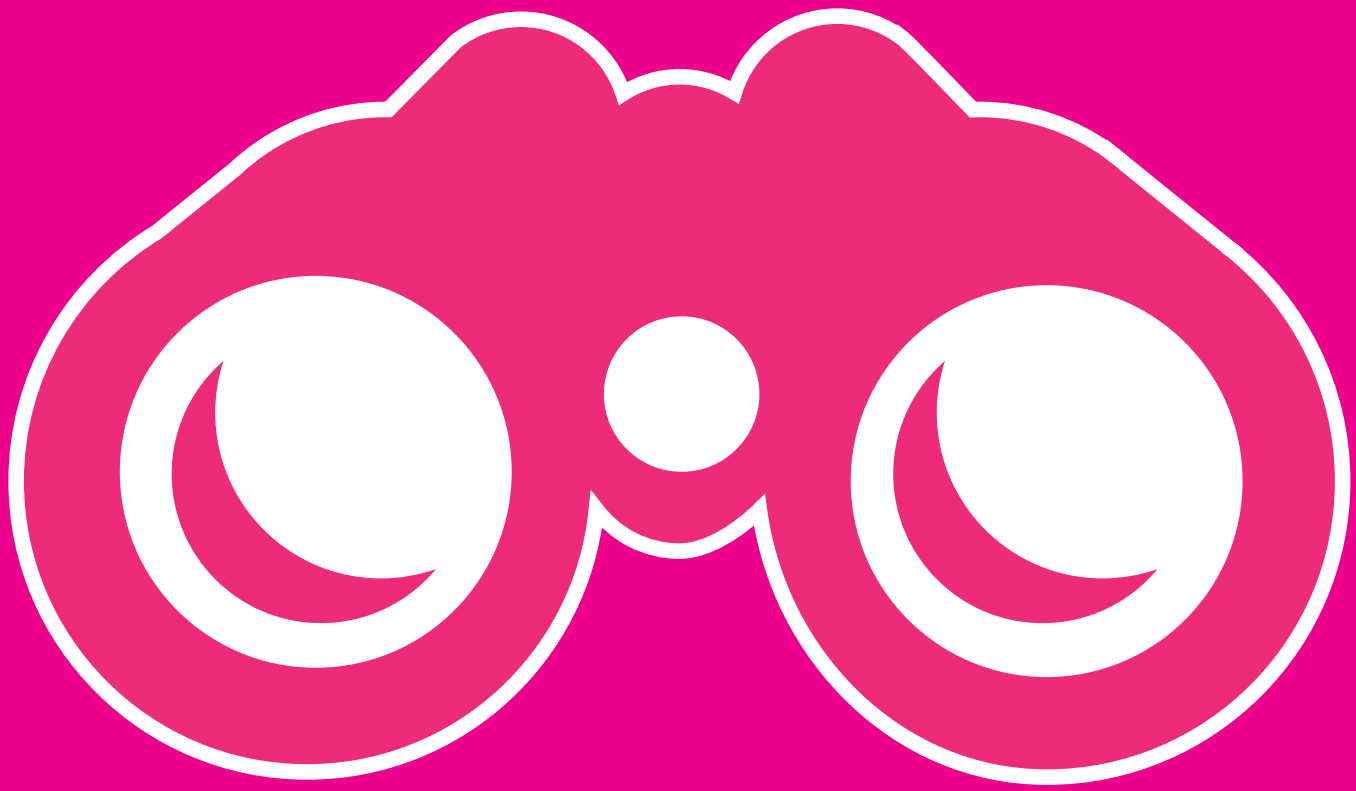
ISO 15189 Quality Management System Implementation: Look Before You Leap



Best Practice Guidance Document

KNCV TUBERCULOSIS FOUNDATION
To eliminate TB

Royal Tropical Institute

ISO 15189 Quality Management System Implementation: Look Before You leap

Best Practice Guidance Document

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TB CARE I

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Executive Summary

This guidance document is primarily designed to provide public tuberculosis (TB) laboratories with best practices when considering embarking on implementing a quality management system (QMS) and seeking ISO 15189 accreditation. The document draws upon lessons learned from QMS implementation at three public National Tuberculosis Reference Laboratories (NTRLs) in Africa—specifically in Botswana, Uganda and Benin — with expert opinion from international consultants in QMS implementation.

The target audience of this guidance document consists of TB laboratory managers, quality officers (QOs), National Tuberculosis Program (NTP) managers, policy makers and other stakeholders involved in TB laboratory strengthening, primarily in low- and middle-income countries (LMIC) in sub-Saharan Africa, but also in LMIC in regions outside the African continent. It is recommended that laboratory professionals who are planning to implement a QMS take note of the advice provided in this document before they initiate the process. This will enable them to determine whether the challenges mentioned in this document are also present in their laboratory and, if so, to start efforts to mitigate those that could become obstacles to the efficient QMS implementation process.

A mixed-method approach was used to evaluate the QMS implementation projects at the aforementioned NTRLs, including a desk review, a literature review, the collection of quantitative data on laboratory performance and the collection of qualitative data to identify factors that either propelled the QMS implementation forward, or alternatively, hindered the process.

Interestingly, all the best practices identified in this evaluation are related to two particular areas: organization (including management) of the laboratory, and the resources of the laboratory (personnel, equipment, purchasing & inventory, facilities & safety). This second key aspect can logically be explained as resources form the basis of the QMS and the primary laboratory process in general. Sub-optimal resources influence the quality of services at all levels. For good quality resources the laboratory is partly dependent on external factors. This requires timely assessment of the quality and availability of resources and identification and anticipation of potential challenges at an early stage. Because the implementation a QMS is a big process of change that affects all laboratory processes, strong management, leadership and organizational skills are needed to facilitate and coordinate this process such that the change is achieved as efficiently as possible.

The findings of this evaluation led to the following best practices for the efficient rollout of a QMS in TB laboratories:

1. Laboratory management should ensure funding for the entire QMS implementation process. The amount needed should be estimated based on identification of the required improvements through a thorough pre-QMS implementation assessment.
2. Laboratory management should try to ensure sustainable funding for QMS maintenance (including equipment maintenance and calibration), e.g. through a dedicated budget line in the Ministry of Health (MoH)/government budget.
3. Laboratory management should initiate and lead the QMS implementation process and show active commitment by spearheading the QMS implementation, providing direction and applying leadership skills from the start to ensure that all staff are engaged in the process.
4. Laboratory management should create efficient and effective internal and external communication channels. Internal communication fosters staff engagement and provides clarity on the quality objectives. External communication allows the laboratory to identify customer requirements and enables the laboratory to inform stakeholders about the needs of the laboratory and what the stakeholders can expect from the laboratory.
5. Laboratory management should appoint a competent, qualified and dedicated QO from the start of the QMS implementation process. The position of QO should be full-time and they should not undertake any other tasks.
6. Laboratory management should create possibilities for physical access to already accredited laboratories at the beginning and during the QMS implementation process, especially for key personnel. This provides them with a tangible example of an accredited laboratory and enables them to have a clearer picture of the desired

end result of QMS implementation.

7. Laboratory management should arrange communication with peers (if possible in-country peers) for the QO to discuss issues related to QMS implementation and to enable setting up bilateral support mechanisms between the laboratories (such as assessment schemes, shared equipment maintenance capacity, bench marking, exchange of equipment as well as parts and supplies).
8. Laboratory management should be competent to using change management principles and apply the proper management and leadership skills to facilitate the process of change created by QMS implementation.
9. Laboratory management should create transparency in the QMS implementation process for all staff and ensure that all staff are involved when a technical expert provides advice. This facilitates staff engagement. Yet, caution must be taken by the technical expert to not demand too much time from the laboratory staff members when advice is not relevant to them. There is no use in providing advice that is for specific positions to all staff members. In this case, a summary of this advice should be provided to all staff members during a debriefing.
10. At the start of the QMS implementation process laboratory management should ensure adequate training for key positions particularly for the laboratory manager, QO, and Biosafety Officer (BSO). This enables them to perform their tasks competently and to be able to effectively engage staff.
11. Laboratory management and, if applicable, external experts, should ensure that all laboratory staff understand their role in the QMS implementation through targeted, relevant continuous internal and external training.
12. Relevant stakeholders (e.g. laboratory representatives, national and international public health organizations) should advocate at the level of national government and education sector to make training on laboratory quality management principles part of the pre-service laboratory training curriculum, to maximize indoctrination on QMS implementation and maintenance on a national scale.
13. Laboratory management should anticipate the initial increased workload when initiating QMS implementation and take appropriate measures. The increase in workload depends on the availability of staff and the amount of work to be done to achieve ISO 15189 compliance. The latter could be estimated by performing a thorough pre-QMS implementation assessment to identify the improvements that need to be made to achieve full ISO 15189 compliance.
14. The laboratory management should continuously monitor workload through regular workload assessments. This enables the laboratory management to adequately react when workload becomes too high and prevent that this hampers QMS implementation and affects routine work.
15. Laboratory management should assess adequate equipment maintenance capacity for all critical laboratory equipment at the start of the QMS implementation process. This activity could be part of a pre-QMS implementation assessment. If in-country equipment maintenance capacity is inadequate, laboratory management must timely plan to compensate for this, as this may cause delays due to the fact that this often lies beyond the control of the laboratory. The appropriateness of the strategies used to compensate inadequate maintenance capacity depend on the local situation. Examples of possible interventions could be:
    a. Training of one or more staff members to perform equipment maintenance themselves.
    b. Outsourcing equipment maintenance to competent companies in-country or otherwise abroad, dependent on in-country capacity (and timely anticipating the extra funds required).
    c. Including a service contract for preventive maintenance as requirement in the tender when purchasing new equipment.
16. If in-country equipment maintenance capacity is inadequate, relevant stakeholders (laboratories/laboratory societies, national and international public health organizations, etc.) should advocate at the level of national government to increase in-country equipment maintenance capacity for the (medical) laboratory sector.
17. Prior to QMS implementation the laboratory management should assess the capacity of procurement and supply chains to provide quality supplies and cope with a potential increase of demand for supplies. This activity should be part of a pre-QMS implementation assessment. If the capacity of the procurement and supply chains is inadequate timely actions should be taken as improvement of this situation can take long due to the fact that this often lies beyond the control of the laboratory. The appropriateness of the strategies used depends on the local situation. If the routine procurement of supplies lies beyond the control of the NTRL, the NTRL management should advocate to the relevant authorities for having its own budget available for procurement of supplies in case of failures in the supply chain and for emergencies that require an extra demand for supplies.

18. If lead times for supply delivery are long due to circumstances that have their root cause within the country, relevant stakeholders (laboratories/laboratory societies, national and international public health organizations, etc.) should advocate to the proper sources to eliminate these causes and improve supply chains.
19. Laboratory management should assess if the facilities comply with the (bio)safety and biosecurity requirements prior to QMS implementation. This could be part of a pre-QMS implementation assessment. If the facilities do not meet the requirements the laboratory management must immediately set the improvement of the facilities in motion as funding limitations and limited in-country availability of contractors competent to renovate or newly construct laboratory facilities can affect QMS implementation.

Applying these best practices, based on empirical data and experiences, enables NTRLs to more efficiently and successfully implement a QMS and achieve ISO 15189 accreditation.

Abbreviations

AFB	Acid-Fast Bacilli
AGHPF	A Global Healthcare Public Foundation
APHL	Association of Public Health Laboratories
ASLM	African Society for Laboratory Medicine
BOBS	Botswana Bureau of Standards
BOTUSA	Botswana-United States of America Partnership
BSL	Biosafety Level
BSO	Biosafety Officer
CDC	US Centers for Disease Control and Prevention
DST	Drug Susceptibility Testing
EQA	External Quality Assessment
FHI	Family Health International/ FHI 360
FM	Fluorescence Microscopy
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GLI Tool	GLI Stepwise Process towards TB Laboratory Accreditation
GLI	Global Laboratory Initiative
KIT	Royal Tropical Institute (The Netherlands)
KNCV	KNCV Tuberculosis Foundation (The Netherlands)
LIMS	Laboratory Information Management System
LMIC	Low- and Middle-Income Countries
LPA	Line-Probe Assay
MGIT	Mycobacteria Growth Indicator Tube
MoH	Ministry of Health
MTB	Mycobacterium tuberculosis
NTP	National Tuberculosis Program
NTRL	National Tuberculosis Reference Laboratory
PCR	Polymerase Chain Reaction
QMS	Quality Management System
QO	Quality Officer
RIF	Rifampicin
SADC	Southern African Development Community
SANAS	South African National Accreditation System
SCMS	The Partnership for Supply Chain Management Systems
SLIPTA	Stepwise Laboratory Improvement Process Towards Accreditation
SLMTA	Strengthening Laboratory Management Towards Accreditation
SOP	Standard Operating Procedure
TAT	Turnaround Time
TB	Tuberculosis
UPS	Uninterrupted Power Supply
WHO	World Health Organization

1. Introduction

This guidance document is primarily designed to provide public TB laboratories with best practices when considering embarking on the implementation of a QMS as well as seeking ISO 15189 accreditation. This guidance document draws upon lessons learned from three public NTRLs in Africa — specifically in Botswana, Uganda and Benin — with the expert opinion from international consultants in QMS implementation.

