendations)

8.4 SOURCES OF INFORMATION

Documents Reviewed

UNITAID and Project Background Documents:

- WHO DLT Web site: http://www.who.int/diagnostics_laboratory/en/
- UNITAID Web site: http://www.unitaid.eu/diagnosticsqa
- UNITAID 5-Year Evaluation Summary Report – October 2012
- Update on the WHO Prequalification of Diagnostics Programme – Powerpoint presentation by Gaby Vercauteren, Geneva, Jan 2012
- Global Medical Technology Alliance (GMTA) web site, comments on WHO PQ for diagnostics (http://www.globalmedicaltechnologyalliance.org/position-paper-the-world-health-organization%E2%80%99s-prequalification-of-diagnostics-impacts-on-diagnostics-and-medical-technology-to-patients.html
- WHO Global TB report 2011

Official project and PQDx programme documents:

- UNITAID Letter of Agreement – March 13, 2009
- UNITAID Memorandum of Understanding (MOU) – March 13, 2009
- WHO Certified Financial Statement Dec 31, 2009 (Contribution from UNITAID)
- Final UNITAID PQDx budgets Dec 2010, Dec 2011
- Diagnostics and Laboratory Technology (DLT) Prequalification of Diagnostics Business Plan 2009-2013 (WHO)
- List of HIV diagnostics eligible for procurement by WHO in 2011, 2012
- WHO Bulk Procurement Scheme Specifications of HIV Test Kits 2009, 2010

Presentations and Market Reports:

- Diagnostic market analysis: HIV simple/rapid, enzyme immunoassay (EIA), and supplemental tests -- Available data and implications for future funding (June 2011)
- Diagnostic market analysis: CD4 and HIV virological technologies -- Available data and implications for future funding (March 2011)
- PowerPoint Presentation to Malaria RDT Landscape Workshop (May 2011) – Update and Perspectives on RDT Prequalification
- Manual for procurement of diagnostics and related laboratory items and equipment (2011 Draft marked “not for distribution)
- PowerPoint presentation by Gene Walther of Gates Foundation – WHO Diagnostics Prequalification: Potential Areas for Improvement (4 April 2011)
- UNICEF Supply of Diagnostic Devices in Health – 6th Consultative Meeting of UN PQ of Diagnostics, Medicines, and Vaccines Programmes (April 2011)
- Presentation by Anita Sands: Current pipeline for WHO PQ of Diagnostics programme: How WHO is bringing innovative POC diagnostics to the field and assuring quality. AIDS2012 Satellite Session, 25 July 2012, Washington DC

Project progress reports:

- 1st Annual Report (March 2009-March 2010) and PUDR – March 15, 2010 (May 15, 2010 final?)
- 2nd Annual Report – March 15, 2011
- 3rd Annual Report – Aug 2012
- 1st Interim Progress Report – Oct 1, 2009
- 2nd Interim Progress Report – Mar 23, 2009 – Mar 15, 2010 – Oct 30, 2010
- 3rd Interim Progress Report – Jan 1st - Sep 30th 2011 – Oct 1, 2011
- Logframe for 3rd Interim Progress report 2011 – Jan 1-Sept 30, 2011
- 4th Interim Progress Report – Jan 1st- Aug 31st - Oct 28, 2012
- Logframe for 4th Interim Progress Report – Jan-Aug 2012 (submitted Nov 26, 2012)
- 4th Interim Progress Report Budget– Oct 28, 2012 (Nov 25, 2012 final?)

Pilot Country documents:

