



Practical Guide to Implementing a Quality Assurance System for Xpert MTB/RIF Testing

(“Xpert QA Guide”)





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Disclaimer

The mention of specific companies or of certain manufacturers' products does not imply that they are recommended in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

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Acronyms and Abbreviations

AFB	Acid-fast bacilli
CDC	U.S. Centers for Disease Control and Prevention
CQI	Continuous quality improvement
DCS	Dried culture spots
DNA	Deoxyribonucleic acid
DST	Drug susceptibility testing
DTS	Dried tube spot
EQA	External Quality Assurance / Assessment
GLI	Global Laboratory Initiative
ISO	International Organization for Standardization
M&E	Monitoring and evaluation
MDR-TB	Multidrug-resistant tuberculosis
MGIT	Mycobacteria Growth Indicator Tube
MOH	Ministry of Health
MTBC	<i>Mycobacterium tuberculosis</i> complex
NHLS	National Health Laboratory Service
NTP	National TB Programme
NTRL	National TB Reference Laboratory
PPE	Personal protective equipment
PT	Proficiency testing
QA	Quality assurance
QC	Quality control
QMS	Quality management system
RIF	Rifampicin
SOP	Standard operating procedure
TB	Tuberculosis
TWG	Technical working group
TOT	Training of Trainers
WHO	World Health Organization
WRD	WHO-recommended rapid TB diagnostic

Glossary of terms

	What is it?	Why do you need it?	How does it work?
Quality assurance (QA)	Sum total of all testing site activities undertaken to ensure accurate & reliable results.	To ensure quality diagnostic results.	QA covers the entire test process, from pre-analytical to analytical & post-analytical, including sample collection, transport, personnel, procedures, processes, equipment, environment & reagents.
Quality control (QC)- see also IQC [ISO 15189 Clause 5.6.2]	Measures put in place during the testing phase to ensure the procedure assures quality results; e.g., known negative & positive slides for every staining batch. Testing site staff performs QC concurrently during testing.	To ensure that the information generated by the testing site is accurate, reliable & reproducible & serves as a mechanism by which testing sites can validate the competency of their diagnostic services.	QC materials are made to mimic patient samples & are tested with the patient samples to evaluate the examination component. Positive controls have known reactivity & negative controls are nonreactive for the test being evaluated.
Quality improvement [ISO 15189 Clause 4.1.1.4]	Process of continuous analysis, & remedial & preventative action to improve quality.	To ensure the most effective & long-lasting improvements by anticipating & preventing problems before they occur, rather than by identifying & correcting defects after they arise.	Data collection, analysis & creative problem solving are key components of this process that involves identification of defects, followed by remedial action to prevent recurrence of problems.
Onsite supervisory visits	Direct supervision	To ensure that testing sites run smoothly & to motivate technicians to improve or maintain performance.	Testing sites are visited by qualified personnel & are evaluated using standardized checklists.
Performance indicators [ISO 15189 Clause 4.14.7]	Performance indicators are objective measures of testing site practices.	To give an objective viewpoint of the structure & processes of the testing site.	Performance indicators can be used to monitor all activities from sample receipt to the time the patient is placed on treatment.
Internal quality control (IQC) [ISO 15189 Clause 5.6.2]	Similar to QC; the ISO standard indicates that these terms are sometimes used interchangeably in different settings.	See QC	See QC
Competency assessment [ISO 15189 Clause 5.1.6]	A theoretical & practical test to determine proficiency.	To determine whether users are following a procedure as documented in the SOP.	Users are tested theoretically & practically to determine if they have sufficient understanding of the test procedure to troubleshoot problems that may arise during testing.
Proficiency testing (PT) or Quality Assessment [ISO 15189 Clause 5.6.3]	An independent & unbiased assessment of the testing performance at of the testing site. Provides an assessment of the validity of testing at the testing site.	To assure the quality of the results generated at the testing site.	Test results reported by each testing site are compared to the reference test results. The testing site is then provided with a report indicating the accuracy of their results.

About this guide

The *Practical Guide to Implementing a Quality Assurance System for Xpert MTB/RIF Testing* (Xpert QA Guide) provides practical guidance and tools to establish and implement a quality assurance (QA) system for the Xpert MTB/RIF test across the diagnostic network. Such a system is designed to ensure the following are in place and sustained:

- All testing is done in compliance with national testing algorithms and standard operating procedures (SOPs);
- A cadre of competent users is available to perform the test;
- Testing sites provide uninterrupted diagnostic services and testing services are unaffected by stock-outs and module failures;
- Good quality samples are collected, quality testing is done in a timely manner and the Xpert MTB/RIF test results are reported without delay;
- Technical assistance, guidance and on-site supportive supervision are provided to testing sites, in particular those that need it most;
- The TB diagnostic network is monitored, using electronic systems where possible, and the collected data are analysed, evaluated and used to inform decision-making.

The strategies and approaches described in this document are not unique to the Xpert MTB/RIF test. This guide can therefore be used to inform development of a quality improvement approach for other tests using the GeneXpert platform, as well as other molecular, near point-of-care and point-of-care, instrument-based diagnostic tests or platforms.

Target audience

This guide is intended for implementers of the Xpert MTB/RIF test and QA managers across the laboratory diagnostic network. Specifically, this guide is intended to inform Ministry of Health officials, National TB Programme officials, National TB Reference Laboratory personnel, donors, implementing partners, QA unit personnel, programme managers, testing site managers, supervisory staff and GeneXpert users at national, regional or testing site level on the how to implement activities to assure the quality of Xpert MTB/RIF results.

Part 1 of the guide (National and Supervisory Levels) focuses on establishing or integrating Xpert MTB/RIF QA activities into the TB diagnostic network in a country or region and Part 2 (QA at Xpert MTB/RIF Testing Sites) addresses key activities to be carried out at the testing sites to ensure the production of quality Xpert MTB/RIF results. Each part is divided into sections, each dealing with an aspect of assuring a quality Xpert MTB/RIF test result. Links are provided to supporting documents, checklists, forms and training materials.

Note: In this guide, the term ‘testing site’ is used to denote a site where the Xpert MTB/RIF test is being performed and includes both traditional laboratories and point-of-care or other clinical testing sites where the Xpert MTB/RIF test is being performed. Furthermore, to ensure the quality of the overall diagnostic process, some of the QA processes (e.g., use of SOPs, participation in supervisory visits, monitoring performance indicators, training, etc.) target activities at participating clinical sites (e.g., specimen collection sites, sample referral centers, clinics).

Note: In this guide, the term Xpert MTB/RIF test is used to denote either the Xpert MTB/RIF test or the Xpert MTB/RIF Ultra test. When the two tests differ (e.g., whether or not a ‘trace’ result is generated), the tests will be described separately.

Background

The World Health Organization (WHO) End TB Strategy calls for an end to the global tuberculosis (TB) epidemic, aiming to reduce deaths by 95%, cut new TB cases by 90%, and ensure that no family is burdened with catastrophic expenses due to TB (WHO, 2014)¹. Despite TB mortality having fallen globally by 47% since 1990, it remains the world's top infectious killers of our time, claiming more than 1.6 million lives in 2017 alone (WHO, 2018)². Many people die from TB due to delayed diagnosis and treatment initiation.

The End TB Strategy highlights the critical role of laboratories in the post-2015 era and emphasizes that in order to meet the targets of the End TB Strategy, WHO-recommended rapid TB diagnostics (WRDs) should be available to all persons with signs or symptoms of TB; all bacteriologically confirmed TB patients should receive drug-susceptibility testing (DST) at least for rifampicin (RIF); and fluoroquinolone resistance should be ruled out, preferably using WRDs³. The Xpert MTB/RIF[®] test is a cartridge-based, automated WRD run on the GeneXpert[®] platform (Cepheid Inc.; Sunnyvale, CA, USA). The test can simultaneously detect *Mycobacterium tuberculosis* complex bacteria (MTBC) and resistance to RIF in less than two hours. Since its launch in 2010, a total of 29,865 instrument modules and more than 23 million Xpert MTB/RIF cartridges have been procured in 130 high TB burden developing countries (Cepheid data, December 2016).

The Xpert MTB/RIF test has the potential to significantly decrease diagnostic delays, increase the detection of drug resistance and impact TB transmission. However, there are a variety of challenges to providing quality Xpert MTB/RIF results:

- Inadequate training and mentoring
- Lack of, or poor adherence to, standard operating procedures (SOPs)
- Stock-outs and use of expired reagents
- Absent or inadequate maintenance of equipment
- Poor quality of samples being tested
- Lack of regular on-site supportive supervision
- Lack of monitoring and evaluation of the TB diagnostic network

Failure to provide a quality Xpert MTB/RIF result can result in either under- or over-diagnosis of TB. Under-diagnosis (i.e., a falsely negative result) can lead to worsening of disease and can contribute to the spread of TB (including drug-resistant TB) in the community (Bailey, 2011)⁴. Over-diagnosis (i.e., a falsely positive result) may result in unnecessary patient treatment and stigma. False results can also undermine confidence in laboratory testing and lead to delayed diagnosis and reduce use of laboratory data for patient care decisions.

A laboratory test is just one part of the diagnostic process which starts with the patient experiencing symptoms and deciding to seek care (i.e., passive case finding) or a healthcare worker identifying a person to be evaluated for TB (i.e., active case finding). At this point, the healthcare worker refers the specimen to the laboratory, where it is analysed. The results of the test are sent to the healthcare worker, who initiates appropriate treatment and monitors response to therapy. A lack of quality or delays in any of the steps in this process can reduce the clinical and public health impact of laboratory testing. As such a system to ensure the quality of laboratory testing must address all the relevant parts of the diagnostic cascade, not just what happens in the laboratory.