What is this document about?

Due to increasing recognition of the importance of QMS implementation in medical and public health laboratories, many TB laboratories in high burden TB countries are considering moving towards QMS implementation and accreditation. Few have achieved this, particularly in the public sector, and many have limited knowledge of what to anticipate and the preparations needed to implement a QMS and achieve accreditation. In 2008, the Maputo declaration was developed which could be seen as the first indication of increased recognition of the need for laboratory strengthening (1). In 2010, sub-Saharan Africa counted 340 accredited laboratories, the majority of which were located in South Africa. Only 28 were located in other sub-Saharan African countries and were almost exclusively private, parastatal or donor-supported research facilities (2). Since the Maputo declaration, many guidance materials have been developed such as the Global Laboratory Initiative (GLI) Stepwise Process towards TB Laboratory Accreditation (GLI tool: www.GLIquality.org (3)), the Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) checklist (2) and Strengthening Laboratory Management Towards Accreditation (SLMTA) training and mentoring program (4). These tools and programs assist laboratories in translating the ISO 15189 requirements into practice, i.e. they assist with the implementation of a QMS. However, laboratories in LMIC embarking on laboratory strengthening projects are frequently confronted with unexpected challenge, many of which are similar for a majority of the laboratories. This can also be concluded when comparing literature on the topic. This situation leads to unnecessary waste of limited resources (human and otherwise) that could have been avoided if laboratories were aware of, and could anticipate the critical factors that affect QMS implementation before they embarked on this process. However, the identification of the most common challenges and their root-causes has never been systematically and empirically documented.

Over the past eight years, public NTRLs in Botswana, Uganda and Benin were assisted through the USAID funded TB CAP/TB CARE I projects with the implementation of a QMS and in achieving ISO 15189 accreditation. In all projects the laboratories received technical assistance from external experts. Evaluation of the QMS implementation process at these three NTRLs forms an excellent opportunity to draw lessons learned. The purpose of this evaluation project was, therefore, to analyze the progress of implementation of a QMS at the aforementioned NTRLs through a mixed-methods approach and identify common factors that facilitated QMS implementation and challenges that blocked efficient QMS implementation, and to subsequently transform these into recommendations for best practices for efficient QMS implementation. It is envisaged that these best practices can help other laboratories become aware of factors that may affect their QMS implementation efforts and therefore anticipate and mitigate them as much as possible. The question that was central in this evaluation project was:

What are the best practices to facilitate the efficient implementation of a QMS based on ISO 15189?

This guidance document presents the results of this evaluation project and the recommendations for best practices for implementing a QMS based on ISO 15189.

Structure of this document

This document starts by reviewing the experiences of QMS implementation in medical laboratories as published in literature, providing a context to which the findings of this evaluation and resulting best practices can be compared. Chapter 3 describes the methodology used for this evaluation and Chapter 4 describes the progress of implementation of the QMS at each NTRL within this evaluation project and the service characteristics of the NTRLs before/after accreditation. This is the result of an extensive desk review of all reports and other documents produced during QMS implementation at the three NTRLs. Chapter 5 presents the best practices, including the

results of the on site qualitative evaluation and the argumentation of how these results, in combination with the desk review data, led to formulation of each best practice. Chapter 6 discusses the results and best practices and compares these with the literature review findings of Chapter 2. A final overview of the best practices is given in Chapter 7.

Who can use this document and how should this document be used?

The insights presented in this document are likely applicable to other laboratories pursuing QMS implementation. Taking note of the findings and recommendations in this report should therefore be considered key for TB laboratory managers and QOs prior to embarking on the QMS implementation process. Public TB laboratories are dependent on external bodies for many aspects of their functioning. When the decision to initiate QMS implementation at a TB laboratory is made by a higher authority it is essential that this authority has taken note of the best practices for QMS implementation to have the proper insights in the consequences of this decision and to anticipate these. Therefore, this document should also be read by NTP managers, policy makers and other stakeholders involved in TB laboratory strengthening, primarily in sub-Saharan Africa, but also in LMICs outside the African continent.

How does this document fit with the GLI Tool?

The GLI tool translates each individual ISO 15189 requirement into simple practical steps on how to establish a QMS and can be used by TB laboratories worldwide in high-, low- and middle-income countries. The tool does not provide specific instructions on how to overcome common challenges faced by laboratories in LMIC, meaning this best practices guidance document forms a supplement to the GLI tool. The best practices document should be a fixed part in the roll-out of the GLI tool as it makes the laboratories aware of the common challenges and preconditions to QMS implementation (i.e. to implementing the GLI tool), enabling them to anticipate problems at an early stage and prevent interruptions in the process later-on.

2. Review of Literature and Context of this Project

A literature review was carried out to investigate the efforts and experiences of other laboratories worldwide with the implementation of a QMS and accreditation. This enables our findings to be compared with and discussed in the global context.

A tool to guide the process of QMS implementation in TB laboratories is the GLI tool (www.GLIquality.org). The authors used this as a backdrop for the country assessments and analysis. The authors recommend using this tool to guide this process in TB laboratories. Information on the structure and use of this tool is included in this chapter.

Review of Literature on QMS Implementation and Accreditation Experiences

A search of scientific literature engines including MEDLINE and Web of Science (search terms: medical laboratory AND quality management AND ISO 15189 AND accreditation, language filter: English, publication date: 2003-2014) and the (publicly available) KIT Information Portal on Laboratory Quality Strengthening (search term: experience, language filter: English), led to the selection of 13 publications about experiences with the implementation of QMSs in medical laboratories. The rationale for excluding publications before 2003 is the fact that the first edition of the ISO 15189 standard was published in 2003. Since we are only interested in experiences with implementation of this standard, there is no point in searching for QMS implementation experiences prior to 2003.

Many authors state that QMS implementation improves the performance of the laboratory (5-9) and is beneficial to both laboratory customers and laboratory personnel (10). This is based on their own experience, customer feedback and the use of indicators to monitor performance improvement over the course of QMS implementation. The QMS improves reliability, reproducibility, traceability, transparency, uniformity, work satisfaction and focus on critical points (5;6). However, many also indicate that QMS implementation is a time consuming process (6;8;11) which leads to a higher workload (6;11). Despite this, staff prefer to work in an accredited laboratory due to the common idea that staff become more specialized and experienced by working in an accredited laboratory (11). Berwouts *et al*. indicate that the QMS brings with it a danger of losing a critical perspective on laboratory performance and can curb innovations, which emphasizes the importance of creating a culture of continuous quality improvement (6).

The most frequently mentioned requirement for successful QMS implementation is the engagement of staff with the process (5;6;8;10;12), but this was also mentioned as one of the most difficult factors (5;9).

Berwouts *et al*. elaborate on the issue of staff engagement in their article on the accreditation of genetic testing laboratories. They indicate that staff have a natural reluctance to change and that convincing them of the value of a QMS is pivotal to success. The implementation of the QMS is a linear process that can be planned chronologically, but change is a process in which staff members go through different stages of resistance and acceptance at different speeds (Figure 1) which can not usually be planned. This combination of processes can cause tensions that form challenges to QMS implementation. The authors mention several strategies to facilitate the process of change and diminish tensions as much as possible, which include force-field analysis (a group discussion tool to identify enabling and disabling factors towards reaching an objective and discuss solutions to minimize the disabling factors and maximize the enabling factors) and the stakeholder approach (management identifies stakeholders that have varying degrees of influence on realizing objectives and designs strategies to involve, inform or mobilize those stakeholders according to their degree of influence). In addition, Berwouts *et al*. indicate that international workshops on quality management positively influence QMS implementation because they form a platform where ideas can be shared and facilitate discussions with and learning from peers (6). Other authors mention that recognizing staff for excellent performance (5;10) and the organization of regular meetings to create awareness on QMS principles, also contribute to creating staff buy-in (5;11).

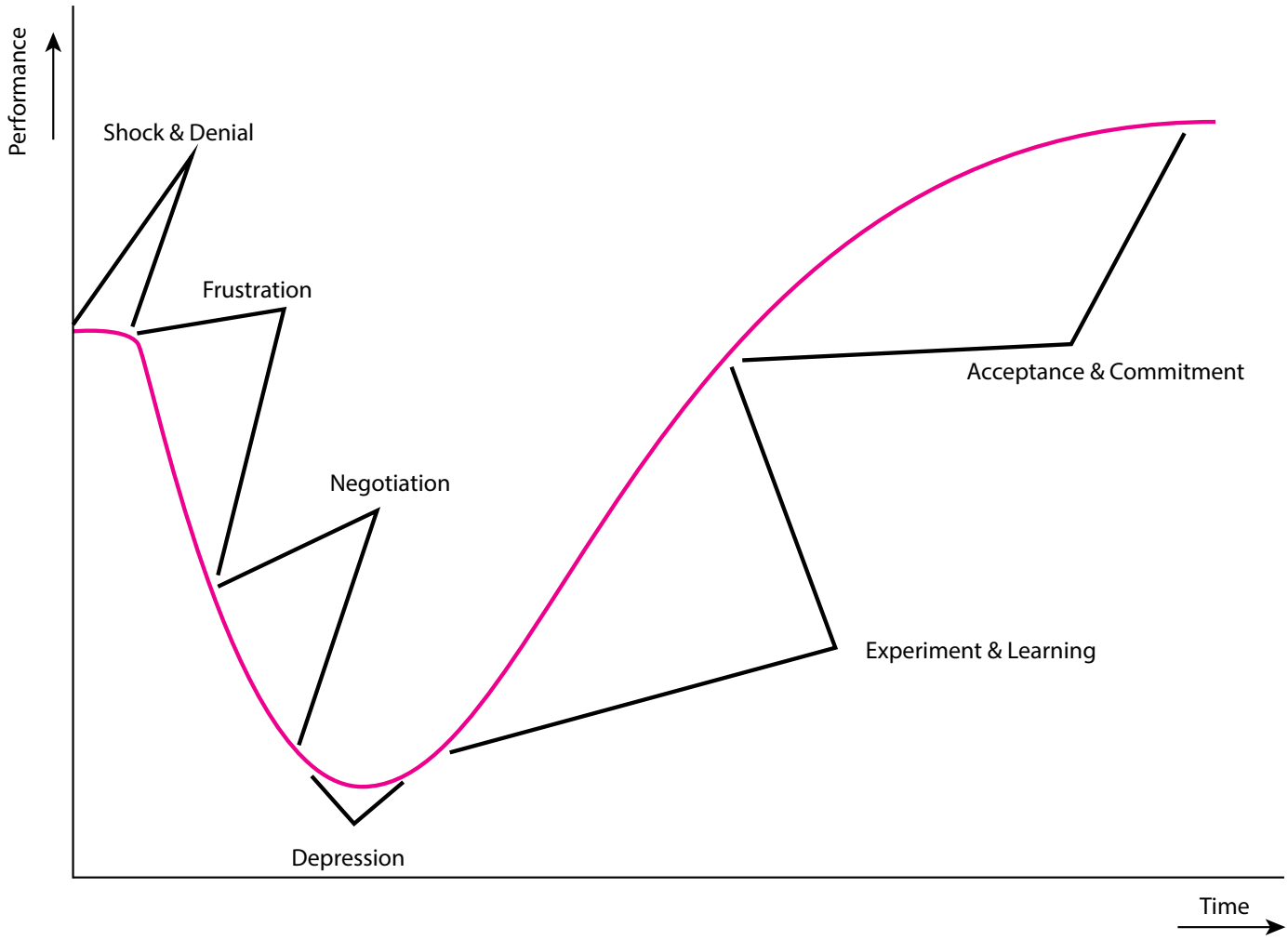

Figure 1: Stages which people go through in times of change and the influence on performance over time. Based on the Kübler-Ross model as presented by Berwouts *et al.* (6)

Many authors indicate factors that are especially important in QMS implementation or provide preconditions to the success of this process, including the following:

- QMS implementation requires strong commitment from management and laboratory staff.
  Commitment is required from the top management to the most junior positions (8;10). Management at all levels should propagate QMS implementation. The decision to initiate the accreditation process should be made by top management (7) and top management should fully support the laboratory team in every aspect (8;10;11). The management has to define responsibilities and authorizations (7) and advocate the laboratory's needs (5). In addition, QMS implementation is a team approach and requires motivation of all personnel (8;10).
- QMS requires considerable and continuous training.
  Continuous training of staff is needed to decrease errors (7) and to get staff to engage in the QMS implementation process (5;8;12).
- Fostering a culture of continuous improvement.
  Communication is pivotal in creating a culture of continuous improvement. Frequent and regular meetings create staff buy-in and serve to address issues in the accreditation process (5;13). Kibet et al. also mention that intentional and sustained interaction with clinical staff contributed to QMS implementation (13). It was indicated by several authors that performing internal audits, recording non-conformities and complaints, and monitoring quality indicators was important to foster communication and create a culture of continuous improvement. It helped to identify many errors which sped-up the implementation of the QMS and made the QMS more alive (7;9-11). It is important to prevent a blame culture: people should be encouraged to identify and react to non-conformities but discouraged from denouncing individuals because this discourages reactions to problems and severely impairs the possibility of quality improvement (8).