- Information Document on Pilot Countries: Strengthening regulatory and post-market surveillance capacity for diagnostics in resource-limited settings -- Prequalification of Diagnostics Pilot Project in five WHO Member States: Burkina Faso, Côte d'Ivoire, South Africa, the United Republic of Tanzania and the People's Republic of China
- TOR MOU with South Africa & invitation letter
- Letter from WHO to the Department of Health South Africa with comments on their draft legislation. (CONFIDENTIAL)
- Draft Mission Report: Executive Summary -- REVIEW OF PROCUREMENT PROCEDURES AND EVALUATION METHODS FOR HIV RAPID TEST KITS IN REPUBLIC OF SOUTH AFRICA - August 2012
- WHO STATEMENT RELATED TO THE ASSESSMENT OF PROCUREMENT PROCEDURES AND EVALUATION METHODS OF HIV TEST KITS IN SOUTH AFRICA - 31 August 2012
- WHO Report of the mission on strengthening of capacity for regulation and post market surveillance of diagnostics in Tanzania, 3-5 November 2009.
- Memorandum and costing from Tanzania
- Leveraging the Prequalification Process for National Regulatory Decisionmaking – Powerpoint presentation by A. Fimbo, Tanzania National Food & Drugs Authority (International Conference of Drug Regulatory Authorities, Oct 2012)
- Strengthening of regulatory and post-market surveillance capacity for diagnostics in resource-limited settings. Generic Framework Country Action Plan for PMS: Sept 2009-Dec 2012
- Strengthening of regulatory and post-market surveillance capacity for diagnostics in Tanzania: Country Action Plan for PMS: Sept 2010- August 2011
- Strengthening of regulatory and post-market surveillance capacity for diagnostics in Tanzania: Country Action Plan for PMS: Jan 2012- Dec 2012
- Strengthening of regulatory and post-market surveillance capacity for diagnostics in Tanzania. Country Action Plan for PMS: Jan 2012- Dec 2012. PROGRESS REPORT AUGUST 2012
- List of Batches of HIV Test Kits sent to NHL-QATC for Quality Checking Dec 2011-July 2012 (Tanzania)
- Meeting Report: Launch of the Program on Strengthening of Regulatory and Post Market Surveillance (PMS) Capacity for Diagnostics in the United Republic of Tanzania. New Africa Hotel, Dar es Salaam, Tanzania. 13 – 14 December 2011
- Annual Technical Report- 2011: Strengthening of capacity for regulation and post market surveillance of diagnostics in Tanzania
- Burkina Faso Action Plan & memorandum
- STRENGTHENING OF REGULATORY AND POST-MARKET SURVEILLANCE CAPACITY FOR DIAGNOSTICS IN RESOURCE-LIMITED SETTINGS-TANZANIA. Assessment Report. July 2010
- RAPPORT INTERMEDIAIRE DU PROJET DE RENFORCEMENT DE LA REGLEMENTATION ET DE SURVEILLANCE POST-COMMERCIALISATION DES TESTS DE DIAGNOSTIC DU VIH AU BURKINA -Août 2012
- Rapport de la mission de renforcement des capacités de réglementation et de la surveillance du marché des tests de diagnostic au Burkina Faso, 15 - 18 Décembre 2009
- MISSION AU BURKINA FASO 30 avril – 04 mai 2012 -Compte rendu
- Memorandum Burkina Faso – Formation sur le Renforcement des Capacites de Reglementation des Produits de Diagnostic – Jan 15, 2013
- Rapport de la mission de renforcement des capacités de réglementation et de la surveillance du marché des tests de diagnostic en Côte d'Ivoire, 10 - 11 Décembre 2009
- Proposal for Post Market Surveillance of HIV Diagnostics in P.R. China Division of HIV/AIDS and Sexually-transmitted Virus Vaccines, National Institutes for Food and Drug control (NIFDC), P.R. of China.

- Proposal for Post Market Surveillance of HIV Diagnostics in PR of China -National AIDS reference Laboratory, NCAIDS
- WHO Prequalification of Diagnostics China TB and HIV – PPT by Anita Sands, Shanghai, Sept 2012

Partner organization documents:

- TOR and Redesignation Form – collaboration with ITM Antwerp – July 2008
- TOR and Redesignation Form – collaboration with ITM Antwerp – Sept 2012
- Agreement with PEPFAR/OGAC on coordination of efforts on lab aspects WHO-CDC (Joint Strategic Framework of WHO and PEPFAR Cooperation on HIV/AIDS 2010-2013) Dec 10, 2009

ANNEX: Published Feedback on PQDx programme from Stakeholders:

- From Tanzania Food and Drugs Authority (A.M. Fimbo) ….presentation to International Conference of Drug Regulatory Authorities, Oct 2012: http://icdra.ee/attachments/article/17/3-Adam-Mitangu-Fimbo.pdf

The WHO PQP has greatly assisted TFDA to develop guidelines and procedures for approving medicines, vaccines and medical devices.

- Ahimsa Partners - Ahimsa Partners was invited to participate in a panel of experts appointed in October 2011 to review the scope and effectiveness of the WHO's prequalification program for medicines, vaccines and diagnostics. At the end of the review, the panel proposed that a strategic analysis be conducted to identify the program's successes and failures as well as the main challenges and the opportunities for improving the process. http://www.ahimsa-partners.com/mission/organisation-mondiale-de-la-sante-prequalification-2012/

One of the report's main recommendations was that the procedures and governance of the WHO's PQDx program should be tightened. The search for partners and funding to implement these recommendations is under way.

- Global Medical Technology Alliance (GMTA) – Position paper on WHO PQDx

http://www.globalmedicaltechnologyalliance.org/position-paper-the-world-health-organization%E2%80%99s-prequalification-of-diagnostics-impacts-on-diagnostics-and-medical-technology-to-patients.html

The GMTA strongly supports the mission of WHO to increase access to affordable diagnostics of assured quality in underserved regions of the world.
The current WHO diagnostic prequalification program, however, creates unnecessary additional regulatory hurdles for manufacturers who already comply with product registration and Quality System requirements under stringent regulatory authorities such as those in the US, EU, or Japan. For companies that routinely and reliably manufacture diagnostics already meeting stringent regulatory requirements, the program adds significant delay and potentially undermines WHO's important mission to increase access to much needed diagnostics in underserved regions of the world.
We echo WHO's longstanding concern for the quality and suitability of diagnostic products intended for use in critical regions of the world, and we recognize the potential need for a product and quality system review of manufacturers not already subject to appropriate regulation. We urge WHO to adopt a two-tiered approach similar to that outlined in this paper as the best means of addressing the organization's concerns over regulatory, quality, and manufacturing standards to be met by diagnostic products procured through its programs. This important step provides a means for WHO to improve regulatory requirements for all products while opening the way for timely access to high quality diagnostics. This also allows

better utilization of both industry and WHO resources to specifically address the unique requirements of products for use in underserved regions of the world