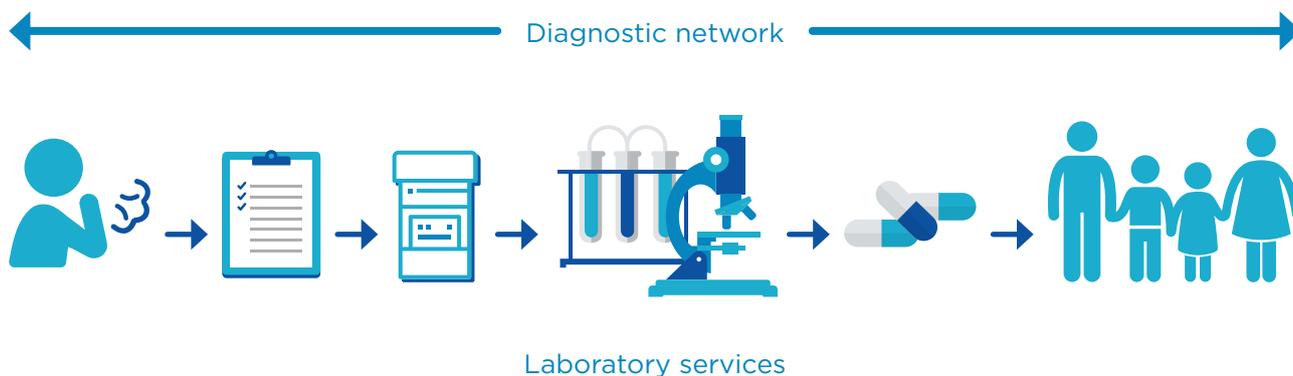
¹ The End TB Strategy – Global strategy and targets for tuberculosis prevention, care and control after 2015. http://www.who.int/tb/strategy/End_TB_Strategy.pdf

² Global tuberculosis report 2018. Geneva: World Health Organization; 2018. WHO/CDS/TB/2018.20. https://www.who.int/tb/publications/global_report/en/

³ World Health Organization. WHO consolidated guidelines on drug-resistant tuberculosis treatment. <https://apps.who.int/iris/bitstream/handle/10665/311389/9789241550529-eng.pdf?ua=1>

⁴ Bailey S.L., Roper M.H., Huayta M., Trejos N., López Alarcón V. & Moore D.A. 2011. Missed opportunities for tuberculosis diagnosis. *Int J Tuberc Lung Dis* 15: 205-10

Figure 1: The TB diagnostic cascade



Introduction to quality assurance and continuous quality improvement

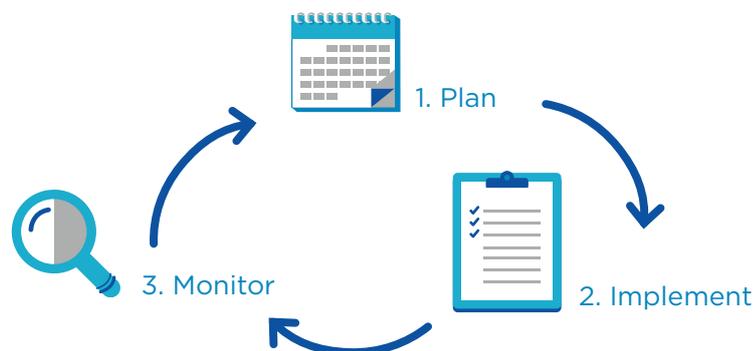
Quality Xpert MTB/RIF test results are essential to ensure patients are correctly diagnosed in a timely manner and rapidly initiated on an appropriate treatment regimen.

▶ *Quality assurance (QA) is a system that monitors the various aspects of a diagnostic process ensuring that the results it produces are accurate, reliable and timely.*

Implementation of quality assurance (QA) activities across the TB diagnostic network is part of the continuous quality improvement (CQI) process. CQI is a cyclical, continuous process-based, data-driven approach to improving the quality of diagnostic testing.

▶ *CQI operates under the belief that there is always room for improving operations, processes and activities to increase quality.*

Figure 2: Continuous quality improvement process



- The **PLAN** phase includes establishing a governance structure for QA activities, assembling a QA management team, conducting situational analysis of current QA activities, setting quality targets and developing an action plan for their implementation.
- The **IMPLEMENT** phase includes implementing QA and quality improvement activities in a phased manner at both existing and new testing sites.
- The **MONITOR** phase includes establishing a monitoring and evaluation (M&E) framework to monitor the diagnostic network; assigning responsibilities for data collection, analysis and reporting; collecting and analyzing data; and evaluating progress toward established targets.

Standards and key activities for assuring quality

Quality standards are goals toward which efforts and resources to assure quality Xpert MTB/RIF testing should be directed. Standards that were developed to measure the performance of the TB diagnostic network form the basis of the standards for the Xpert MTB/RIF QA system. The TB diagnostic network standards are based on criteria developed by the Global Laboratory Initiative (GLI) for ensuring the quality of acid-fast bacilli (AFB) smear microscopy⁵, by the African Society of Laboratory Medicine (ASLM) and the Association of Public Health Laboratories (APHL) for evaluating diagnostic networks⁶, and by USAID and partners for evaluating TB diagnostic networks in Nigeria and India⁷. The standards, associated QA activities and corresponding sections of this guide are described in Table 1.

⁵ TB Microscopy Network Accreditation. An assessment tool. Global Laboratory Initiative. 2013. http://www.stoptb.org/wg/gli/assets/documents/TB-Microscopy_Network_Accreditation_Web.pdf

⁶ Ondo, P. et al. A new matrix for scoring the functionality of national laboratory networks in Africa: introducing the LABNET scorecard. African Journal of Laboratory Medicine, 5, Oct. 2016. <http://www.ajlmonline.org/index.php/ajlm/article/view/498/712>

⁷ Albert, H. Essential standards for a TB diagnostic network. ASLM2016.

Table 1: Diagnostic network standards and key quality assurance activities

Diagnostic Network Standards	Key QA Activities
Structures & policies are in place that enable continuous, country-wide availability of free, quality assured diagnosis according to the national guidelines.	<p>Governance (Element 1)⁸</p> <ul style="list-style-type: none"> • Establish procedures & structures with clearly defined roles & responsibilities • Appoint, train & empower quality officers <p>Planning (Element 2)</p> <ul style="list-style-type: none"> • Conduct a situational analysis • Develop a prioritized action plan for phased implementation of the required QA activities • Adequately budget for QA activities
A minimum package of tests & quality standards is defined for each level of the TB diagnostic network.	<p>QA documentation (Element 3)</p> <ul style="list-style-type: none"> • Use standardized documents, records & forms for recording & reporting sample requests & results at all testing sites
Adequate numbers of competent, well-trained & motivated technical & managerial staff are available at all levels of the diagnostic network.	<p>Training & certification (Element 4)</p> <ul style="list-style-type: none"> • Adopt standardized curricula for trainings • Train at least two users per site; assess competency • Train sufficient advanced users to provide supervision & advanced troubleshooting
Inter-operable & inter-connected electronic recording & reporting systems are in place that generate reliable data that are monitored & analysed in real time.	<p>Data connectivity & remote monitoring (Element 5)</p> <ul style="list-style-type: none"> • Utilize remote monitoring systems to collect & analyse data relating to performance indicators, QA & supplies management
Testing is performed in a manner & in facilities that ensure the safety of the staff, customers, community & environment.	<p>A safe & functional testing site (Element 6)</p> <ul style="list-style-type: none"> • Assess each testing site for suitability and readiness prior to GeneXpert installation using a standardized checklist • Ensure that the site is not hazardous for the staff, patient, community or environment • Ensure that a good working environment is available
Testing is performed with state-of-the-art, well-maintained equipment & an uninterrupted supply of quality reagents & consumables.	<p>Supply chain (Element 7)</p> <ul style="list-style-type: none"> • Ensure uninterrupted supply of Xpert MTB/RIF supplies & reagents • Perform new lot testing on new batches of reagents <p>Equipment servicing and maintenance (Element 7)</p> <ul style="list-style-type: none"> • Ensure that all GeneXpert instruments undergo routine maintenance & calibration • Verify all instruments are fit for use at installation, after service or calibration, or after moving instruments
Continuous quality improvement targets all facilities within the network & includes quality indicator monitoring, external quality assurance & regular on-site supervision.	<p>Proficiency testing (PT) (Element 8)</p> <ul style="list-style-type: none"> • Enroll each testing site in a PT programme • Provide testing sites with timely feedback from PT events • Investigate incorrect PT results & take corrective actions <p>Site supervision (Element 8)</p> <ul style="list-style-type: none"> • Assess each testing site for readiness prior to GeneXpert installation using a standardized checklist • Make on-site supervisory visits on a regular basis (at least yearly) by competent personnel <p>Monitoring & evaluation (Element 9)</p> <ul style="list-style-type: none"> • Collect, analyse and report performance indicator data monthly for trends that may inform operational decisions • Review performance indicator data locally & nationally to inform overall programme planning & improvement

⁸ The element numbers correspond to the numbers of the sections in Part 1 and Part 2 of this guide that describe the activities needed to accomplish the standard.