- Creating better job security, career attractiveness and remuneration conditions.
  Some countries deal with high staff turnover and brain drain (or "brain circulation"), this affects the efficient implementation of a QMS. Measures such as creating better job security, career attractiveness and remuneration conditions were mentioned as being pivotal to laboratory quality improvement and retaining and recruiting personnel (5;14;15).
- Good cooperation is needed with laboratory suppliers and service engineers.
  A QMS has high demands with regards to supplies and equipment. Discussion between laboratory management and the suppliers/vendors is needed to provide clarity about these requirements and demands and resolve issues with supply delivery (5) and equipment maintenance (7).
- Hiring an external consultant is advised for QMS implementation.
  Both Guzel et al. and Wadhwa et al. advise to hiring a consultant to guide QMS implementation. This helps save time and effort (11;16).
- Establishment of a quality team.
  A quality team or unit facilitates QMS implementation by coordinating the implementation process and nurturing of a quality culture (9;11).
- Designating responsible persons for each item of equipment.
  This helps the management to oversee equipment and provides clarity on who to contact in case of malfunctioning or other equipment-related issues (8).

Several articles reported about QMS implementation and laboratory strengthening specifically in LMIC. Specific challenges related to this environment were mentioned to be:

- Supply availability and quality (5;9;17).
  Adequate availability of supplies is reported by many to be problematic in LMIC and the root of the problem is often beyond the control of the laboratory (5). Stringent government procurement laws and the fact that supplies often have to come from abroad are reported as factors that lead to long lead times (9).
- Equipment maintenance (9).
  Availability of specialized service engineers for equipment maintenance is reported to be problematic in LMIC. These services often have to be hired from abroad which increases costs (9;14) Kibet et al. partly solved this issue by making maintenance part of the placement contract when purchasing equipment (13).
- Human resource availability, turnover and training (5;9).
  High staff turnover rates were mentioned as a factor causing problems with retaining skills and competence. Audu et al. mention the brain circulation syndrome: staff frequently move to another job in search of better wages and conditions (5). Severe lack of health workers due to inadequate training capacity, brain-drain and low career attractiveness also affect laboratory strengthening on national scale (14;15). Insufficient in country availability of training capacity, especially on QM, increases the cost of accreditation (9).
- The majority of laboratories in LMIC lack adequate physical and man power infrastructure to implement international quality standards (14;15).
  Ahmad et al. reported that nearly 90% of the laboratories in one country studied fell into this category. To make laboratory quality improvement also accessible to these laboratories the ISO 15189 standard was simplified into a national standard (14). Alemnji et al. indicate that the development of a checklist and training program for step-wise laboratory improvement (called SLIPTA and SLMTA respectively) contribute to resolving this problem (15).

Many problems specific to LMICs require action from authorities (e.g. national governments and international agencies) and are beyond the direct control of the individual laboratories (14;15). The resolution of these types of problems often ask for action (in the form of dialogue and advocacy) from management. Examples are procurement, supply and maintenance of equipment, and also the education of the personnel. Audu *et al.* indicate that problems with supply/delivery at the Human Virology Laboratory in Nigeria were resolved when the management of the laboratory discussed the issue with supporting partners (5). Dahim *et al.* describe the attempt to resolve the problem related to availability and quality of equipment and supplies in Iran by creating a national directory of reliable providers and manufacturers of supplies and equipment (17).

National governments play an important role by creating national laboratory policy and strategic plans (14;15). Alemnji *et al.* indicate that the creation of an international coordination and support society in sub-Saharan Africa

(called the African Society for Laboratory Medicine, ASLM) is key in increasing awareness and advocacy for laboratory strengthening (15). They further indicate that countries should also take greater responsibility for public health laboratory challenges and rely less on the global community to increase the sustainability of laboratory strengthening, given the global economic recession which threatens donor funding (which many laboratories in LMIC still heavily rely on). The establishment of public-private partnerships is also important in this context. Alemnji *et al*. further indicate that the establishment of national laboratory networks should be encouraged to ensure better coordination and effective utilization of available resources (15).

About the GLI Tool

The GLI tool was developed with the purpose of assisting national TB laboratories with implementing a QMS and complying with ISO 15189. It is constructed in such a way that laboratory quality improvement is already gained from step one of the process.

The GLI tool is a digital guidance tool in the form of a website that provides a stepwise plan for implementing a QMS in compliance with ISO 15189:2012. The tool divides the QMS implementation process into four phases with each phase having a specific focus and the next phase building logically on the activities of the previous one. However, is also constructed in such a way that if laboratories are stuck with implementation of certain activities of the previous phase, they can still proceed with other activities in the next phase, i.e. the plan is not rigid and allows for significant adaptation to the laboratory's specific situation. The individual steps explain the activity that should be done in a standardized format, explaining why the activity should be done, what should be done, how it should be done and by whom (the most appropriate laboratory position for implementing the activity). Where appropriate, background reading, document templates and other tools are provided.

The first phase of the GLI tool focuses on implementing the absolute basic elements that all laboratories should have in place regardless of size or location. Without these elements it is impossible to guarantee adequate and safe services. Phase 2 focuses on the fundamentals of the QMS: quality control and quality assurance. Quality control mechanisms are implemented in the complete primary process of the laboratory (3;18). Quality assurance is further improved with establishment of a standardized stock and ordering system, equipment management system, document control and information management system and the development of SOPs for all procedures performed in the laboratory.

Implementing a QMS is a systems approach, meaning it is not limited to merely implementing controls, procedures and forms, but it also affects the management and structure of the organization. Proper organization, management and leadership are needed to coordinate the quality management activities, which Phase 3 will focus on (3;18).

A QMS according to ISO 15189 is based on the Plan-Do-Check-Act cycle developed by Edward Deming (Figure 2). Not only mechanisms are implemented to assure quality, but the organization must also learn from mistakes and use these to continually improve the work. In Phase 4 systems are implemented that enable passive and active identification of points for improvement and use these to optimize quality services. This phase ends with the finalization and optimization of all quality system elements so that the laboratory is ready to apply for accreditation (3;18).

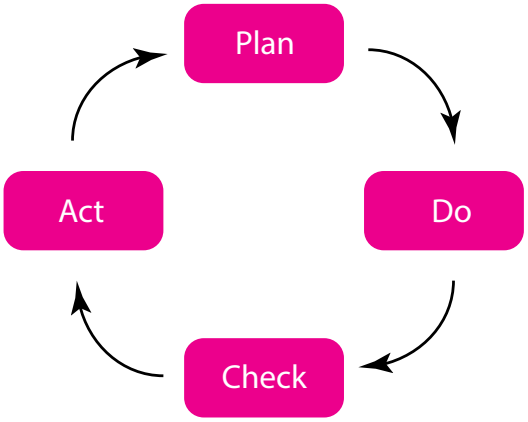

Figure 2: Plan-Do-Check-Act cycle for continuous improvement

Each phase provides a roadmap that presents the activities in an order ideal for day to day implementation (Figure 3).

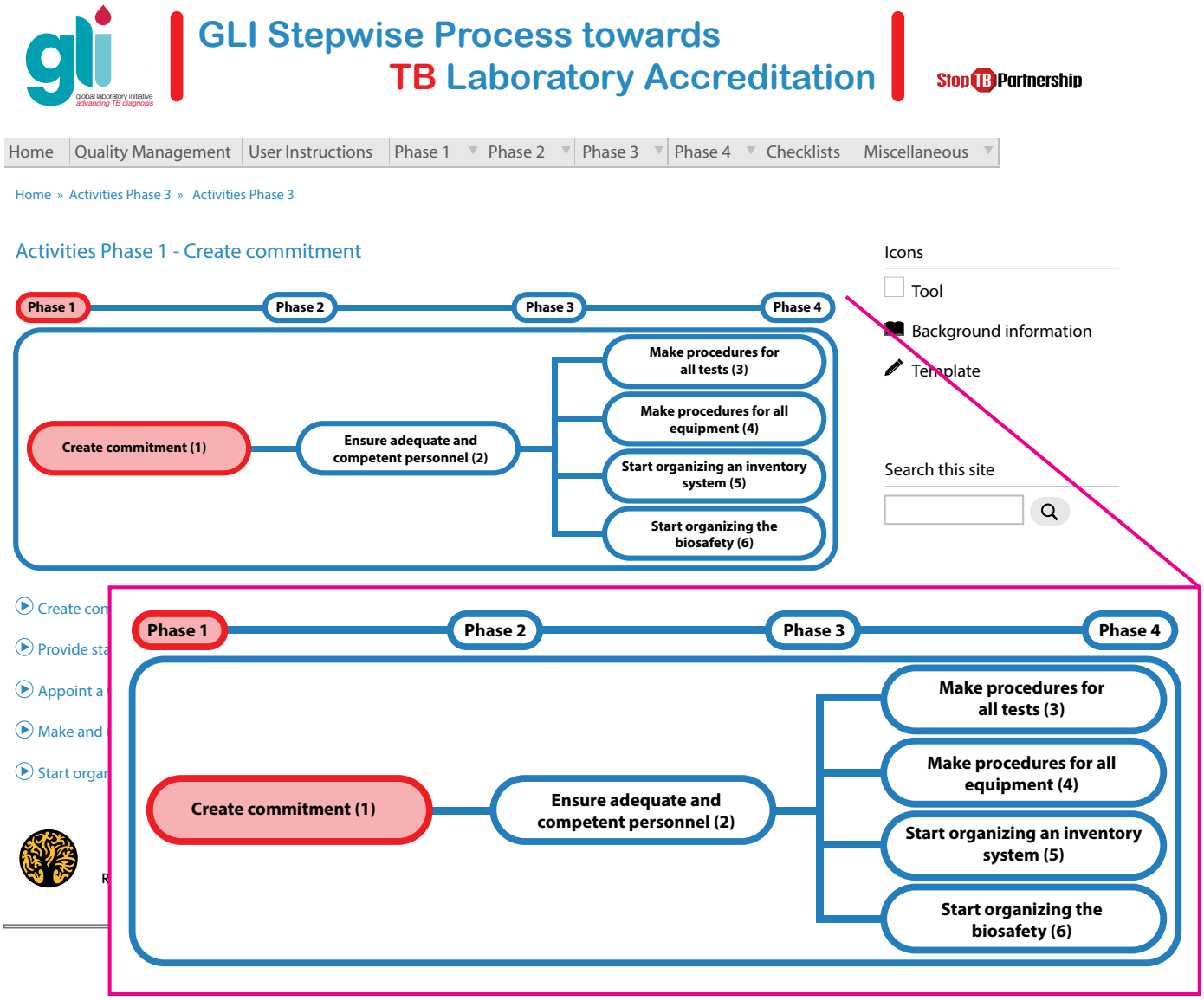

Figure 3: Activities presented in ideal order for day-to-day implementation using the roadmaps

In addition, the activities can also be structured according to the 12 Quality System Essentials to gain insight into what needs to be done for specific parts of the QMS, such as equipment management, facilities and safety, or process management (Figure 4).

Figure 4: Activities structured according to the 12 Quality System Essentials

Besides providing guidance on the implementation of the QMS, the GLI tool also provides the means to assess the implementation process through an option that allows the user of the tool to develop tailor-made checklists based on the desired focus of the assessment. These checklists can be used as support during internal audits, to map progress or to verify correct implementation of the QMS.

The GLI tool is an online tool for which users need to have access to a reliable internet connection. It is possible to request a copy of the tool for offline use for those users that do not have access to a reliable internet connection. This allows the users to download the entire tool once, after which it can be used without an internet connection.

3. Methodology

Study Sites

Three NTRLs in Africa were supported with the implementation of an ISO 15189 QMS under the TB CAP and TB CARE I projects between 2009 and 2014. The NTRL of Botswana was supported by KNCV Tuberculosis Foundation which provided an embedded expert for technical support and hired a QO for QMS implementation. The NTRLs of Uganda and Benin were assisted by KIT which provided three to four one-week mentoring visits per year to guide the QMS implementation process. The NTRL of Botswana (enrolled in 2007) received ISO 15189 accreditation from the South African National Accreditation System (SANAS) in 2012. The NTRL of Uganda (enrolled in 2008) was accredited by SANAS in 2013. The NTRL of Benin (enrolled in 2011) plans to apply for accreditation in 2015. These NTRLs were selected as study-sites for this evaluation project.

Conceptual Framework and Evaluation Questions

The formulation of the evaluation questions and the development of the evaluation materials was guided by the conceptual framework which includes the quality system essentials as used in the GLI tool (3;18).