Diagnostic Network Standards	Key QA Activities
<p>An efficient diagnostic-clinical interface allows for appropriate diagnostic tests to be ordered & performed, & ensures the timely linkage of diagnosed patients to appropriate care & treatment.</p>	<p>Strengthen the clinical-laboratory interface & the diagnostic cascade (Element 10)</p> <ul style="list-style-type: none"> • Provide training on all aspects of the diagnostic cascade that affects the quality of TB testing to all laboratorians, clinicians, nurses & other healthcare providers • Ensure that national testing algorithms are followed & that the correct test is ordered for each patient • Ensure that quality specimens are collected, properly labelled, correctly stored, & promptly transported to the testing site • Enforce the use of standardized test requisition forms; ensure that they are completed with all the required information • Report accurate results to clinicians & TB & MDR-TB treatment focal persons; include information on the interpretation of test results. Use standardized reporting forms • Monitor performance of the diagnostic cascade

From standards and procedures to implementation

A QA system targets all facilities within the diagnostic network (e.g., clinics, specimen collection and referral sites, testing laboratories, treatment centers, etc.) and all the pertinent steps in the diagnostic cascade. A comprehensive QA system includes standardized procedures (i.e., SOPs), document control, quality indicator monitoring, internal quality controls, external quality assessment, proficiency testing, regular on-site supervision, as well as timely feedback, corrective actions and follow-up.

Many countries have been implementing the Xpert MTB/RIF test for a number of years, with varying degrees of maturity of individual elements of QA. However, QA activities are often inconsistently implemented or are not documented. Also, data from QA activities are often not reviewed and used for decision-making and quality improvement. For example:

- Laboratories are enrolled in an external proficiency testing (PT) programme, but they do not receive feedback on their performance. As a result, no corrective action is taken in the poorly performing testing sites and they continue to generate poor-quality results.
- A country has recently implemented standardized training for GeneXpert users, but there is no participant training log. During supervisory visits, it is reported that many GeneXpert users are not certified as competent (see Section 4), calling the accuracy and reliability of test results into question.

This guide to operationalizing a QA system can be used by countries to prioritize and plan the implementation of a QA system to strengthen the quality of their Xpert MTB/RIF testing. The following parts and sections in this guide describe practical steps for the implementation of a system for ensuring the quality of Xpert MTB/RIF testing at all levels of the TB diagnostic network.

Part 1: National and Supervisory Levels focuses on establishing or integrating Xpert MTB/RIF QA activities into the TB diagnostic network in a country or region. This part covers the planning, implementation and monitoring of Xpert MTB/RIF QA at the central and supervisory levels.

Part 2: QA at Xpert MTB/RIF Testing Sites addresses key activities to be carried out at the testing sites to ensure the production of quality Xpert MTB/RIF results.

Each part is divided into sections, each dealing with one of the QA elements (Table 1) required for assuring quality Xpert MTB/RIF test results. Links to additional resources are provided at the end of the guide. Links to customizable checklists, forms, supporting documents, tools and job aids to assist with the implementation of QA activities are also provided. These templates can be customized as required.

Part 1: National and Supervisory Levels

Background

In many countries, implementation of national policies and procedures are coordinated at central level by the Ministry of Health (MOH), national TB programme (NTP) or national TB reference laboratory (NTRL). In some settings, particularly in large countries, these activities may be decentralized to the regional level. Commonly, the coordinating levels provide general guidance and tools for standardized QA activities. At the regional or district level, supervisory laboratories are responsible for the supervision of the QA activities and monitoring of the adherence to the procedures in testing sites.

Pillars of a Quality Assurance System

National Planning

- Governance
- Situational analysis
- Planning & budgeting

Procedures & training

- Quality procedures & documentation
- Training & certification
- Clinical–laboratory interface

Testing infrastructure & supplies

- Safe & functional site
- Equipment & supplies
- Data connectivity

Monitor impact

- Remote monitoring
- External quality assessment (EQA)
- M&E

At the national and supervisory levels, the key steps required to develop, implement and monitor a QA system include:

1. **Governance:** establish procedures and structures with clearly defined roles, responsibilities, linkages and focal persons at the national, regional and district levels to plan, implement, manage and monitor a CQI-based QA system for Xpert MTB/RIF testing.
2. **National strategic planning:** i) conduct a situational analysis to determine the current quality of diagnosis using Xpert MTB/RIF and the status of implementation of Xpert MTB/RIF QA activities; ii) use the data from the situational analysis to design a QA system customized to the country's situation; iii) engage private sector and implementing partners; iv) develop a prioritized action plan for phased implementation of the required QA activities including measuring impact of the plan; v) adequately budget the activities and set a time line for implementation.
3. **Quality procedures and documentation:** develop, standardize and disseminate the SOPs, forms, documents and records that will be needed to ensure the quality of testing.
4. **Training and certification:** develop and implement a training (initial and refresher training), competency assessment and certification program to ensure the availability of qualified laboratory staff.
5. **Data connectivity:** use remote monitoring systems where possible to collect and analyse data relating to performance indicators, QA, procurement and supplies management.
6. **A safe and functional testing site:** assess each testing site for readiness prior to GeneXpert installation using a standardized checklist and upgrade facilities and procedures as needed to create a safe and functional working environment.
7. **Equipment and supplies**
 - a. **Equipment service and maintenance:** implement a system to ensure that all GeneXpert instruments undergo routine maintenance and recalibration according to the manufacturer's recommendations.
 - b. **Quality supplies:** implement a system to ensure uninterrupted availability of quality-assured reagents at the testing sites.

8. **External quality assessment (EQA):** develop and implement an EQA program that includes quality and performance indicator monitoring, proficiency testing, regular on-site supportive supervision, and timely feedback, corrective actions and follow-up.
9. **Monitor performance** of Xpert MTB/RIF testing and of the QA/CQI system: establish an M&E framework; monitor and evaluate appropriate performance indicators; collect and analyse the data, using remote monitoring where possible; and use the data for decision making.
10. **Clinical-laboratory interface:** strengthen the clinical-laboratory interface to ensure that national testing algorithms are followed, the correct test is ordered for each patient, quality samples are collected and submitted to the laboratory, accurate results are reported to the clinician, results are correctly interpreted and patients are promptly placed on appropriate therapy.

Detailed guidance for implementing a functional QA system is provided in the subsequent sections for each element (however, the order is not meant to be a prescriptive step-by-step one, i.e., complete element 1 before element 2, etc.). As part of the strategic planning process (Element 2), countries will prioritize activities and develop a phased implementation plan and time line. Such plans should focus on providing the appropriate structures (e.g., quality teams, data monitoring units), support (e.g., training, supportive supervision, constructive feedback) and monitoring and evaluation processes (e.g., collection and regular analysis of key performance data) needed to implement a functioning CQI process. For example, implementing a PT program without implementing a corresponding system of timely feedback, corrective actions and supervisory visits will greatly limit the usefulness and impact of PT on the quality of testing.

Element 1. Governance

It is important to note that while these guidelines focus on Xpert MTB/RIF QA programs, governance structures already exist for other programs such as HIV, TB, QA and biosafety of laboratory services. Xpert MTB/RIF QA activities should be incorporated wherever possible into existing governance structures with clear lines of communication and reporting.

The governance structure at the national and supervisory level will likely vary by country. In many countries, the central level provides policies, guidance and tools for standardized QA activities, while the regional and district levels operationalize and supervise the QA activities and monitor adherence to the procedures. In turn, data collected at the testing sites are reviewed regionally and centrally and used to inform and update policies and procedures, thereby closing the CQI cycle (Figure 3).

How do I establish a governance structure?

- Establish a working group on Xpert MTB/RIF QA with appropriate authority and reporting structure to senior management within MOH to develop or review the governance structure of the Xpert MTB/RIF QA system
- Assign roles and responsibilities (see Table 2). Develop terms of reference
- Identify the gaps in the capabilities required to perform the assigned roles and responsibilities. As necessary, develop the needed capabilities
- Develop an organogram of the governance structure that clearly delineates relationships and lines of supervision
- Establish lines of communication and reporting within the governance structure. Map out the flow of information and identify points of contact

Activities at a glance

- Establish a governance structure
- Establish National QA Office or Coordination team with a National Laboratory QA Officer
- Establish lines of communication across the diagnostic network

Figure 3: Continuous quality improvement cycle

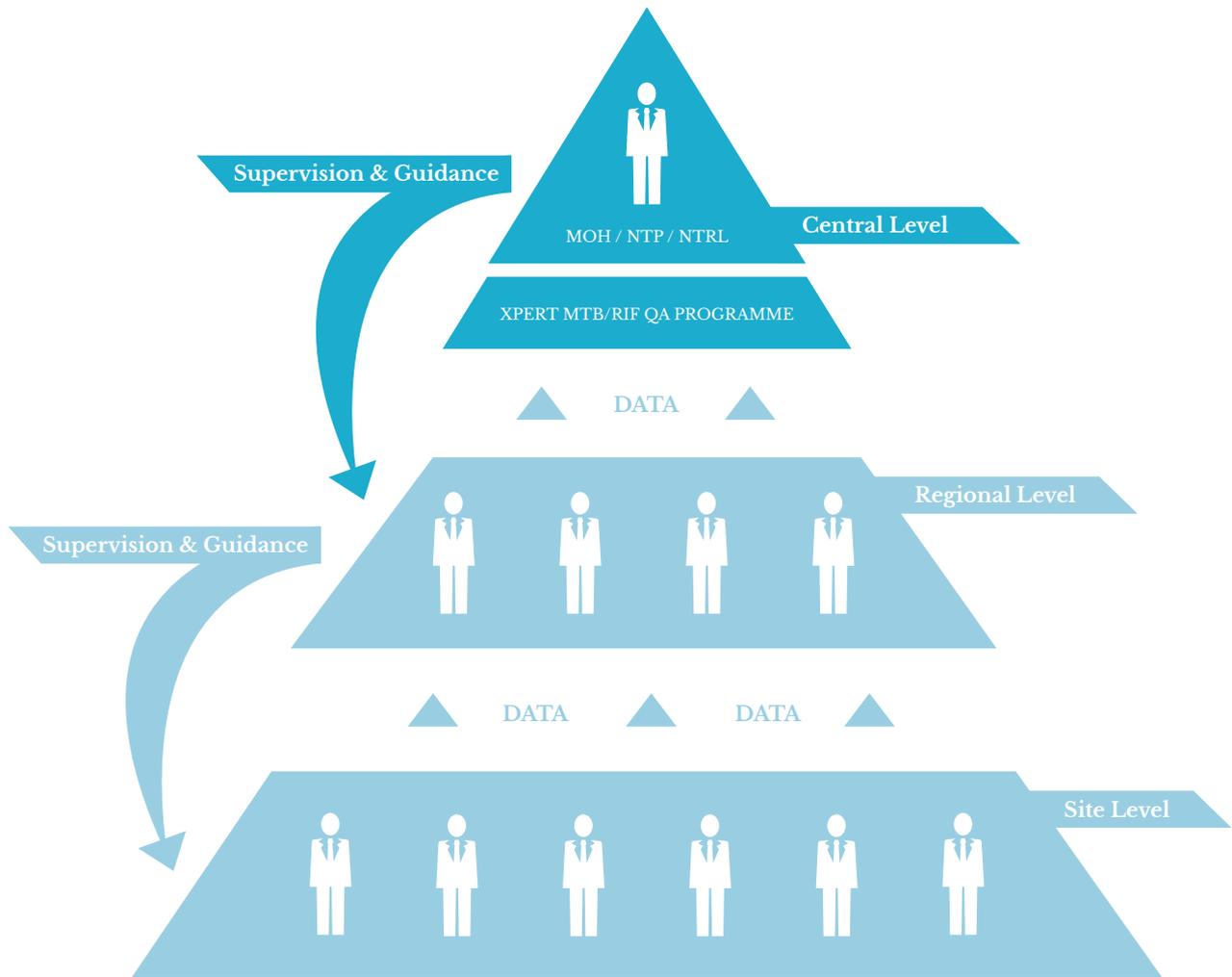


Table 2. Example of a governance structure with defined roles and responsibilities

Entity	Roles and responsibilities
MOH	<ul style="list-style-type: none"> • Establish the CQI strategy, vision and mission • Establish a National QA office or Coordination team and appoint a National Laboratory QA Officer who works closely with the National Clinical Services QA Officer • Engage implementing partners and private sector in QA processes • Establish Laboratory Technical Working Group (TWG) to assist in the formulation and implementation of national policies and procedures • Oversee a process to develop Xpert MTB/RIF EQA policies and procedures • Oversee a strategic planning process that includes <ul style="list-style-type: none"> – a situational analysis – design of a QA system customized to the country’s situation – development of a costed, prioritized action plan for phased implementation with targets and time line • Allocate an adequate budget for QA activities
Other Ministries	<ul style="list-style-type: none"> • Ministry of Education: ensure that CQI and QA knowledge forms part of the core curriculum of academic and training institutions and part of the scopes of practice of relevant healthcare professionals as appropriate (laboratory, doctors, clinical officers, nurses, programme managers, etc.) in collaboration with the relevant statutory Professional Councils • Ministry of Finance: manage financial issues related to laboratory programs
NTP	<ul style="list-style-type: none"> • Develop and implement the National Strategic Plan for TB Control (NSP) • Oversee the TB diagnostic network • Participate in the development of Xpert MTB/RIF QA policies and procedures • Enforce TB QA policies and procedures throughout the TB diagnostic network, in particular focusing on pre- and post-analytical processes • Provide training, guidance and technical assistance • Oversee monitoring and evaluation programmes
NTRL	<ul style="list-style-type: none"> • Provide technical input for the development of Xpert MTB/RIF QA policies and procedures • Enforce TB QA policies and procedures throughout the TB laboratory network • Provide guidance and technical assistance • Develop, standardize and distribute the SOPs, forms, documents and records needed to ensure the quality of testing • Develop, implement and manage systems to: <ul style="list-style-type: none"> – train, assess competency and certify laboratory workers for Xpert MTB/RIF testing – ensure that all GeneXpert instruments undergo routine maintenance and recalibration according to the manufacturer’s recommendations – ensure uninterrupted availability of quality-assured reagents at the testing sites – remotely collect and analyse data relating to performance indicators, QA and procurement • Coordinate the QA activities and provide samples for proficiency testing • Supervise and manage regional and district facilities responsible for supervising testing sites • Establish an M&E framework; monitor and evaluate performance and quality indicators; collect and analyse the data; and use the data for decision making
Regional and district supervisory laboratories	<ul style="list-style-type: none"> • Enforce TB QA policies and procedures in the testing sites • Conduct supervisory visits of testing sites and provide supportive supervision • Evaluate QA indicators, provide timely feedback, recommend corrective actions and follow-up on corrective actions • Provide training, guidance and technical assistance to testing sites • Collect and compile data on performance and quality indicators and report to central level
Health Facility Quality Committee	<ul style="list-style-type: none"> • Ensure accountability, leadership and governance at health facility level • Provide oversight and coordination for QA and CQI activities at the institution • Provide regular progress reports to the regional QA structure • Translate policy into practice

Element 2. Strategic planning

The strategic planning process should include 1) a situational analysis to determine the current status of Xpert MTB/RIF QA activities; 2) design of a QA system customized to the country's situation; 3) development of a costed prioritized action plan for phased implementation of the required QA activities with targets and a time line; and 4) allocation of an adequate budget and resources for the implementation and annual operation of QA activities.

What you need to do

2.1. Understanding the current quality of the Xpert MTB/RIF testing network

A situational analysis should be conducted in order to i) determine which Xpert MTB/RIF QA activities are being implemented at central, supervisory site and testing site levels, ii) measure their impact on testing quality and iii) identify the gaps in providing quality assured Xpert MTB/RIF results. A situational analysis should be conducted as an initial step in developing or revising a QA system and periodically (e.g., every 3 to 5 years) thereafter to evaluate progress.

A strong commitment from the MOH and implementing partners is essential if QA activities are to be successfully implemented. The activities must align with applicable existing national, regional, and testing site priorities. The MOH/NTP/NTRL should delegate the responsibility for conducting the situational analysis and planning of the Xpert MTB/RIF QA activities to a team led by a suitably qualified individual.

Who should lead the situational analysis?

- The QA focal person should coordinate the situational analysis, in collaboration with an implementing partner where needed, this may be the National Laboratory QA Officer, GeneXpert focal person, NTRL Quality Officer or other delegated individual or team identified by MOH/NTP/NTRL.

How do I select the team?

- Assemble a team that includes representatives of:
 - a. MOH (laboratory and clinical services)
 - b. NTRL
 - c. Xpert MTB/RIF implementing partners
 - d. Testing site managers
 - e. Data analytics
- Make a list of stakeholders to be consulted during the process. These should include:
 - a. Programme managers
 - b. Regulatory bodies
 - c. Private sector
 - d. Clinical staff
 - e. Other local experts, such as implementing partners
- Identify key individuals who may contribute to establishing or integrating the QA activities
- Set up a meeting with the key stakeholders. Consider using existing meeting structures (e.g., MOH quarterly meetings) to engage individuals
- Introduce the QA activities and QA system to the key stakeholders
- Determine stakeholder willingness to participate in the QA team

Activities at a glance

- Assemble the team
- Define roles and responsibilities
- Conduct situational analysis
- Develop a strategic plan to implement and sustain the QA system
- Set the budget and time line

What does the team do?

- Coordinate, conduct and report results of a situational analysis
- Advise MOH/NTP/NTRL on strategies to implement Xpert MTB/RIF QA activities
- Develop action plans that ensure all aspects of quality are met
- Oversee the rollout of the QA activities
- Assess the impact and scale-up of the Xpert MTB/RIF QA activities

How do I plan the situational analysis?

- Use the Situational Analysis Checklist and Xpert MTB/RIF Continuous Quality Improvement (Xpert CQI) Assessment Checklist for Testing Sites (ACTS)
- Arrange a planning meeting to review the checklists
- Select the testing sites to be included in the analysis (see the box below)
- Assign a timeframe for conducting the assessment
- Assign responsibilities to stakeholders
- Provide the necessary data collection tools and sensitize all stakeholders responsible for data collection on the checklist and means for data verification
- Supply stakeholders with a list of documents (e.g., policies, reports, forms, etc.) that need to be collected as part of the assessment
- Designate the responsibility to compile the situational analysis report to members of the Technical Working Group, sub-group or other designated persons

How do I select the testing sites?

- Divide the country districts into areas defined by difficulty to access, geography, epidemiologic situation or other criteria
- Randomly select one district per area
- Select all the testing site(s) located in the identified districts for analysis(consider sampling if there are a large number of sites in any selected districts)
- To assess the entire diagnostic network, include (even if they are not contained in the selected districts):
 - facilities at different levels of the health system
 - private sector facilities
 - at least one testing site from each major implementing partner
 - facilities that refer and receive specimens
 - non-laboratory point-of-care testing sites

What should be included in the situational analysis report?