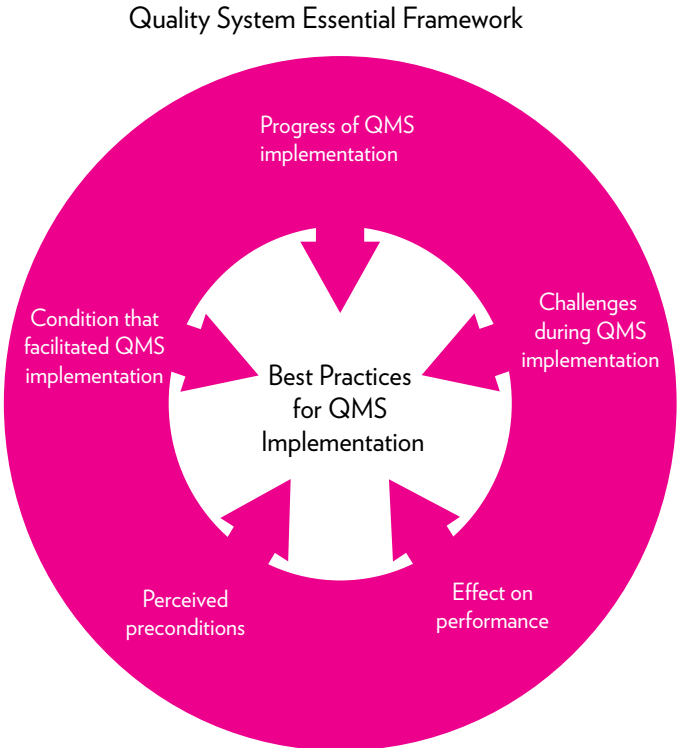

Figure 5: Conceptual framework

A mixed-method approach was used to evaluate the accreditation projects at the above-mentioned NTRLs. The evaluation was guided by the following question:

What are the best practices to facilitate the efficient implementation of a QMS?

This evaluation question was defined by the following sub questions:

A. What were the consequences of receiving ISO 15189 accreditation for the laboratory services?
B. Which internal and external conditions of the laboratory formed challenges to the implementation of the QMS?
C. Which internal and external conditions of the laboratory facilitated the efficient implementation of the QMS?
D. What are the preconditions for efficient implementation of the QMS?

Evaluation Procedure

Data to answer the evaluation questions were collected both quantitatively and qualitatively. Quantitative data informed primarily sub question A. Qualitative data informed primarily sub questions B, C, D and to a lesser extent sub question A.

Quantitative Data Collection

To obtain insight into the consequences of receiving ISO 15189 accreditation for the laboratory, the effect of implementation of the QMS on laboratory services was measured. The following indicators were collected:

1. Analytical methods offered at the NTRL (including the names of these methods), in the year before initiation of the accreditation project and the year after receiving accreditation.
2. Number of tests performed in the year before initiation of the accreditation project and the year after receiving accreditation.
3. Average percentage of incorrect results in proficiency testing for AFB microscopy and culture/DST in the year before initiation of the accreditation project and the year after receiving accreditation.
4. Number of staff members working at the laboratory in the year before initiation of the accreditation project and the year after receiving accreditation.
5. Average number of staff members that left and the number of staff members recruited each year during the accreditation process.

This data was collected during on-site visits to each laboratory. Laboratory registers were used for indicators 2 and 3, and laboratory management/quality officers were asked to provide data for indicators 1, 4 and 5. Data was only collected if records could be provided.

To ensure proper data collection, a standardized form was used to collect the quantitative data.

The quantitative data was not sufficient for extensive statistical analysis, it was used as descriptive information to support findings from qualitative data collection and to inform the qualitative data collection process during the on-site visits.

Qualitative Data Collection

To be able to evaluate the accreditation projects at the three study sites it was necessary to get a deeper insight into the progress of the accreditation project per NTRL. This provided the context against which the challenges and conditions that facilitated efficient QMS implementation could be viewed. Desk review was the preferred method for this part of the evaluation.

The TB CAP and TB CARE I mission reports/progress reports formed the backbone of the desk review. In addition, audit/assessment reports, minutes, and action plans collected during the QMS implementation projects were scrutinized. A standardized form was used to list the main findings from each document. This form included the following parameters:

- Description of major activities carried out to implement the QMS.
- Date/period over which these activities were carried out.
- Names of person(s)/organization(s) that carried-out the activities.
- The deliverables, findings and challenges encountered.
- Reference for the document from which the information was extracted.

The interviewing of laboratory employees was the preferred evaluation method for the identification of the conditions that facilitated efficient QMS implementation and the challenges encountered during the accreditation projects. These persons were the ones actively engaged in QMS implementation and therefore were directly confronted with the challenges and conditions that facilitated QMS implementation. Both semi-structured interviewing and focus group discussion methods were utilized. Semi-structured interviews were held with individuals from all layers of the organization. Focus group discussions were held with all employees of the NTRL except for the management. The argumentation was that semi-structured interviewing provides better insight in personal experiences and allows for comparison of these experiences in relation to the hierarchical positions.

Focus group discussion provides the possibility to obtain an indication of the severity/significance of the different challenges encountered and could also reveal challenges or conditions that facilitated QMS implementation that were not brought up during semi-structured interviews. The semi-structured interviews may reveal experiences which individuals might be reserved from sharing during the focus group discussion. The focus group discussions were held after the semi-structured interviews to allow the findings of the latter to inform the former. Management was excluded from participation in the focus group discussions to maintain objectivity in the answers of laboratory employees (e.g. with management present the employees might not be comfortable sharing specific experiences about the process of implementing the QMS out of fear of repercussions). The interviews were conducted in the national languages, which meant that an interpreter was hired in Benin.

Semi-Structured Interviews

The development of the interview guides was directed by the conceptual framework which included the evaluation questions and the quality system essential framework as used in the GLI tool (Figure 5). A general guide was made that was tailored to the different positions of the laboratory. Interviews began with the consent procedure (see below) and lasted between 45 and 90 minutes (partly depending on the positions of the interviewees). After the interviewee had consented to participate, the interview continued with several closed questions to record personal details (nationality, education, year interviewee started working at the NTRL, current position and year interviewee started working in his/her current position). The interview continued with open questions to gain insight in the interviewee's daily work, the workload and the fringe benefits, both in the present time and during the implementation of the QMS. Next, questions were asked to gain insight in the work atmosphere and environment, The interview subsequently proceeded with in-depth questions regarding the process of implementing the QMS. This part focused both on the process itself, the challenges, the conditions that facilitated the process, and the method of external assistance that was provided.

Focus Group Discussions

The focus group discussion guide were also constructed based on the conceptual framework presented above (Figure 5). The duration of the focus groups discussion was 1.5 to 2 hours and began with a presentation of the purpose/aim of the evaluation project and an introduction of the facilitators. The facilitation team consisted of one discussion leader and one person making notes. A PowerPoint presentation was used to guide the focus group discussion. After introduction of the facilitators the consent procedure was performed (see below). Subsequently, the method of the focus group discussion was explained to the participants: they were shown a statement that was meant to provoke discussion. The discussion leader probed when necessary and fueled the discussion with questions which provoked further discussion and exploration of interesting areas. The following statements were shown (in chronological order):

1. The implementation of the QMS was difficult.
2. The quality of the facilities has changed over the past few years.
3. The quality of equipment has deteriorated over the past few years.
4. The quality and availability of supplies has improved over the past few years.
5. The safety in the laboratory has not improved over the past few years.
6. The workload over the past few years has not changed.
7. I have plenty of opportunities to participate in trainings/courses.
8. The work atmosphere at the laboratory could be better.
9. Without the QMS the laboratory performance would be the same.

Consent Procedure

A two-person team, consisting of a lead interviewer who asked the questions and a second person making notes, conducted both the semi-structured interviews and focus group discussions. The interviews were conducted with permission from the management of the NTRLs and during the interviewees' working hours and were recorded with the interviewee's permission. Participation was voluntary and they were conducted in a private office without any other persons present. At the start of the interview the persons present were introduced by the lead interviewer, the interview procedure was explained and the consent letter was read to the interviewee.

The following explanations were given to the interviewees:

- This interview is part of an international research project within the USAID TB CARE I project.
- The information gained will be used to optimize the GLI tool and be reported in a document called a "Best Practices Document" that will be submitted to TB CARE I.
- The interview will be conducted to learn more about the interviewee's experiences and perspectives on the process of implementing the QMS.
- The interview will have a duration of a maximum 1.5 hours (for the focus group discussion a maximum of 2 hours).
- The interviewer will ask for permission to record the interview.
- The interview is not a test.
- The information provided by the interviewee will solely be used to gain knowledge on QMS implementation, which will be used to help other laboratories in LMIC by learning from the interviewee's experiences.
- The interviewee will remain anonymous.
- Participation in the interview is voluntary and the interviewee can stop participation at any time.

The interviewee was given the consent letter (in their national language) and allowed to read it before providing their consent by signing the form. Interviews followed the flow of discussion while making sure all topics were covered. Probing questions were asked to gain more clarity on certain points. At the end of the interview the interviewee was thanked for their participation and again allowed to ask any questions or discuss any issues. The interviewees were provided with the contact details of the principle evaluator to allow them to ask questions at a later stage.

To ensure confidentiality and anonymity the interview reports were coded and all the personal identifiers were removed. Only the principal evaluator had access to the coding sheet enabling the direct connection of interview reports to specific persons.

Data Processing and Analysis

Directly after the interviews were conducted interview reports were made using the notes made during the interview and the sound recording of the interview. Validation of the interview processing method was done by having both members of the interview team process a subset of interviews separately after which they compared and merged their interview reports. There were no significant differences between the interview reports of both team members, indicating that the method of processing interviews was reliable.

After conducting all the interviews during the on site visits, the interview reports were scrutinized and relevant statements in each interview report were categorized according to the four sub evaluation questions. One compilation sheet per evaluation question was made with statements from interviews from all three countries which facilitated comparison of statements. A list of observations was made per research question, per country, by accumulating and grouping similar statements that all pointed to the same observation.

Data was further analyzed during a final workshop where the evaluation team reviewed the findings of the desk review, the quantitative data and the observations from the qualitative evaluation activities. They proceeded by listing all their observations per country, categorized according to the quality system essential framework. The team subsequently continued with addressing their observations per quality system essential and formulating best practices through a discussion and consensus approach. The team formulated their general findings per best practice and recorded their argumentation on how the findings resulted in the formulation of the best practice. The final list of best practices and the underlying findings and argumentations were transformed into this best practices document.

4. Implementation of a QMS at the NTRLs

The data in this chapter are the result of the desk review of each accreditation project. General characteristics of the NTRLs are provided and a chronological description of the progress of the implementation of the QMS at each laboratory is provided.

Table 1: General characteristics of the NTRLs within this study

	NTRL Botswana	NTRL Uganda	NTRL Benin
Human Resources	23	29	21
Governance	MoH > Dept. of Clinical Services > National Health Laboratory > NTRL	MoH > National Tuberculosis and Leprosy Program > NTRL	MoH > NTP > NTRL
Priority Functions	• Supporting routine TB testing incl. culture, DST, identification (excl. routine microscopy) • Conducting operational research • Organizing EQA for the national TB laboratory network	• Supporting routine TB testing • Conducting operational research • Organizing EQA for the national TB laboratory network	• Testing for diagnosis of TB and Buruli ulcer • Conducting operational research • Organizing EQA for the national TB laboratory network
Disease Program	NTP	National Tuberculosis and Leprosy Program	NTP
Level of Functioning	National reference laboratory and supranational reference laboratory for the SADC[1]	National and supranational reference laboratory in the SRL network[2]	National reference laboratory and candidate supranational reference laboratory for the SRL network

1. SADC: Southern African Development Community.
2. This is the worldwide supranational reference laboratory network coordinated by the World Health Organization (WHO).

NTRL of Botswana

Pre-QMS Implementation

The Botswana NTRL was established in 1999 through the assistance of the U.S. Centers for Disease Control and Prevention (CDC) Botswana (formerly Botswana-United States of America partnership (BOTUSA)).

The NTRL exists to provide quality TB culture and DST with regard to diagnostic services. It also has a role as the overseer of all the laboratories in Botswana performing Acid Fast Bacilli (AFB) microscopy through its coordination of the four pronged external quality assurance program which involves on site supervisory visits, proficiency testing, blinded rechecking and training. As the reference laboratory, the NTRL also provides TB research support to the health system in Botswana.

First Year

The implementation of the QMS at the NTRL of Botswana was started in 2007 after a gap analysis revealed that the NTRL was ready for this process (19). There was no progress on QMS implementation in the first months of the QMS implementation project due to staff shortages (20), so a QO was appointed in March 2007. With the help of external consultants the documentation of the NTRL was developed using a documentation development plan drafted in April 2007 (21). In August 2007 an audit showed that the required documentation was in place, but that the QMS was still in its infancy. The major non-conformities indicated that it was imperative that more

training as well as full control had to be given to the technical management team to facilitate the effective implementation of the QMS. With training the NTRL attempted to increase the ownership of the staff over the QMS implementation process (22). A corrective action plan was developed and implemented to address gaps raised during this audit (personal communication O. Kachuwaire, November 2014). In addition, from 2007 onwards the NTRL received support from the Association of Public Health Laboratories (APHL) by appointment of an embedded mentor for technical support. This mentor continued from 2008 under TB CAP and under the guidance of the mentor the liquid media system was validated in August of 2008 (personal notes O. Kachuwaire, (23)).

Second Year

In the second year of the project, six new members of staff were hired to cover the increase in workload caused by an increase in routine testing and a drug resistance surveillance study being performed by the NTRL (personal notes O. Kachuwaire). The implementation of the QMS continued with a gap analysis, revealing six major and five minor non-conformities related to quality assurance and three major and 21 minor non-conformities related to safety (24). In August of 2008 the first management review was organized by the QO revealing that some progress was made by the laboratory in terms of reducing the non-conformities noted, but there were problems with calibration, maintenance and infrastructure. The BSL-3 laboratory facility was not able to maintain negative pressure, there were challenges with the laboratory infrastructure characterized by aging of facilities and equipment (25)and no funds were allocated to address these challenges (personal communication O. Kachuwaire, November 2014).

Third Year

In 2009, the third project year, the NTRL received support from many different sources: A Global Healthcare Public Foundation (AGHPF) started to provide backstopping support to QMS implementation, The Partnership for Supply Chain Management Systems (SCMS) procured new equipment and the QO was trained in ISO 15189 by the Botswana Bureau of Standards (BOBS). Subsequently, the QO trained laboratory staff on ISO awareness (personal notes O. Kachuwaire).

AGHPF performed an audit using the SLIPTA checklist and reported that the laboratory scored 46 out of 100 points (26). A later progress report revealed that the NTRL still had work to do on all areas of the QMS, it had made the most effort on documents and records and the least on occurrence management, process improvement and customer service (27).

In November 2009 a laboratory information system was installed by CDC/APHL as a country pilot site (personal notes O. Kachuwaire).

Fourth Year

In February 2010, the start of the fourth project year, an assessment was done by Family Health International (FHI)/AGHPF to assess readiness for accreditation. This assessment revealed that the laboratory had adequately posted safety signs and controlled access, and sufficient eye wash and safety shower stations were also present. The laboratory had appointed a safety officer and a deputy safety officer. Although the terms of reference of the safety committee of the NTRL state that safety committee meetings should be held every fortnight, the safety committee meetings had not been held for two years. The assessment revealed that the laboratory was in possession of a validated Laboratory Information Management System (LIMS) and information was backed up automatically and the reports were stored in a central location on a separate server. With regard to documentation the assessment showed that the NTRL had a quality manual and Standard Operating Procedures (SOPs) in place as required by the standard. However, in many areas the assessment revealed discordances between documentation and practice. A lack of adequate corrective actions affected all areas of the laboratory: discordant External Quality Assessment (EQA) results were not followed-up and problems with supply management were not addressed. Internal audits were not held in accordance with the internal audit plan. The laboratory was also not registered by any legal body or the government. The assessment revealed also that personnel files were present but there was no continuous education program for staff members and competency assessment was not performed. There were no service contract present for laboratory equipment (28). In the subsequent months of

2010 the NTRL worked on correcting these non-conformities. Many activities were undertaken such as arranging equipment calibration and servicing through support from CDC/SMCS (personal notes O. Kachuwaire). In September 2010 the NTRL deemed itself ready for accreditation and sent the application for accreditation to SANAS.

Fifth Year

In January 2011 the NTRL received a document review report from SANAS which indicated that the documentation was deemed to be assessable but that there were several areas of noncompliance with ISO requirements. Therefore corrections had to be submitted before the initial on site assessment by SANAS could be scheduled (29).

The fifth project year was further marked with renovation of the laboratory. After having bought new equipment in 2009, the CDC now financed significant renovation of the laboratory, including the separation of administrative areas from testing areas, ensuring access to the safety shower by all laboratory technologists, the installation of a new epoxy coated floor and new BSCs in the Biosafety Level (BSL)-3 laboratory, reworking of the heating, ventilation and air conditioning system in the entire laboratory building and separation of air-conditioning systems to single units in each laboratory area (personal notes O. Kachuwaire).

Delays in renovations were experienced which caused the laboratory to close for a period of 3 months (between May and July 2011), therefore the initial site assessment by SANAS, scheduled for July 2011 was postponed to October 2011. This site assessment revealed eight findings of which five were major and three were minor. The NTRL was recommended for accreditation by SANAS after the findings were resolved and accreditation was received in February 2012 (personal communication O. Kachuwaire, July 2014; (30)).

NTRL of Uganda

Pre-QMS Implementation

A pre-QMS implementation assessment was performed at the NTRL of Uganda in 2007 to determine readiness to initiate the process. The main findings of this assessment were that the NTRL had already invested efforts in QMS implementation through the preparation of several SOPs and planning the renovation of its facilities. Points for improvement were the absence of a personnel training plan, no implementation of safety practices, absence of SOPs on culture and drug susceptibility testing (DST), and no possibility for quantification and specification of supplies in the procurement system for the TB laboratory network, leading to a substandard quality of reagents (31). The latter affected both the TB laboratory network and the NTRL, although the procurement system of the NTRL itself was found to be running well (32;33). This issue was eventually solved by improving communication between the NTRL and the national procurement office (personal communication M. Engelberts, June 2014; (34)).

First Year

The implementation of the QMS formally began in 2008. The external expert performed an assessment of which the main findings were similar to the assessment performed in 2007 (31). Organization of EQA was found to be impressive; data were consistently and properly verified and archived, but the documentation of procedures was less well organized. The NTRL was found to be understaffed by 15 employees and infrastructure, equipment and biosafety management were evolving very slowly. Nevertheless, staff showed a great commitment to QMS implementation and had enthusiastically begun the writing of SOPs (32).

Directly after the assessment the external experts provided a one-week introductory training on quality management principles for all members of staff, as well as for people from other organizations such as the Mulago Hospital, Central Public Health Laboratories, government laboratories and health care centers (35).

An external assistance visit at the end of the first project year found that the NTRL had not made progress since the training provided 5 months earlier due to understaffing and insufficient daily coordination and renovation of facilities and SOP development had also not progressed (33).

Second Year

This situation changed in the second project year (2009): a laboratory administrator was appointed, internal quality control improved, personnel files were updated and SOPs and worksheets were introduced. Internal audit training was provided by the external expert. The main bottleneck was the organization of the NTRL: the view of the MoH on the laboratory organization did not reflect reality which gave rise to problems when designing the organogram. There was a lack of control over the work being done due to continued vacancy of the positions of laboratory manager and technical supervisor (36;37). This situation changed at the end of the second project year when a laboratory manager was appointed (38). At this time a start was also made with renovation of the laboratory facilities. Therefore the laboratory operations were temporarily moved to Mulago hospital. Due to the high number of changes the laboratory personnel struggled to comply with procedures (38) and the fact that the quality team members were still part of the routine operational process slowed down QMS implementation (37).

Third Year

The third project year was marked by poor laboratory staff motivation caused by a high workload that failed to yield any visible benefits. The rapid rotation system used in the laboratory meant staff members never saw the results of their work which also decreased motivation and affected QMS implementation. To tackle this situation the external expert organized a workshop to increase the intrinsic motivation of staff members by making them realize that they do the work to help patients and decrease morbidity and the burden of TB (39). This, in combination with improvement of the rotation system increased staff motivation significantly, after which QMS implementation got back up to speed in the second half of the third project year (39-41). From that moment internal communication improved, many SOPs were developed, the internal audit system was running properly and the management started establishing a policy cycle. A BSO was trained and appointed, but there were still some organizational issues such as infrequent meetings between management, director and QO and no clarity for staff members about the roles and responsibilities of the QO and laboratory manager. This led to conflicts in the coordination of QMS implementation and increased the workload of the QO (40;41).

Following-up the high number of action points started to become a problem in the second half of the third project year, this was solved by better communication and coordination. A refresher training on QM, provided by the external expert improved communication (41).

Fourth Year

At the start of the fourth project year the QMS was nearing completion and the process of implementation gradually moved to optimization. Nearly all the SOPs were implemented and the quality manual was ready for to be put into action. The number of action points was drastically cut, but there were still problems with staff members not indicating when they did not understand action points, use of non-realistic deadlines and not signing off on completed action points, all of which were addressed by the external expert (42).

In the fourth project year the QMS implementation process was marked by equipment and method validation, which was perceived as a complex process. A start was also made with the implementation of non-conformity and complaint management. The renovation of the facilities was completed but deployment of the BSL-3 laboratory was delayed due to lack of an Uninterrupted Power Supply (UPS) (43;44). The implementation of a suitable LIMS was also a challenge: the NTRL switched supplier three times before finding an adequate LIMS for the laboratory's data management (44). Although meetings between the QO, laboratory manager and director were still on an ad hoc basis (affecting proper planning and communication within the QMS), in the middle of the fourth project year, the NTRL was deemed ready for an external audit to determine readiness for accreditation (42).

This audit was performed by an independent external auditor at the end of the fourth project year. Strong points noted were: quality awareness of staff, communication of quality issues, designation of staff to different duties, personnel training and competency assessment. Areas for improvement noted were implementation of assurance procedures, involvement of staff in document review and lack of information on the results of improvement activities (no information on follow-up of non-conformities and complaints, and no trend analysis was performed). It was not surprising that this was flagged as an area of improvement given the fact that this area was part of one of the last stages of the QMS implementation plan (45;46).

Fifth Year

In the fifth project year the technical assistant focused on the follow-up of action plans resulting from the external audit, optimization of the analytical process to decrease the turnaround time (TAT), and optimization of the complaints and non-conformity management system (34;47). In March 2012 the NTRL was deemed ready for accreditation (47). SANAS performed a documentation audit followed by the accreditation audit in 2012. In March 2013 the NTRL received ISO 15189 accreditation and in July 2013 it was formally appointed as an SRL by the WHO (48).

NTRL of Benin

Pre-QMS Implementation

The accreditation project at the NTRL of Benin started in 2011. Before this time the NTRL was assessed by different partners to determine readiness for QMS implementation and identify strengths and weaknesses in the laboratory system. These assessments revealed that the NTRL functioned well and had already assured technical quality to a certain extent (49). Points of concern were:

- Non-compliance of facilities and staff with biosafety regulations.
- Sufficient equipment and backup equipment was available but equipment maintenance possibilities were limited (49-51).

Points that were not of immediate concern, but attention points for the future were:

- Supply management: the NTRL could only order supplies once a year at a central stock center. There laboratory did not have insight in the budget, orders were sometimes not received and the orders took several months to be delivered. However, after years of working with this system the NTRL was able to mitigate most of the problems arising from this system (52).
- Staff management: dependence on Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) for most technician salaries, ageing of key staff and increasing demands on both the head and deputy head were marked at points of concern (53).

First Year

The QMS implementation was started in the first half of 2011 with two trainings on QM provided by external experts (51;54). After provision of these trainings the first practical steps towards implementation were the analysis of the primary process and developing flowcharts of various analytical techniques to identify the SOPs that needed to be written. The development of SOPs started with the design of the master SOP, which provides the guideline for writing all types of SOPs.

Other activities started in the first year were the design of the digital document control system and the NTRL decided to send the aspirant equipment officer on a one-year training course on equipment maintenance in France to increase equipment maintenance capacity. In addition, the organizational chart was reviewed and revised and personnel files were developed (55;56).

At the NTRLs own request internal auditing was started by the provision of training by the external experts. This turned out to be too ambitious: the first internal audits yielded a high number of non-conformities which could not be immediately solved. It was decided to continue internal auditing after implementation of all the SOPs needed for the sections to be audited (50;52).

Second Year

In the second year of QMS implementation, significant progress was made with SOP development and validation, with most technical and general SOPs drafted and validated (57). The document control system was further expanded with establishment of a physical document archive. The external expert noticed that the NTRL already had a good policy cycle in place and that this only needed streamlining to get it in compliance with the ISO 15189 requirements, which was done during the second year (50;55).
At the end of the second year several issues already noted during the pre-implementation assessments started to become obstacles to QMS implementation: the high workload of laboratory management started to spread to other staff members which put the implementation of the QMS under pressure. This problem was addressed by

recruiting more personnel, which was a slow process and beyond the control of the NTRL (58). The high workload demanded extra effort in planning capacity which demanded a change in culture (57).

Third Year

The application of biosafety regulations in facilities and by staff started to become an obstacle to the progress of the QMS implementation. At the start of the QMS implementation the NTRL had already decided to construct a new laboratory building with the capacity to house a BSL-3 laboratory compliant with all the biosafety regulations (49). Due to slow tendering processes the construction of the new building only started at the beginning of the third project year (59). In addition, the provision of the biosafety training to staff, initially planned for the end of the first project year, was postponed by the supplier several times and was delayed by one year in total (50;55;57;60). The training was ultimately provided at the end of the second project year (60). This all delayed the biosafety improvement and therefore the QMS implementation as well. As a consequence, the TB CARE I accreditation project was put on hold at the beginning of the third project year. Two assessments were performed to re-determine the NTRL's capacity to achieve accreditation within the span of the project period. Both assessors concluded that biosafety needed urgent attention, but indicated that the TB CARE I project should continue. Both assessors noted the high level of motivation and commitment of NTRL staff to the QMS implementation (59;60), and this was also noticed by the external expert who observed that the NTRL staff had continued QMS implementation activities during the disruption of TB CARE I support (58).