- Introduction and objective: State why Xpert MTB/RIF QA activities are needed and define activity objectives
- Situational analysis: State the need for the situational analysis; explain how the situational analysis was conducted; and describe who and what was assessed
- Findings: Report the findings of the situational analysis. Consider organizing the findings according to the key steps in the roadmap for the national and supervisory levels and for the testing site
- Recommendations: Outline the problems that were identified during the situational analysis, how and by whom they may be addressed and provide a time line for resolution. Budget: Include a detailed budget for the proposed activities and the resources required to address the identified gaps and implement recommendations

The situational analysis report should describe gaps identified, recommendations for how to implement QA activities and propose a time line for implementation based on the current level of implementation (e.g., some testing sites will already have implemented a high proportion of recommended activities while others have not). Recommendations should address gaps at the national and supervisory levels and at the testing site level. The report should be reviewed and endorsed by the Xpert MTB/RIF Technical Working Group (TWG) before presenting the report to senior management at MOH/NTP. An excerpt from an example situational analysis checklist with commonly observed outcomes and recommendations, can be found in the Supporting documents/forms and templates⁹.

Based on the country governance structure, the responsibility for prioritizing implementation of the report recommendations and developing an operational plan may be at national level or may be delegated to the regional level. In any case, priorities should be agreed at national level by the TWG and this body should receive regular updates on progress towards implementation (see Element 9). It is important to include implementing partners and all stakeholders involved in implementation, particularly with respect to mobilization of resources and technical assistance.

2.2. Prioritize interventions

The outcome of a situational analysis informs the implementation of QA activities at the central, regional, testing site and clinical site level. Some activities might or might not have already been implemented, some with and without QA components. The phased implementation plan and time line should focus on providing the appropriate structures (e.g., quality teams, data monitoring units), support (e.g., training, supportive supervision, constructive feedback) and monitoring and evaluation processes (e.g., collection and regular analysis of key performance data) needed to implement a functioning QA process. For example, implementing a PT program without implementing a corresponding system of timely feedback, corrective actions and supervisory visits will greatly limit the usefulness and impact of the PT program on the quality of testing.

Depending on the nature of a QA activity, it may be implemented simultaneously at all testing sites (e.g., establishing a national PT programme) or may rely on individual site level implementation (such as conducting routine maintenance tasks), and therefore the progress will depend on site level motivation, capacity and resources. Monitoring of indicators at a national level will highlight such differences and should help in addressing challenges in implementation, and in learning from best practices in well-performing sites or regions.

Depending on available human resources and funding, countries may decide to prioritize implementation of certain activities that could rapidly produce improvements in the quality of testing with a limited investment. That is, certain activities require limited resources, beyond initial development of data collection tools and training of staff. Others may require national level action and decisions, such as development and availability of national training curricula and recording and reporting forms. As such, individual sites may rely on higher level input in order to meet these criteria.

Countries may focus on implementation of all QA components and monitoring of all indicators at a selected number of sites initially, and once successfully implemented, go on to develop a plan for scale-up to all sites. Alternatively, countries may work on establishing a selection of QA activities at all sites, then expanding the range of QA activities once the initial implementation has been completed. Either way, an important focus should be on clinical and programmatic indicators and process indicators, and not just on laboratory performance indicators.

⁹ The example contains excerpts from a situational analysis checklist, and is not fully inclusive. The situational analysis checklist must be used to provide a comprehensive overview of Xpert MTB/RIF quality assurance activities.

2.3. Set the budget and time line

Successful implementation of QA activities for the Xpert MTB/RIF test will require financial commitment from MOH and NTP and the testing sites, with support of the implementing partners. In some countries, funding will also be allocated by state or regional governments and by institutions. A budget should be developed to address both the implementation of recommendations from the situational analysis and the implementation and sustainability of the QA activities thereafter. A GeneXpert costing tool is available on the FIND website:

<https://www.fnndx.org/implementation-resources/#tb>

Table 3: Budgetary considerations for QA activities

QA activity	Budgetary considerations
Generate QA documentation	<ul style="list-style-type: none"> • Preparation & printing of standardized test request & results reporting forms • Preparation & printing of standardized logbooks • Regular review of all Xpert MTB/RIF documents (SOPs, checklists, etc.) based on national requirements
Remote monitoring	<ul style="list-style-type: none"> • Costs associated with providing a remote monitoring system in-country
Maintain & service equipment	<ul style="list-style-type: none"> • Site upgrades, calibration kits and warranty costs
Strengthen the supply chain	<ul style="list-style-type: none"> • Material cost per test, including but not limited to Xpert MTB/RIF test reagents, consumables, sample collection items, printing paper, etc. Additional equipment costs, such as printer, computer, printer cartridges, shipping & courier costs
Conduct training, competency testing & certification	<ul style="list-style-type: none"> • Preparation of training materials for each of the QA activities: <ul style="list-style-type: none"> – Training of Trainers (TOT) – Training of GeneXpert users & advanced users • Costs associated with facility and classroom-based training including travel, accommodation, printing materials, venue hire & catering. Personnel wages are excluded, as these are not expected to add additional costs to the activity • Costs of competency testing • Costs of refresher trainings and trainings of test updates
Conduct onsite supervisory visits	<ul style="list-style-type: none"> • Preparation of checklists for supervision and troubleshooting • Site visits (including printing checklists, travel to sites, daily subsistence allowance for visits to remotely located sites)
Implement PT testing	<ul style="list-style-type: none"> • Costs associated with management of externally produced panels: consider distribution of panels, analysis of reports, visits to participating sites • Costs associated with providing PT panels produced in-country. Costs do not include human resource and laboratory setup costs: <ul style="list-style-type: none"> – Determine the capacity that exist in-country to manufacture panels – Map out financial resources that will be required: consider preparation, dissemination, collection, analysis and reporting of data, visits to sites participating in PT – Include costs associated with establishing the capacity in country including any needed trainings, technical assistance – Include costs associated with external quality assurance and internal quality control of the PT panels

Element 3. Quality procedures and documentation

Without accurate and complete documentation, the quality of Xpert MTB/RIF test results may be compromised. The documentation must address activities throughout the diagnostic cascade including documentation for clinical activities (e.g., specimen collection and referral) and laboratory activities.

Standardized documents and forms should be developed at the national level and distributed to all testing sites in order to assure conformity

Standardization of documents and forms will take time. Therefore, plan the implementation of standardized documentation in a systematic manner.

SOPs, forms and other documents must be up-to-date, accurate and readily accessible at all testing and participating clinical sites.

A document control system is needed to ensure regular review of quality management documents (e.g., SOPs) and to ensure the correctness of the documentation that supports laboratory testing.

How do I generate QA-related documentation?

- Review the list of required documents (see above)
- Review the situational analysis - what needs to be written/revised/ standardized?
- Assign writing and review responsibilities
- Review the revised documents for approval
- Provide training in the use of the documents
- Disseminate to the testing sites
- Review documentation implementation during supervisory visits

How do I create a document control system?

- Write an SOP for Document Control including the Document Retention List
- Create a Document Retention List: determine storage time and location for all types of documents used
- Make a Document Control Log
- Design a Document Revision Form
- Add a front page to each quality document used in the laboratory to track versions
- Create folders for storing SOPs at the most convenient locations (at the testing site) for staff to have access to the SOPs when needed
- Develop personnel files for all staff members to document their knowledge of the correct documents
- Provide training and roll out the document control system

Activities at a glance

- Generate QA documents
- Disseminate QA documents
- Implement a document control system

Table 4: SOPs, forms, and other documents that must be available at all testing sites

Resource	Description
National TB Diagnostic Algorithm	Describes a step-by-step protocol for diagnosis of TB at healthcare facilities
Document Control SOP http://www.gliquality.org/activities/2/33	Describes the procedures to ensure that the correct documentation (e.g., SOP) is used for laboratory testing
Specimen Collection & Transport SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedures to be followed to ensure collection of good quality specimens & safe, rapid transport of specimens to the testing site
Test Requisition Form	Form for requesting Xpert MTB/RIF testing
Laboratory Register	Register for recording patient, specimen, & test information
Specimen Referral SOP & forms	Describes a procedure for specimen referral & provides the necessary forms
Xpert MTB/RIF test SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedures for performing the Xpert MTB/RIF test
Xpert MTB/RIF Ultra test SOP ¹⁰	Describes the procedures for performing the Xpert MTB/RIF Ultra test
Proficiency Testing (PT) SOP	Describes the general principles and procedure for testing PT samples, resulting, reporting, and corrective action for unacceptable results
GeneXpert maintenance log	Form for recording GeneXpert maintenance tasks
Temperature monitoring records https://www.finddx.org/implementation-resources/#tb	Form for recording daily temperature monitoring in testing and kit storage areas
Non-conformity & corrective action log https://www.finddx.org/implementation-resources/#tb	Form for capturing non-conformities and corrective actions
Waste management SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedure of safely disposing consumables and Xpert MTB/RIF reagents (may be included in a Biosafety SOP)
Spill management SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedure to follow in the event of a biohazard spill at a testing site (may be included in a Biosafety SOP)
Xpert MTB/RIF WHO reporting codes http://www.who.int/tb/publications/definitions/en/	Describes the standard WHO reporting codes for reporting Xpert MTB/RIF test results
Xpert MTB/RIF performance indicator reporting form	Form for capturing Xpert MTB/RIF performance indicator data
Xpert MTB/RIF test reporting form http://www.who.int/tb/publications/definitions/en/	Form for reporting Xpert MTB/RIF test results to clinicians
PT failure investigation and corrective action form	Form for documenting the results of the investigation of PT failures and remedial action taken

¹⁰ Xpert MTB/RIF and Xpert MTB/RIF Ultra package inserts can be requested from: <http://www.cepheid.com/en/support/package-inserts-uk/package-insert-entry-form>

Element 4: Training, competency assessment and certification

Training, competency assessment and certification are critical components of providing quality assured Xpert MTB/RIF test results. The implementation of the Xpert MTB/RIF test in a quality assured manner requires training beyond the steps required to carry out the test. Manufacturer-supplied, on-site training following installation is often too short to cover QA activities. The testing site manager must ensure that users receive adequate training in QA and other key aspects of testing.

To date, most countries have relied upon national trainings, which have generated well-trained users and advanced users. However, testing sites have found that this system does not always guarantee sufficient numbers of GeneXpert users. In some settings, national training is not offered frequently enough or trained users may be lost due to staff attrition, both situations leading to inadequate testing coverage. One proven solution is to develop capacity of testing sites to conduct training and competency assessment of their staff using nationally developed guidelines and training materials. The evolving role of the national level is to develop national training curriculum, to provide implementation guidance, and to monitor training and competency assessment activities.

Activities at a glance	
<input type="checkbox"/>	Customize training package
<input type="checkbox"/>	Conduct training
<input type="checkbox"/>	Perform competency assessments

What you need to do

4.1 Develop a national training curriculum for the Xpert MTB/RIF test

- The training programme should be standardized by the MOH/NTP and include training curricula for trainers, users and advanced users. A significant portion of the training should be devoted to hands-on training that incorporates quality assurance elements.
- All training (whether at national or site level) should use a single nationally developed curriculum.
- Training of clinical healthcare workers is also critical in ensuring quality Xpert MTB/RIF test results. Clinical healthcare workers must understand how to interpret Xpert MTB/RIF test results, as well as the limitations of the test (http://www.stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF_Ultra.asp).
- Training should be provided for programme and laboratory managers and their implementation partners on key topics for diagnostic network strengthening including implementing a QA system (http://www.stoptb.org/wg/gli/TrainingPackage_Programme.asp).
- A Training-of-Trainers (TOT) approach should be used to establish and sustain a team of competent local trainers and mentors. Competency of trainers and mentors should also be assessed by master trainers and mentoring provided over time to develop all necessary skills required to independently manage the programme.
 - The GLI training package contains modules (Table 5) that can be customized and adapted to include country-specific elements
 - GeneXpert Users: Modules are selected and customized to provide testing site personnel with the skills and knowledge to perform the Xpert MTB/RIF test, understand the testing algorithms, interpret Xpert MTB/RIF test results, maintain the GeneXpert instrument, perform quality assurance procedures, and supply the NTP with relevant performance indicators.
 - Module 12 of the GLI training package: It is dedicated to QA of the Xpert MTB/RIF test. This module needs customization once country-specific performance indicators and documentation have been identified.
 - GeneXpert Advanced Users: Modules are selected and customized to provide advanced users with the skills to co-ordinate Xpert MTB/RIF test implementation activities, such as supervisory visits, competency assessments and troubleshooting in their regions.

- Criteria for competency should be agreed and documented, and only training participants who meet the criteria should be certified as competent.
- Certificates should be issued to competent users and training reports provided to MOH/NTP for all trainings.
- All implementing partners should use the National Training Curriculum for the Xpert MTB/RIF test for training users.
- A register of certified users and advanced users should be kept by MOH/NTP.
- Criteria for retraining at regular intervals and for personnel who do not pass the initial assessment should be determined.

How do I develop a training and certification programme for Xpert MTB/RIF?

- Review the situational analysis to determine how many trainers (or potential trainers) are available compared with country need for training
- Review the situational analysis to determine the number, level and location of users who need training
- Review GLI training materials and develop or revise training materials. Have training materials reviewed and approved by MOH
- Develop a register of certified users, advanced users and trainers and assign responsibility for managing register
- Conduct a TOT. Consider using local or international trainers from implementing partners if there is no in-country expertise to conduct the training
- Conduct GeneXpert user trainings and competency assessments. Consider using centralized trainings or training on testing sites
- Identify potential advanced users from the cadre of trained GeneXpert users
- Conduct advanced user training and competency assessments
- Deploy the advanced users to introduce regular competency assessments at testing sites
- Review training records and participants' performance during supervisory visits and conduct refresher training where needed

In situations where nationally conducted Xpert user's training is not sustainable, a standardized training curriculum for training of users at the testing sites may be developed. Onsite training may be conducted by trained users with documented competency level 4 or 5 and by supervisors during supportive supervisory visits at the testing sites. A standardized, approved training checklist should be used to document training and to ensure all technical and QA activities were included.

4.2. Perform competency assessments

- Competency assessments should be performed after training and periodically thereafter (e.g., annually). Competency assessment should include assessment of skills for performing on-site supervision, training and mentoring as well as performing the test. Templates for recording the results of a competency assessment for a GeneXpert user and an advanced user are available in the Supporting Documents/forms and templates.

Table 5: Available training packages

Contents of the GLI training package for Xpert MTB/RIF (Ultra)	
Module 1	TB Biosafety
Module 2	Specimen Collection & Referral
Module 3	Procurement & Inventory Management
Module 4	Recording & Reporting Results
Module 5	Monitoring Quality Indicators
Module 6	Quality Assurance of the Xpert MTB/RIF (Ultra)
Module 7	External Quality Assurance
Module 8	Clinical Guide to Xpert MTB/RIF (Ultra)

http://www.stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF_Ultra.asp

Contents of GLI training package: Programme modules for diagnostic network strengthening	
Module 1	TB Diagnostics: Global Policies and Strategies
Module 2	Implementing TB Diagnostics: Practical Considerations
Module 3	Plan and Establish a Sample Referral Network for TB Diagnosis
Module 4	Plan and Implement a Quality Assurance Programme
Module 5	Plan and Implement Connectivity Solutions
Module 6	Monitor and Evaluate Your Programme
Module 7	Funding Your Programme
Module 8	Plan an Integrated Diagnostic Approach

http://www.stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF_Ultra.asp

Element 5. Data connectivity and remote monitoring

Diagnostics connectivity refers to the ability to connect diagnostic test devices that produce results in a digital format, such as GeneXpert instruments, in such a way as to transmit data rapidly and reliably to a variety of users. Key features of the systems are the ability to remotely monitor performance, conduct QA and manage inventory. With remote monitoring, designated persons can use any internet-enabled computer to access the software platform, providing them with an overview of the facilities, devices and commodities in their network. For example, the head of a supervisory laboratory or other authority can easily see how many tests are being performed and where; what are the results; and which sites are underperforming or experiencing abnormal results or errors, which may highlight a need for troubleshooting, device repairs, targeted on-site supervision, or retraining of technicians. Software can track consumption and inventory to avoid stock outs and expiring cartridges as well as potentially identify commodity lots or specific instruments with poor performance and abnormal error rates for QA purposes and can provide a highly cost-effective way to ensure proper functioning of a diagnostic device network.

Activities at a glance

- Select a data connectivity solution
- Connect all GeneXpert instruments
- Prepare SOPs and train users

Data can also be transmitted automatically to 1) clinicians and patients which allows for faster patient follow-up, 2) laboratory information management systems or electronic registers, reducing staff time and the chance of transcription errors, and greatly facilitating monitoring and evaluation processes and 3) the NTP to assist with surveillance of trends on disease or resistance patterns as well as enhance the capacity of NTPs to generate performance indicators and to provide the data needed for several of the top 10 indicators of the End TB Strategy. Because of the promise to improve recording, reporting and monitoring of data and performance indicators, diagnostics connectivity has been incorporated into two of the indicators for laboratory strengthening under the End TB Strategy:

- Indicator 4: all sites that use WHO-recommended rapid diagnostics should be transmitting results electronically to clinicians and to information management systems using data connectivity solutions no later than 2020
- Indicator 9: remote monitoring via data connectivity solutions should be used to monitor key performance indicators at all sites that use WHO-recommended rapid diagnostics no later than 2020

Diagnostics connectivity solutions, especially for Xpert MTB/RIF testing, are the way of the future. Countries should give high priority to investing in developing and maintaining such systems and in training personnel to operate them and to use the data generated for decision making. Detailed information on the design and implementation of a diagnostics connectivity solution may be found in the *GLI Quick Guide to TB Diagnostics Connectivity Solutions*.¹¹



Diagnostics connectivity solutions typically comprise: 1) a connectable diagnostic device that produces electronic data, 2) a software platform that receives and interpret and displays data and 3) a means to transmit data from the device to the software platform and to a server. Systems have been developed by Cepheid, USA (C360), SystemOne (GxAlert™/Aspect™), Savics (DataToCare™) and Blue Frontier (Connected Diagnostics Platform). See *TB Connectivity Solutions* for a comparison of the available systems. Importantly, the developers are collaborating to ensure the compatibility of the systems. The systems connect GeneXpert instruments to central in-country servers or cloud-based servers via the internet or short message service (SMS). Instrument data can be accessed via web-based dashboards. The software can usually be configured so that subsets of data can be securely made available to those who need access to it. Security protocols also protect the privacy of the patient.

However, remote monitoring systems only help with collection of instrument-related data, and systems need to be put in place to collect and review other data, as described above. Nonetheless, they can greatly simplify and improve speed and quality of test data collection and access to automated reports at testing site, regional or national level.

¹¹ GLI Quick Guide to TB Diagnostics Connectivity Solutions. 2016. <http://www.stoptb.org/wg/gli/gat.asp>

How do I select a data connectivity solution?