Upon resumption of the QMS implementation support in mid-2013, the external expert noted that the NTRL's capacity did not meet the demand for training, support and supervision activities. The follow-up of action points remained an issue, as well as the receipt of supplies. At this point the external expert provided training on the registration of non-conformities and complaints and an internal audit plan was developed, after which internal auditing was restarted (58).

Fourth Year

External experts noticed that at the start of the fourth year the workload of the NTRL staff and management increased due to their involvement in many supervision tasks, meetings, training of students and project activities. On top of that, four member of staff retired and an additional staff member left the laboratory for another job (61). This resulted in a delay of the QMS implementation: the NTRL was not able to register non-conformities and complaints, and perform internal audits according to planning (62). At the same time it became known that the initial five-year duration of the TB CARE I project for accreditation support was to be cut short by one year.

The external expert provided training in root cause analysis to address non-conformity and complaint management and provided assistance in planning techniques to get the NTRL ready for the external audit to determine readiness for accreditation, that was now planned for the end of the fourth project year (62). By this time, the NTRL had to make most progress on biosafety improvement and establishing the continuous improvement cycle. Nevertheless, during the second visit of the external expert in the fourth project year, it became clear that the NTRL would not achieve full QMS implementation at the end of the fourth project year. The NTRL had decided to implement the QMS at its own speed, creating a more sustainable system having all the staff on board. The NTRL itself had made provisions to guarantee continued external support to QMS implementation which is another sign of its commitment to the process (63). When the TB CARE I project closes out, the NTRL will receive continued support from external experts from the Institute of Tropical Medicine in Belgium. The NTRL envisages readiness for accreditation in the first half of 2015, which is in line with the initial planning made in 2011 at the start of the TB CARE I project (64).

Consequences of Implementing a QMS

Table 2 provides an overview of several service characteristics of the three NTRLs before and after QMS implementation.

The qualitative data revealed that accreditation of the NTRLs of Botswana and Uganda brought numerous positive consequences for the NTRLs. Amongst others, the capacity and quality of services of the NTRLs improved considerably. This resulted in both NTRLs acquiring a better reputation, which led to more test requests and research projects. Staff said that they experience a sense of pride to work at the accredited NTRLs.

Table 2: Quantitative performance characteristics of the NTRLs before and after accreditation

	NTRL of Uganda			NTRL of Botswana			NTRL of Benin		
Number of routine diagnostic tests in the year before the start accreditation project	No data	Period over which this was calculated:	No data	3200	Period over which this was calculated:	2006	17220*	Period over which this was calculated:	Jun 11 – May 12
Number of routine diagnostic tests in the year after receiving accreditation	No data	Period over which this was calculated:	No data	21492	Period over which this was calculated:	2012	19212*	Period over which this was calculated:	Oct 13 – Sep 14
List of analytical methods available at the NTRL before the start of the accreditation project	• FM and ZN smear microscopy • LJ culture • MGIT culture • 1st line LJ DST • 1st line MGIT DST • 2nd line LJ DST • 2nd line MGIT DST • Identification (MP64 antigen)			• Direct FM smear microscopy • Concentrated FM • LJ culture • 1st line LJ DST			• FM and ZN smear microscopy • LJ culture • 1st line LJ DST • LPA • Serology • Biochemical testing • Buruli ulcer culture • Buruli ulcer PCR		
List of analytical methods available at the NTRL after receiving accreditation	• FM and ZN smear microscopy • LJ culture • MGIT960 liquid culture • 1st line LJ DST • 1st line MGIT DST • 2nd line LJ DST • 2nd line MGIT DST • LPA • RIF/geneXpert • Identification (MP64 antigen)			• Concentrated FM microscopy • MGIT960 liquid culture • 1st line LJ DST • LPA • Capilia/SD Bioline for identification of MTB			• FM and ZN smear microscopy • LJ culture • 1st line LJ DST • LPA • Serology • Biochemical testing • Buruli ulcer culture • Buruli ulcer PCR • RIF/GeneExpert • Spoligotyping.		

*The data on number of routine diagnostic tests for Benin were not available in the year before accreditation. Therefore this parameter was calculated over the first year of QMS implementation at the NTRL of Benin. The same applies to this result of this parameter in the year after accreditation: since the NTRL of Benin was not yet accredited at the time this evaluation was conducted, this parameter was calculated from the date of the evaluation visit until the same date one year earlier.

5. Best Practices Towards TB Laboratory Accreditation

The quality system essential framework is used to present the findings, argumentations and resulting best practice recommendations in a structured way. All findings are related to the organization and the resources of the QMS and laboratory: personnel, equipment, purchasing & inventory, and facilities & safety.

Organization

Funding:

Findings/Observations:

All three NTRLs received some level of financial support from their respective government for funding the basic routine activities of the NTRLs. However, the donors' contribution was larger than the financial input by the governments. Donors provided financial support to fill in the gaps when government funding was insufficient/ not available. Lack of funding resulted in a delay of the QMS implementation process. For example, all three NTRLs were lacking BLS-3 facilities and needed either renovation of the existing facilities or construction of a new building which required a substantial financial input. All three NTRLs faced a delay of this facility upgrade due to, amongst other things, a lack of funding.

Extra funding accelerated the QMS implementation process. When funding became available to fill in key positions (e.g. QO and laboratory manager), to buy equipment (e.g. safety cabinets, centrifuges, autoclaves) and to arrange for maintenance of equipment (for example for pipettes and to provide training of a staff member to do maintenance and calibration of equipment) the implementation process gained momentum.

Argumentation/Analysis:

Additional funding led to the acceleration of the QMS implementation process whilst lack of funds led to a delay of the QMS implementation process. Implementation of the QMS requires many elements of the laboratory to be improved such as the equipment and facilities, which is an additional effort to the routine laboratory work and requires extra staff time. The QMS also requires the sustained maintenance of these elements. Depending on the initial state of these elements additional funding is required for improvement and establishing continuous maintenance.

Best Practice Recommendations:

Laboratory management should ensure funding for the entire QMS implementation process. The amount needed should be estimated based on identification of the required improvements through a thorough pre-QMS implementation assessment.

Laboratory management should try and ensure sustainable funding for QMS maintenance (including equipment maintenance and calibration), e.g. through a dedicated budget line in the MoH/government budget.

Laboratory Management:

Findings/Observations:

In the NTRLs where the management showed good leadership and commitment to the QMS, the implementation process went faster and smoother and staff engaged earlier in the implementation process. Examples of strong leadership demonstrated at the NTRLs:

- Pro-active fund raising resulting in sufficient staff and functional equipment.
- Restructuring of the organization in collaboration with the staff, resulting in clear organograms and the appointment of backup staff for key positions.
- Ensuring that job descriptions were in place so that all roles and responsibilities were clear to all staff creating a conducive work environment with efficient collaboration and team work.
- Adequate planning, resulting in the delegation of tasks and the timely maintenance of equipment.
- Supportive supervision, resulting in competent staff as they were trained when needed, leading to assured standardization and competence in conducting laboratory procedures.

- Supporting the QO. The QO's role is to monitor QMS implementation and maintenance, and provide advice about this to the management. The management needs to make decisions and direct staff on quality management, based on the advice of the QO (The QO cannot assign tasks and duties to fellow staff members).

Argumentation/Analysis:

In the NTRLs where the laboratory management was spearheading the QMS implementation process by providing direction and showing leadership to engage and involve staff, the QMS implementation process was smoother compared to those where this was not the case.

Best Practice Recommendation:

Laboratory management should initiate and lead the QMS implementation process and show active commitment by spearheading the QMS implementation, providing direction and applying leadership skills from the start to ensure that all staff are engaged in the process.

Communication:

Findings/Observations:

At NTRLs with short, clear and effective communication lines at all levels (internally and externally) the implementation process was more efficient. Internally it helped to get all the laboratory staff engaged and to increase team spirit. Good external communication meant partners and donors stepped in when there was a lack of resources as they were quickly consulted.

Argumentation/Analysis:

Good communication helps to engage staff, government, donors and partners in the QMS implementation process and to mitigate problems.

Best Practice Recommendation:

Laboratory management should create efficient and effective internal and external communication channels. Internal communication fosters staff engagement and provides clarity on the quality objectives. External communication allows the laboratory to identify customer requirements and enables the laboratory to inform stakeholders about the needs of the laboratory and what the stakeholders can expect from the laboratory.

Quality Manager:

Findings/Observations:

In one laboratory a full-time QO was appointed three months after the initiation of the implementation process and at that moment tangible implementation began. In another laboratory, the QO was involved in other activities besides the QMS tasks, which had an impact on the speed of QMS implementation.

Argumentation/Analysis:

The absence of a QO delayed the start of the QMS implementation process and when the QO was occupied with other activities besides the QMS implementation activities, the process was delayed. This indicates that efficient QMS implementation needs a full-time dedicated QO without involvement in activities unrelated to QMS implementation.

Best Practice Recommendation:

Laboratory management should appoint a competent, qualified and dedicated QO from the start of the QMS implementation process. The position of QO should be full-time and they should not undertake any other tasks.

In-country Laboratory Quality Peers:

Findings/Observations:

All countries expressed the need to have access to peers in quality management. For the QO this would enable more accessible discussion possibilities with experts to find (alternative) solutions to issues related to QMS implementation. For the general laboratory staff this would provide an example of the desired end result of QMS implementation so that they have a better picture of what they should work towards.

Argumentation/Analysis:

All three NTRLs in this project were the first TB laboratories in the public sector to implement an ISO 15189 QMS. This meant they did not have access to other routine diagnostic TB laboratories that were already accredited. Not having an example situation made QMS implementation more complex for staff as they did not have a clear vision of the necessary end results. The QOs of two NTRLs did not have access to a discussion forum in addition to the external expert. Having access to this would help in finding alternative solutions to issues arising in the QMS implementation and could also contribute in terms of equipment maintenance, setting up assessment schemes, bench marking, learning from each other, exchange of equipment and supplies, etc.

Best Practice Recommendations:

Laboratory management should create possibilities for physical access to already accredited laboratories at the beginning and during the QMS implementation process, especially for key personnel. This provides them with a tangible example of an accredited laboratory and enables them to have a clearer picture of the desired end result of QMS implementation.

Laboratory management should arrange communication with peers (if possible in-country peers) for the QO to discuss issues related to QMS implementation and to enable setting up bilateral support mechanisms between the laboratories (such as assessment schemes, shared equipment maintenance capacity, bench marking, exchange of equipment as well as parts and supplies).

Personnel Change Management:

Findings/Observations:

In all the NTRLs the staff initially showed different levels of reluctance and lengths of time to fully take part in the QMS implementation process. Better involvement of staff in the QMS planning and implementation process by the management, and the presence of short communication lines within the organization, led to increased acceptance of the new working culture. Thorough training and explaining the importance of the QMS helped to get staff on board.

Argumentation/Analysis:

Reluctance to any change is normal and the implementation of a QMS is a big process of change. Laboratory staff need to adopt and get used to a new way of working, which takes time. The implementation of a QMS also requires a change in culture.

Best Practice Recommendations:

Laboratory management should be competent in using change management principles and apply the proper management and leadership skills to facilitate the process of change created by QMS implementation.

Laboratory management should create transparency in the QMS implementation process for all staff and ensure that all staff are involved when a technical expert provides advice. This facilitates staff engagement. However, technical expert should not demand too much time from the laboratory staff members when the advice is not relevant to them. There is no use in providing advice that is for specific positions to all staff members. In this case, a summary of this advice should be provided to all staff members during a debriefing.

Training:

Findings/Observations:

At all three NTRLs the QOs and laboratory managers were trained in QMS principles, only two NTRLs trained all other staff on QMS principles. At two NTRLs the staff indicated they needed more training on QMS principles and implementation and at all three, new staff were inducted to the QMS by the QO which resulted in rapid engagement. The BSOs of all the three NTRLs were trained on (bio)safety issues. All NTRLs were supported in continuous education through trainings provided by the external experts, which was positively perceived by staff.

In all three countries laboratory quality management principles are not part of the pre-service training curriculum.

Argumentation/Analysis:

Training facilitates the implementation process by increasing staff knowledge and competence with regard to quality management, which in turn results in better staff engagement in the QMS implementation process. Training also enables laboratory management to apply better management and leadership skills and guide the process of change. Continuous training ensures that all staff remain engaged in the QMS implementation process.

Best Practice Recommendations:

At the start of the QMS implementation process laboratory management should ensure adequate training for key positions particularly for the laboratory manager, QO and BSO. This enables them to perform their tasks competently and to be able to engage staff effectively.

Laboratory management and, if applicable, external experts, should ensure that all laboratory staff understand their role in the QMS implementation through targeted, relevant and continuous internal and external training.

Relevant stakeholders (e.g. laboratory representatives, national and international public health organizations) should advocate at the level of national government and education sector to make training on laboratory quality management principles part of the pre-service laboratory training curriculum, to maximize indoctrination on QMS implementation and maintenance on a national scale.