- Conduct an in-country assessment of existing systems and infrastructure (both laboratory and connectivity). Technical assistance from a diagnostics connectivity expert may be needed. Key considerations include:
 - Is on-site internet service or 2G/3G cellular services available and sufficiently stable for the remote monitoring system?
 - What hardware and software will need to be installed and maintained at the testing site?
 - Who will have access to the data?
 - What training will be required for testing site staff to access the system? How will data be secured?
 - How, and at what frequency, is the system backed-up?
 - What are the associated costs of implementing and maintaining a remote monitoring system (e.g., internet access charges, information technology support, software licenses)?
- Based on the assessment, develop recommendations for the planned diagnostic connectivity solution and data needs
- Develop a costed roadmap
- Develop an operational budget that provides for:
 - Project management, data monitoring and supervision costs
 - Remote or in-country technical support, IT-support and updates, costs
 - Running costs for connectivity, e.g., monthly mobile data costs, server hosting, etc.

How do I connect all GeneXpert instruments?

- Determine if an internet-based or cellular systems-based solution will be used
- Install all needed hardware and equipment at each site, e.g., routers, modems, server, or SIM cards and establish maintenance plans
- Set up the connectivity solution at each site, technical assistance from the diagnostics connectivity solutions provider may be needed
- Establish units at the national, regional and local level to systematically monitor data on a weekly or biweekly basis
- Develop SOPs for access, reporting, data entry, data security and data back-up

How do I train users?

- Conduct implementation workshops and trainings that include data collection, data use and management and day-to-day operations of connectivity solution
- Provide initial training for new users and refresher training for existing users as needed

How do I monitor and evaluate a diagnostics connectivity system?

- Develop or adopt objectives, outcome measures, impact indicators, process indicators and performance indicators for the diagnostics connectivity systems
- Routinely collect and analyze the data to inform connectivity management and inform policy

Element 6. A safe and functional testing site

Failure to provide a safe and functional work environment can impact the quality of testing in several ways including:

- An unsafe testing site is a hazard to staff, patients and the environment
- In an unsecure testing site, test results may be delayed if there is equipment failure or theft
- Testing sites that do not maintain uninterrupted power, optimal working temperature and a clean environment can have equipment failures and high error rates that delay reporting and waste reagents

The selection of which sites will conduct Xpert MTB/RIF is usually directed by the NTP or NTRL and is based on factors such as the testing workload, the efficiency of referral networks and patient access to services. The Xpert MTB/RIF testing sites may be located in a peripheral clinic, district laboratory, or a high-throughput reference laboratory.

In addition to evaluating new sites, existing testing sites should also be regularly assessed for providing a safe and functional testing site using a standardized checklist.

What you need to do

As part of the QA process, each testing site should be evaluated for readiness using a standardized checklist¹² prior to the installation of the GeneXpert instrument and any testing of clinical specimens. Key infrastructure requirements are:

- a stable and continuous electrical supply
- an uninterrupted power supply (UPS) that will last a minimum of two hours to allow completion of a run
- an ambient temperature of 15–30°C in the room where the instrument is used (humidity control may also be needed)
- a clean environment with little dust
- adequate storage space for the cartridges with a consistent temperature of 2–28°C, monitored daily
- security to protect against theft of the instrument or computer
- adequate ventilation to meet WHO biosafety requirements
 - when appropriate microbiological techniques are used, processing of specimens for the Xpert MTB/RIF assay may be carried out on an open bench in an **adequately ventilated** area.
 - when the climate or use of air conditioning prevents the use of natural ventilation (e.g., from open windows), mechanical ventilation systems may be needed to provide an inward flow of air without recirculation in the room or the use of ventilated workstations or certified biosafety cabinets may be needed to ensure a safe working environment.
- appropriate facilities and equipment (e.g., autoclaves or incinerators) to safely dispose of biohazardous waste

Activities at a glance

- Assess each testing site for readiness
- Upgrade facilities as needed to create a safe functional work environment
- Regularly assess existing testing sites for safety and functionality

¹² Xpert pre-installation checklist. https://www.finddx.org/wp-content/uploads/2016/03/Pre-installation-checklist_10-2014.pdf

Similarly, the sites should be assessed to determine if all the required policies and procedures (e.g., SOPs for waste disposal) for safely conducting the Xpert MTB/RIF test are in place.

If the Xpert MTB/RIF testing site does not meet the infrastructure requirements, the national and supervisory levels should work with the testing sites to upgrade facilities and procedures to create a safe and functional working environment.

How do I create a safe and functional testing site?

- Have an experienced assessor evaluate the readiness of each testing site using the Xpert pre-installation checklist (https://www.fnnddx.org/wp-content/uploads/2016/03/Pre-installation-checklist_10-2014.pdf)
- Pay particular attention to the required electrical supply, ambient and storage conditions, physical security, biosafety and waste disposal
- As necessary, work with the facilities to upgrade infrastructure and procedures and provide training in safe working practices
- Regularly assess existing sites by an experienced assessor using the Assessment Checklist for Testing Sites (ACTS). This may be done as part of a supervisory visit

Element 7. Equipment and supplies

The GeneXpert is a precision instrument that requires regular maintenance to ensure that it provides accurate and precise results. A robust inventory system is required to monitor Xpert MTB/RIF cartridge consumption. Accurately forecasting the Xpert MTB/RIF test supply needs reduces the risk of an interruption in service due to shortage of reagents. Failure to maintain an adequate, uninterrupted supply of quality-assured reagents can affect quality because 1) stock-outs result in delayed testing and delayed reporting of results and 2) use of poor quality or expired reagents can result in high error rates and inaccurate test results.

What you need to do

7.1. Equipment service and maintenance

Without regular maintenance and servicing, the GeneXpert instrument cannot generate accurate and reliable Xpert MTB/RIF test results:

- All GeneXpert instruments must be evaluated as being “fit for purpose” through verification with known positive and/or negative material prior to commencing testing of clinical specimens. Instrument verification is conducted at installation, after service or calibration, or after moving instruments.
- All GeneXpert instruments must undergo routine maintenance and recalibration according to the manufacturer’s recommendations.
- Basic preventative maintenance should be carried out daily and weekly by users at the test site and some advanced maintenance can be done by superusers during supervisory visits.
- Servicing and repair of instruments should be carried out by authorized service providers.

Detailed guidance for equipment maintenance can be found in the **Tuberculosis Laboratory Maintenance Plan (LMP) for Preventive and Routine Maintenance of Laboratory Equipment**¹³ developed by the European TB Laboratory Initiative.

Remote monitoring systems can identify specific instruments or modules with poor performance or high error rates which indicate a need for service or repair. Also, some remote monitoring systems track the status of warranties as well as the status of the calibration of instruments and alert users to schedule renewal of maintenance agreements or recalibration service.

How do I ensure well-functioning GeneXpert instruments?

- Ensure that all GeneXpert instruments are evaluated as being “fit for purpose” at installation, after service or calibration, or after moving instruments
- Ensure that all GeneXpert instruments undergo routine maintenance according to the recommended daily, weekly and monthly schedules. Records of maintenance must be kept and reviewed at least monthly by the testing site manager and during supportive supervisory visits
- Ensure that all GeneXpert instruments are recalibrated according to the manufacturer’s recommendations. Monitor recalibration schedules at the national or supervisory levels
- Use remote monitoring capabilities to monitor the performance of GeneXpert instruments and individual modules
- Obtain servicing and repair of instruments from authorized providers. Develop a national SOP for obtaining service
- Purchase extended warranties or service contracts for each GeneXpert instrument

¹³ Tuberculosis Laboratory Maintenance Plan (LMP) for preventive and routine maintenance of laboratory equipment. European TB Laboratory Initiative. 2017. Available at http://www.euro.who.int/__data/assets/pdf_file/0009/355788/WHO-ELI-TB-Lab-Maintenance-Plan_ENG.PDF

Activities at a glance

- Develop and implement plans to ensure maintenance and servicing of the GeneXpert instrument
- Establish a system to ensure an uninterrupted supply of quality-assured reagents
- Implement a system for new lot testing of batches of cartridges

7.2 Quality supplies

The quality of the Xpert MTB/RIF testing service depends on the uninterrupted availability of quality-assured reagents at the testing sites.

7.2.1. Strengthen the supply chain

Distribution of Xpert MTB/RIF test reagents to testing sites requires special consideration, as the reagents have a limited shelf life and temperature-controlled storage requirements. The testing site performance indicators are used to calculate consumption rates. The regular TB supply chain should be used for distribution of reagents; however, due to transport issues, it may be necessary to implement a district-level stock buffer to ensure stock-outs do not occur.

Effective supply chain management is a complex process that includes product specification, product selection, forecasting of needs, procurement, distribution and storage and use. Managing a laboratory's commodities involves careful planning and coordination and should follow the well-recognized cycles of selection, procurement, distribution, and use. General guidance can be obtained from various sources, including USAID/Deliver: Guidelines for Managing the Laboratory Supply Chain¹⁴.

Remote monitoring systems can facilitate inventory management, by allowing stocks to be entered at site-level and forecasting the anticipated stock-out date or potential expiring cartridges based on the consumption rate. Replenishment of inventory can be managed before stock out, or potential expiring cartridges can be prioritized or moved to other sites. In addition, the tracking of lot numbers can identify poor performance and abnormal error rates for quality assurance purposes.