Workload:

Findings/Observations:

All NTRLs indicated shortage of staff although not all NTRLs could provide exact numbers on the level of workload of routine work.

Argumentation/Analysis:

Implementation of a QMS initially increases the workload as it requires work to be done in addition to the routine work of the laboratory. This includes, for example, implementation of new work methods, SOP development and implementation, improvement of recording and reporting of information, development of equipment maintenance programs, etc.

Best Practice Recommendations:

Laboratory management should anticipate the initial increased workload when initiating QMS implementation and take appropriate measures. The increase in workload depends on the availability of staff and the amount of work to be done to achieve ISO 15189 compliance. The latter could be estimated by performing a thorough pre-QMS implementation assessment to identify the improvements that need to be made to achieve full ISO 15189 compliance.

The laboratory management should continuously monitor workload through regular workload assessments. This enables the laboratory management to adequately react when the workload becomes too high and prevent this hampering QMS implementation and affecting routine work.

Equipment

Equipment Maintenance and Backup:

Findings/Observations:

All NTRLs reported insufficient competent in-country maintenance capacity for the maintenance and calibration of equipment.

Argumentation/Analysis:

It is critical that equipment maintenance systems are functional to guarantee good laboratory services and to comply with ISO 15189 requirements.

Best Practice Recommendations:

Laboratory management should assess if there is adequate equipment maintenance capacity for all critical laboratory equipment at the start of the QMS implementation process. This activity could be part of a pre-QMS implementation assessment. If in-country equipment maintenance capacity is inadequate, the laboratory management must plan to compensate for this, as this may cause delays due to the fact that this often lies beyond the control of the laboratory. The appropriateness of the strategies used to compensate inadequate maintenance capacity depend on the local situation. Examples of possible interventions could be:

- *Training of one or more staff members to perform equipment maintenance themselves.*
- *Outsourcing equipment maintenance to competent companies in-country or otherwise abroad, dependent on in-country capacity (and anticipating the extra funds required).*
- *Including a service contract for preventive maintenance as a requirement in the tender when purchasing new equipment.*

If in-country equipment maintenance capacity is inadequate, relevant stakeholders (laboratories/laboratory societies, national and international public health organizations, etc.) should advocate at the national level of government to increase in-country equipment maintenance capacity for the (medical) laboratory sector.

Purchasing & Inventory

Procurement of Supplies:

Findings/Observations:

Inflexible administration of in-country supplies management resulted in slow procurement processes and substandard supplies for all NTRLs. At all NTRLs donors were relied upon for the provision of supplies where the government supply system was insufficient. At one NTRL this was perceived as have a negative impact on QMS implementation. A lack of certified suppliers was an issue for one NTRL.

Argumentation/Analysis:

Timely delivery of good quality supplies leads to uninterrupted quality services and is a requirement of the QMS. In areas where there is a lack of proper suppliers, and/or supply/delivery have long lead times, adequate actions must be taken to find alternative solutions and improve this situation.

Best Practice Recommendations:

Prior to QMS implementation the laboratory management should assess the capacity of procurement and supply chains to provide quality supplies and cope with a potential increase of demand for supplies. This activity should be part of a pre-QMS implementation assessment. If the capacity of the procurement and supply chains is inadequate timely actions should be taken as improvements in these situations can take a long time (as they often lie beyond the control of the laboratory). The appropriateness of the strategies used depends upon the local situation. If the routine procurement of supplies lies beyond the control of the NTRL, the NTRL management should advocate to the relevant authorities to have their own budget available for the procurement of supplies in case of failures in the supply chain and for emergencies that require an extra demand for supplies.

If lead times for supply delivery are long due to circumstances that have their root cause within the country, relevant stakeholders (laboratories/laboratory societies, national and international public health organizations, etc.) should advocate to the proper sources to eliminate these causes and improve supply chains.

Facilities and Safety:

Findings/Observations:

At all the NTRLs the (re)construction of the BSL-3 facility delayed the QMS implementation process due to inadequate planning and/or communication between the NTRL and donor, slow tendering procedures, and/or unavailability of competent BSL-3 laboratory construction firms.

Argumentation/Analysis:

A safe work environment is a prerequisite for health of the staff, especially in TB (culture) laboratories. Renovation of the laboratory facilities can be a long process which requires timely planning.

Best Practice Recommendation:

Laboratory management should assess if the facilities comply with the (bio)safety and biosecurity requirements prior to QMS implementation. This could be part of a pre-QMS implementation assessment. If the facilities do not meet the requirements, the laboratory management must immediately set the improvement of the facilities in motion as funding limitations and limited in-country availability of contractors competent to renovate or newly construct laboratory facilities can affect QMS implementation.

6. General Discussion

Implementing ISO 15189 remains an important pillar in laboratory strengthening to ensure quality healthcare. However, implementing an ISO 15189 QMS is a huge intervention that is a huge challenge for laboratories in high income countries and even more so for laboratories in LMIC. This evaluation sought to determine the best practices that laboratories should take into consideration before embarking on this undertaking.

Consequences of Receiving Accreditation

It is difficult to collect quantitative data on laboratory performance such that the effect of the QMS implementation can be visualized. In unaccredited laboratories many parameters are not structurally recorded, it is therefore often impossible to obtain baseline performance data from the years before accreditation. The same applies to the indicators used in this evaluation project. Data on EQA performance and staff turnover was not complete or could not be obtained. The fact that the proper collection of data from the years before the start of the accreditation projects is not possible while this can be done for the years after QMS implementation is in itself a sign of the effect of implementing a QMS; this indicates that the QMS requirements related to information management indeed optimize accessibility and availability of laboratory data.

Table 2 (page 26) shows that the number of test requests increased both at the NTRL of Benin and Botswana. In Botswana, this increase was said to be due to the improved reputation of the NTRL following accreditation and the fact that TB laboratory testing was included in the national diagnostic algorithms of Botswana. In Benin, the number of tests mainly increased because of the adoption of new techniques, but the effect of accreditation could not be measured as this NTRL is not yet accredited. At the Uganda NTRL data about the increase of test requests could not be collected. This makes it impossible to indicate whether the substantial increase of test requests at the NTRL of Botswana is something that is to be expected by other laboratories after receiving accreditation.

The number of different examinations performed increased at all three NTRLs, this is due to the development of new TB diagnostic test methods. The implementation of the QMS probably did not influence this, although the QMS might have facilitated easier uptake of the new diagnostic test methods.

The qualitative data indicates that the QMS indeed influenced the quality of services according to the majority of those interviewed. The reputation and status of the NTRLs improved and customers are more satisfied with the NTRLs' services.

Implementation of the QMS

The NTRLs in this evaluation have received different levels of support from the respective MoHs. They are situated in low to middle income African countries and represent settings similar to laboratories in other African countries where multi-partner support in collaboration with the government has been used to achieve laboratory accreditation (65;66). As much as partner support is essential to start the implementation of the accreditation processes, without long-term government support national accreditation programs will not improve or be sustainable (15;67). To ensure sustainability, advocacy by relevant stakeholders at the national level will be required for governments to include international ISO 15189 accreditation through QMS implementation in national laboratory policies and national strategic plans (15;66;68;69).

Expected Findings

Many factors that are very likely to affect the implementation of a QMS were observed, such as the availability of funding, the role of laboratory management, training, supply chain and equipment maintenance capacity, and change management/staff resistance. The importance of these elements in implementing a QMS has also been indicated by many other before (5-15;17).

What is striking is that all the best practices are related to two elements in general: the organization (including management) of the laboratory and the resources required for laboratory work (personnel, equipment, purchasing & inventory and facilities & safety). This could logically be explained by the fact that resources are needed to

build the rest of the QMS. Without the proper resources, the rest of the QMS implementation process cannot be completed properly either. As stated before, QMS implementation is a big process of change, as demonstrated in chapter 2, strong management and organization is needed to coordinate and facilitate this process, without these elements, the efficiency of QMS implementation directly decreases.

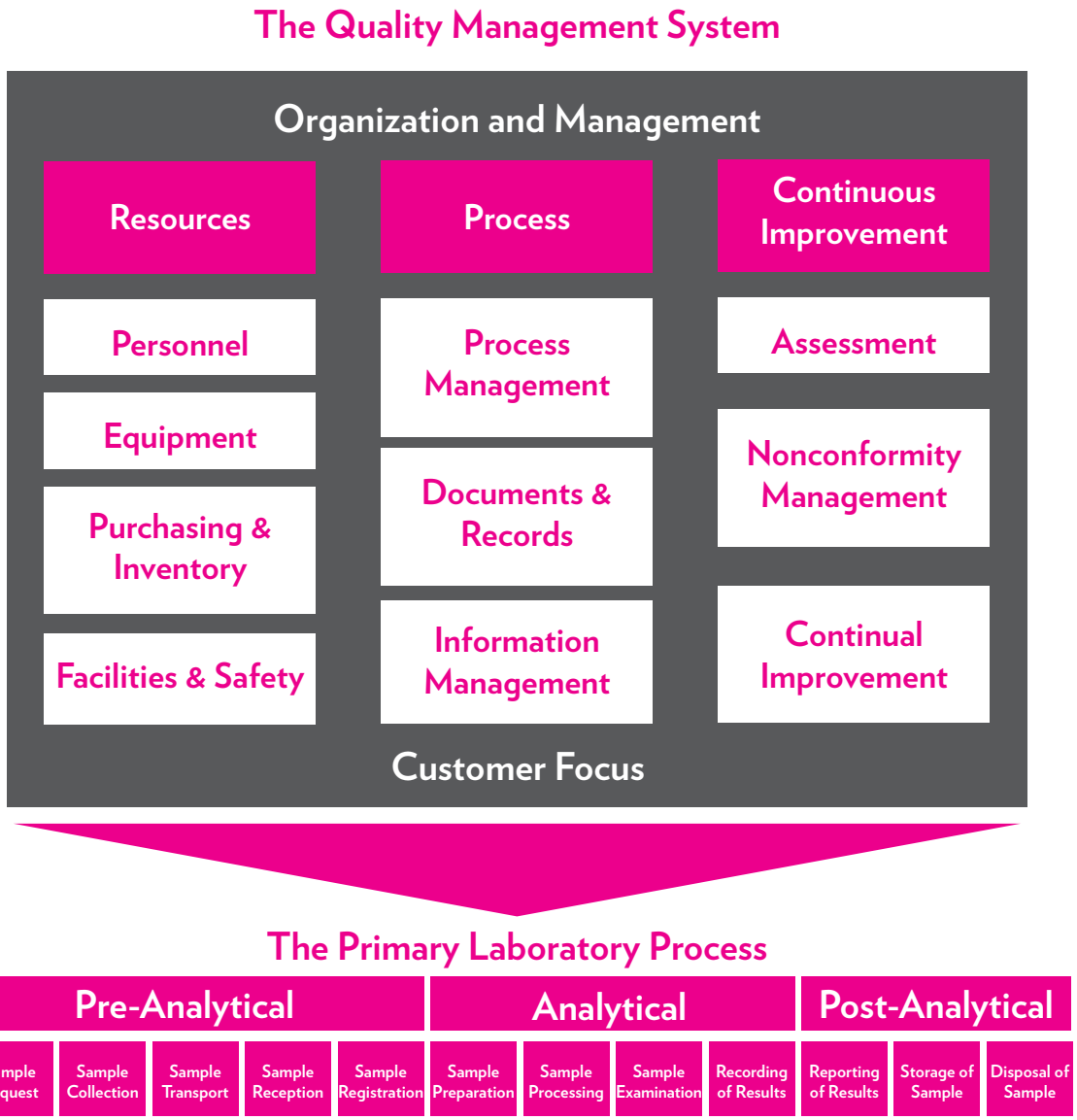

Figure 6: Graphical display of the individual quality system elements within the QMS

Funding facilitated QMS implementation by enabling the recruitment of additional staff, the procurement of reagents, the improvement of facilities, etc. When funding was lacking, it delayed some of the processes at the NTRLs in this evaluation such as the construction of BSL-3 facilities. This obstacle was often resolved by interventions from donors who financially supported the majority of the QMS activities. The same was seen in Ethiopia, where laboratories implementing a QMS using the SLMTA model only progressed in areas that required no financial commitment, which shows the importance of funding for this process (70). The advantage of donor funding is that the QMS implementation process can continue; the disadvantage is that the sustainability of funding is not ensured. The maintenance of the QMS that is required after it has been implemented, requires sustained funding and in the public sector this should ideally be provided by the MoH. This indicates the need for sensitization at MoH level about the requirements of ISO 15189 by the laboratory management as this provides the MoH with insight into the resources required to implement/sustain a QMS. Further to this, the authors recommend that the laboratory management raise awareness about QMS requirements and their implications on the support and resource demands at the authorities that provide the support and resources (including human resources) to the NTRL. This way the extra demand during QMS implementation can be anticipated by these authorities.

It is clear that the role of the laboratory management is crucial to the success of QMS implementation. Nearly all the best practices recommended in this evaluation require action from the laboratory management. Therefore, the fact that the laboratory management is strong, has good leadership skills and actively directs and controls the implementation of the QMS is of critical importance. The laboratory management has the responsibility to propagate the QMS and explain the consequences both internally and externally.

Resistance from staff caused by the required culture change during the accreditation process as shown in this evaluation is similar to the findings from Kenya (9). In Rwanda, to increase staff buy-in, a performance based incentive scheme was employed, which involved financial rewards for continued improvement during implementation (71). In this evaluation the management of one NTRL showed very strong direction and leadership skills with regard to the QMS implementation process. In this NTRL, staff were engaged earlier and committed to the QMS implementation process in comparison to NTRLs where the laboratory management did not actively commit to the QMS implementation process. This finding is supported by examples from other laboratories. In Nigeria buy-in from top management was cited as a factor in the successful implementation of a QMS (5). A culture of open communication also contributed to staff engagement and involvement at one of the NTRLs. These findings confirm the importance of laboratory management showing proper management and leadership skills and applying the principles of change management as described by Berwouts et al. (6).

In this evaluation, all the NTRLs experienced increases in workload, laboratory management must anticipate and manage this change by reorganization and/or the recruitment of new staff.

The availability of a full time QO from the start of QMS implementation process made it move faster and more efficiently, which supports the statement of Zeh et al. and Guzel et al. who point out the importance of establishing a quality team to coordinate the process (9;11). When the QO was assigned duties other than QMS tasks, the implementation process slowed down. It is important that the QO has an advisory position under the laboratory manager/director, instead of a line-position. The QO has no authority to assign tasks to specific staff members and can only provide advice to laboratory management, therefore the laboratory management should not expect the QO to be authoritative and assign tasks to staff members.

This evaluation supports the statement made by many before, that initial and continuous training to build capacity of staff, starting with key personnel, is essential for the QMS implementation process (5;7;8;12). In this evaluation formal training in quality management principles was provided to key personnel at all NTRLs. In-country capacity for QMS training was beneficial in one country as it reduced costs. In other mentoring models training of in-country mentors has been shown to improve the speed of QMS implementation and the presence of a full-time facility-based mentor in Nigeria, Botswana and Kenya had a positive impact on their accreditation processes (4;65). The disadvantage is that the costs of these models are considerable and the presence of a full-time mentor compromises staff ownership over the QMS and thus sustainability of the QMS (9;16). In two NTRLs in this evaluation QMS implementation assistance was provided through four one-week visits by the external expert per year. It was noted by staff and management that this was a suitable model to ensure sustainability and staff ownership over the QMS as they implemented the QMS themselves. However, the external expert said that a visit of a longer duration (two to three months) at the start of the project would facilitate earlier staff engagement and more rapid start-up of QMS implementation.

The availability of a well-functioning supply chain system and reliable suppliers was identified as a necessity by all three NTRLs. For two NTRLs the supply system was managed entirely by donors, while at the other the donors only provided support to supply delivery during stock outs that could not be resolved in time by the routine supply system. Availability of reliable (certified) in-country suppliers was a challenge at all three NTRLs, which made the supply chain system cumbersome. This finding was no surprise as the availability of proper supply systems in LMIC was reported to be challenging by many before (5;9;17). This indicates the necessity to improve this situation and is a call for action by higher level authorities, starting with national governments. The same applies to the frequently reported challenges around equipment maintenance capacity in LMIC (7;9;13;14), which was also challenging for the three NTRLs evaluated in this study. They reported that the availability of a well-functioning equipment maintenance system and qualified equipment maintenance vendors is critical to successful QMS

implementation. In two of the NTRLs the equipment maintenance was carried out by vendors subcontracted by donors, in the third a laboratory technologist was sent abroad for one year to be trained in basic equipment maintenance. Unfortunately this solution was only partly effective in resolving equipment maintenance and especially calibration issues as challenges persisted due to lack of tools required for maintenance and calibration of several pieces of equipment.

The fact that challenges related to equipment maintenance and supply chain systems are similar in many LMIC indicates that urgent action is needed to resolve these issues. Although many supplies have to be imported from abroad which often leads to long lead times, the national governments could play a role in optimizing the administrative procedures around ordering and importing supplies. This will prevent an increase in the already long lead times of imported supplies. National governments can also play a role in the creation of in-country equipment maintenance and calibration capacity by establishing proper policies and providing subsidies for the establishment of these institutions.

Unexpected Findings

Although most of the factors mentioned above were expected to influence the QMS implementation, the complexity of some of the problems was not fully expected, including the difficulties in solving them. These factors were mostly beyond the control of the laboratory. Of note were issues that required policy changes, which took a long time to realize and some that are still a challenge even after accreditation (e.g. supply chain systems, laboratory budgets and ad hoc staff transfers). These findings are not unique to the NTRLs in this evaluation and were also observed in other settings where, even after accreditation, government processes made equipment maintenance and adequate delivery of supplies a challenging process (9).

Staff in some of the NTRLs said that they felt left out during the visits of the external expert because the external expert often focused on working with key laboratory staff (QO and laboratory management). The external experts who provided this assistance were not aware of this issue. This finding shows that deliberate engagement of all staff by the external experts during each visit is necessary to facilitate more active involvement and motivation of staff when implementing the QMS. However, the external expert should find a balance between engaging all staff and aiming assistance at certain key positions that play an important role in the implementation of specific QMS elements, because this type of assistance is often not relevant for the majority of other staff members besides the key position on which assistance is focused.

Staff in two of the NTRLs said that they would have benefited from visiting laboratories that were already accredited as this would enable them to visualize what the end result of their efforts would look like, especially at the beginning of the QMS implementation process. In addition, staff in two NTRLs stated that they thought that it was important to have opportunities to share experiences with a group of peers involved in QMS implementation in laboratories in or outside their countries. Only one of the NTRLs had an in-country quality forum, which was noted to be useful. Other countries would also benefit from setting up such a forum to provide a supporting environment for laboratories implementing a QMS. In Kenya a laboratory implementing a QMS formed an advisory committee with other experts from the US and held quarterly meetings in a formal in-country QA meeting which supports the suggestions found in this evaluation (9). If possible, advisory committees with peers from the same country are preferred to have more approachable discussion possibilities and keep control over the costs.

A safe working environment in TB laboratories is an international requirement to ensure the safety of both staff and patients, and the WHO TB laboratory biosafety manual advises that laboratories conduct a risk assessment (72). This is an approach that promotes the consideration of risk and the development of appropriate biosafety practices in laboratories based on the unique combination of test procedures, staff expertise and facilities present in each laboratory. The NTRLs in all three countries had to upgrade their infrastructure by renovating or even building a new laboratory facility, which resulted in unexpected delay of the process as this was one of the slowest and one of the most expensive steps in implementing a QMS. The delay was augmented by the lack of competent in-country contractors experienced in building BSL-2/3 laboratories in all the three countries. In some of the countries delay was due to construction formalities with donors and the government. In some of the NTRLs the

quality of the upgrades were affected by shortages of funds allocated for the reconstruction. In all three countries donors supported the construction or reconstruction of the laboratories. The challenges around facility upgrading mentioned here confirm the statement made in the roadmap for ensuring quality TB diagnostic services within national laboratory strategic plans as published by the WHO, saying that the establishment of well-maintained TB laboratories with appropriate biosafety measures and equipment presents the greatest challenge for both initial financing and sustainability (73). This shows the necessity to assess and identify the improvements that need to be made to the laboratory facilities at the start of the QMS, so that the improvement process can be started at the earliest convenience, leaving more time to mitigate challenges such as those described above.

Factors 'In' and 'Beyond' the Direct Control of the Laboratory

Prior to start of the implementation, a gap analysis of all the elements of the QMS at the NTRLs was conducted with support from external experts. Following this, plans were developed to address the identified gaps, which allowed for a structured approach to implementation. Despite this planning there were unexpected delays due to some factors over which the NTRLs had no direct control, indicated in Table 3.

Table 3: Factors in and beyond the direct control of the NTRLs

Factors in the direct control of the laboratory	Factors beyond the control of the laboratory
• Staff engagement • Laboratory leadership/management • Trainings • Assessments • Communication channels both internal and external to the laboratory • Appointment of QO, BSO and supplies officer • Fund-raising activities	• Supply chain system • Equipment maintenance • Availability of donors • Availability of peers • Staff shortages/staff transfers

We observed that some of the factors beyond the control of the NTRLs took a longer time to be resolved compared to the factors over which the NTRLs had direct control. All the NTRLs with a strong management actively engaged donors to resolve some of the external factors such as issues with the supply chain and equipment maintenance. Laboratories that are planning to begin the process of implementing a QMS should consider a pre-QMS implementation assessment that also identifies factors over which the NTRLs have direct control and which are beyond their control. When there are elements that are beyond the control of the laboratory but that need to be optimized as part of the QMS implementation process, these should be taken into account in the planning and budgeting process. This basically means that the laboratory management should design strategies to achieve the desired improvements, e.g. through advocacy and/or discussion with external institutions that control these elements.

Technical Assistance

The format in which assistance was provided by external experts was similar at all NTRLs in this evaluation. To date, two NTRLs are accredited and one NTRL is in the final stages of accreditation. At all the NTRLs, it has taken five years of preparation to apply for accreditation. As all three NTRLs evaluated in this process worked with external experts, we cannot make any conclusions on how critical the external assistance is in accelerating the whole QMS implementation process, due to the lack of an appropriate control. However, in Nigeria a laboratory which had intermittent assistance from an external expert progressed much further than one without, despite the latter already having implemented ISO 9001. Some of the reasons stated in this situation were a lack of understanding of audit findings and the ISO 15189 standard at the laboratory that did not receive external assistance, which led to delays in implementation of corrective actions (65). This suggests that assistance of an external expert is preferable when implementing a QMS according to ISO 15189.

Limitations of this Evaluation

This evaluation was performed by the same persons that provided assistance during the QMS implementation processes at the three NTRLs. This could have influenced the answers given during the interviews, predominantly on questions regarding the method in which external assistance was provided. The evaluators minimized the risk for bias by making sure that the interviews were led by evaluators that did not provide external assistance to the NTRL at which the interviews were held, while the evaluator that had provided external assistance to the NTRL before, made notes of the interviews. Answers to questions where evaluators suspected the presence of bias were omitted from analysis.

Another potential limitation is that this evaluation focused on the African setting only, evaluating QMS implementation in NTRLs in three different African countries. Indicating that the best practices are applicable to continents other than sub-Saharan Africa would be an extrapolation that is not supported by empirical data. Nevertheless, the literature review, in which reports of similar projects in other parts of the world were analyzed, yielded similar results to the findings found in this evaluation. Therefore, the authors conclude that the findings and resulting best practices of this evaluation project can to some extent be safely be extrapolated to countries with similar conditions outside the African continent

The geographical location of the three countries where the NTRLs are located form a cross-section of Sub-Saharan African countries. This provides more certainty that the recommendations for best practices in this document are applicable to the majority of countries in sub-Saharan Africa. As the NTRLs that were evaluated were located in one upper middle-income country and two low-income countries, there is also more certainty that the recommendations for best practices are applicable to laboratories in both low- as middle-income countries in sub-Saharan Africa.

7. Conclusion

After a literature review and extensive evaluation of the ISO 15189 QMS implementation processes at the NTRLs of Botswana, Uganda and Benin using a mixed-methods approach, significant insights were obtained on important factors influencing the QMS implementation process. Based on these insights, 19 best practice recommendations were formulated. These best-practices should lead to more efficient implementation of QMSs according to ISO 15189, when they are adhered to by TB laboratory managers, QOs, NTP managers, policy makers and other stakeholders involved in TB laboratory strengthening. These best practices should also be used in the GLI tool roll-out.

Our findings largely corroborate findings published by others. Several unexpected findings were related to the method of assistance provided to the laboratories, the fact that staff often indicated the importance of visiting an already accredited laboratory to obtain a clear vision on the target and know what was expected, and the complexity of some of the problems due to the fact that their causes were not under the direct control of the laboratory.

Interestingly, all of the best practices identified in this evaluation are related to two particular areas: organization (including management), and the resources of the laboratory (personnel, equipment, purchasing & inventory, facilities & safety). The importance of proper organization and management can be explained by the fact that the implementation of a QMS is a big process of change, that affects all laboratory processes. To facilitate and coordinate this process such that the change is achieved as efficiently as possible, strong management, leadership and organizational skills are needed.

The fact that the majority of the best practices are related to the resources of the laboratory is logical as resources form the basis of the primary laboratory process and the QMS and sub-optimal resources influence the quality of services at all levels. In our evaluation we found that problems with sub-optimal or a lack of resources were often caused by factors outside the direct control of the laboratory. This exacerbated the problems and solving them often required large amounts of time, strong management and advocacy skills from the laboratory manager. It is therefore of particular importance that laboratories that are planning to implement a QMS, perform a pre-QMS implementation assessment, focused on the best practices laid out in this document. If points for improvement are identified, actions should be taken immediately to decrease the chance that they will affect QMS implementation at a later stage.

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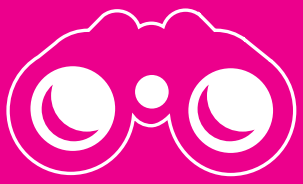

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