7.2.2. New lot testing

New lot testing, also known as lot-to-lot verification, should be performed on new batches of cartridges. New lot testing usually consists of testing a sample of the new cartridges and comparing the results to existing lot of cartridges with known performance. A new lot testing example SOP is available in the Supporting Documents/forms and templates.

- Conditions during transport & storage of cartridges may affect their performance.
- Cartridge test failures could indicate that the new batch of cartridges is not fit for use.
- New lot testing is preferably performed at the central level (e.g., NTRL), thereby ensuring that cartridges with test failures are not distributed, and reducing the burden of testing and number of cartridges used.

New lot testing at regional or testing site level monitors conditions during transport and storage of cartridges in-country.

How do I ensure the quantity and quality of supplies?

- Develop and implement a system to ensure an uninterrupted supply of quality-assured reagents
- Establish a system for monitoring inventories and forecasting supply needs
- Use remote monitoring capabilities to monitor consumption of supplies, demand for supplies, inventories and expiry dates of cartridges.
- Have a mechanism in place to reallocate supplies to avoid shortages and expiration of cartridges
- Conduct new lot testing on each new batch of cartridges (at least at the national level)

¹⁴ Guidelines for Managing the Laboratory Supply Chain: Version 2. USAID | DELIVER PROJECT, Task Order 1 2008. http://deliver.jsi.com/dlvr_content/resources/allpubs/guidelines/GuidManaLabSC_v2.pdf

8. External quality assessment (EQA)

An EQA program includes quality and performance indicator monitoring, proficiency testing (PT), regular on-site supportive supervision, timely feedback, corrective actions and follow-up. On-site supervision should be prioritized to poorly performing sites as identified during proficiency testing, monthly monitoring of performance indicators or after site assessments.

8.1. On-site supervision

On-site supervisory visits for assessment and training are especially critical during early stages of implementing a new test or procedure as they provide motivation and support to staff, especially in peripheral settings. On-site supervisory visits are also good opportunities to provide refresher training, mentoring, troubleshooting advice and technical updates. Strong relationships with GeneXpert users encourage rapid reporting of any problems and enable rapid troubleshooting, re-training and corrective actions. On-site supervisory assessments should be documented using standardized checklists to ensure consistency and completeness of information and to enable monitoring of trends and follow-up on recommendations and corrective actions. An on-site supervisory programme requires substantial planning and resources (both financial and human).

Develop and implement a program for on-site supervision

- Developing the program
 - Adequate numbers of trained staff and funds must be available for on-site supervisory visits and assessments.
 - On-site supervisory visits should be planned at regular intervals with schedules communicated to sites in advance.
 - On-site supervisory visits may be conducted by supervisors, GeneXpert advanced users, national and regional TB coordinators, depending on the nature of the support to be provided.
 - All personnel conducting on-site supervision must receive training in conducting assessments and use of checklists.
- Conducting assessments
 - On-site supervisory assessments should use standardized checklists and include discussions with GeneXpert users, testing site management, review of Xpert MTB/RIF test site documentation and observation of testing site operations. A supervisory checklist (Assessment Checklist for Testing Sites or ACTS) and user's manual are available in the Supporting Documents/forms and templates.
 - Where possible, on-site supervisory visits should be integrated with other on-site supervision (e.g., quarterly NTP site visits, AFB smear microscopy EQA visits).
 - Comprehensive assessments may be conducted less frequently (e.g., annually) by expert testing site staff (e.g., GeneXpert advanced users or NTRL staff), with more frequent (e.g., quarterly) assessments or visits done by district/regional supervisors or other appropriately trained QA teams. The extent of evaluation during each visit will depend on the frequency of the visit, capacity of staff and performance of the testing site (more extensive evaluation is needed in poorly performing sites).
 - Where resources are limited, poorly performing sites should be prioritized for on-site supervisory assessments and support. Poorly performing sites may be identified by monitoring of performance indicators or poor performance in PT events or poor site assessment results.

Activities at a glance

- Develop and implement a program for on-site supervision prioritizing poorly performing sites
- Develop and implement a proficiency testing program

- Providing feedback and follow-up actions
 - A plan must be established for addressing problems identified during the on-site assessment. All problems should be discussed immediately with facility staff, and any follow-up activities including training should be undertaken in a timely manner.
 - A list of the problems identified are included in the supervision report. Interim feedback is given to the Laboratory Manager or facility manager immediately after the assessment. Later the full supervision report is sent to the testing site, NTP/NTRL and designated individual for follow-up.
 - Site supervisory reports and completed checklists should be collated and should be reviewed by the QA or GeneXpert Focal Person.

How do I develop a site supervisory programme?

- Review the situational analysis to determine what the current coverage of site supervision is and where the individuals conducting site supervision are located. Identify the gaps in coverage and supervisors by mapping the testing sites to be covered
- Provide each testing site at least one supervisory visit per year by qualified supervisory staff using a standardized checklist (link1 and link6 to situational checklist or ACTS)
- Determine the number and location of supervisors that need to be trained. Consider the additional supervisors that are being trained as GeneXpert advanced users
- Conduct GeneXpert advanced training (http://www.stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF_Ultra.asp)
- Incorporate specific aspects of site supervisory visits to GeneXpert testing sites into other training curricula (e.g., training for regional TB coordinators)
- Develop a schedule for conducting site supervisory assessments and visits. If supervisors are limited, focus on poorly performing testing sites as identified during review of quality indicators and PT results and result of the testing site assessment
- Alternatively, consider piloting the programme in a few testing sites and scaling-up the programme as the number of trained supervisors increases; or consider reducing the number of visits to all testing sites
- Review reports from site supervisory assessments to determine effectiveness & coverage of the programme
- Report the outcomes of site supervisory visits to MOH/NTP

8.2. Proficiency testing

For many laboratory tests, the EQA program includes proficiency testing (PT). PT is a means to determine the quality of the results generated at the testing site. PT compares testing site PT results with a reference result (and with other laboratory results for the same panel of samples) to determine inter-testing site comparability. The purpose of PT is to:

- Identify testing sites with serious testing deficiencies
- Help to target support to the most poorly performing testing sites
- Evaluate the proficiency of users following training
- An online up-to-date comparison of the various PT panels can be found at: (the connectivity guide is at <http://tinyurl.com/glicconnectivity>)

A variety of PT panels using different sample matrices have been evaluated in a recent publication (Scott, et al. 2014)¹⁵. Included in this evaluation were artificial sputum (WHO/GLI), dried tube specimens (CDC), dried culture spots (National Health Laboratory Service (NHLS), South Africa) and two commercial suppliers of lyophilized samples and liquid samples. All panels showed good compatibility with Xpert MTB/RIF testing.

¹⁵ Scott L., Albert H., Gilpin C., Alexander H., DeGruy K. & Stevens W. 2014. Multicenter feasibility study to assess external quality assessment panels for Xpert MTB/RIF assay in South Africa. J Clin Microbiol 52: 2493-2499

Alternatively, a country may elect to prepare its own PT panels (e.g., NTRL) and distribute these to the testing sites. In-country prepared PT panels must follow a detailed SOP that has been tested and validated and must undergo EQA. Factors affecting the decision to prepare PT panels in-country will include capacity to manufacture panels in the country and manage the logistics of panel distribution, data management and reporting results, cost of commercial panels, ability to manage customs clearance and import panels from outside the country, and eligibility to participate in selected programmes. Forms and checklists for establishing and operating a proficiency testing programme for Xpert MTB/RIF are available in the Supporting Documents/forms and templates.

Table 6: Advantages and disadvantages of country-supplied vs externally-supplied PT panels

Country supplied	Externally supplied
<p>Advantages</p> <ul style="list-style-type: none"> • Control over the frequency of testing and what is included in the PT panel • Control over the scoring and analysis of data • Easily scalable 	<p>Advantages</p> <ul style="list-style-type: none"> • Can be initiated immediately • Cost associated with testing CDC panels are minimal. However, there is a cost associated with panel and result distribution • Requires minimal personnel to oversee the programme • No additional facilities required
<p>Disadvantages</p> <ul style="list-style-type: none"> • Requires extensive planning to initiate the programme • Requires external quality assessment of the PT panels • Cost • Requires dedicated personnel to oversee the programme • Requires specialized culture facilities 	<p>Disadvantages</p> <ul style="list-style-type: none"> • No flexibility on the frequency of testing or what is included in panels • No control over scoring and analysis of data • May not be easy to scale if the programme is over subscribed • Can be costly if multiple sites are enrolled in a paid programme

Irrespective of the source of Xpert MTB/RIF PT panels:

- PT requirements and guidelines for testing and reporting must be communicated to the testing sites.
- When a GeneXpert instrument is installed at a new testing site, it is recommended that the site enroll (i.e., is registered) in the PT programme.
- Testing sites should be supported to implement procedures to investigate incorrect PT results (e.g., performing root-cause analysis).

How do I implement a PT programme?

- Review the situational analysis to determine what PT is currently being performed
- Review the advantages & disadvantages of PT, providing options & deciding on the best approach
- If the option is to produce PT panels in-country, follow the recommendations provided in the Supporting Documents/forms and templates
- If the option is to use an external PT panel provider:
 - Engage the provider
 - Enroll all sites in the PT programme
 - Provide the PT provider with the details of recipient of the PT reports
 - Arrange in-country distribution of PT results
 - Collate and analyse PT panel results
 - Include review of PT results as part of supervision visits

Element 9. Monitor performance of Xpert MTB/RIF testing and of the QA/CQI system

Routine monitoring of quality indicators, also known as performance indicators, is a critical element of assuring the quality of any diagnostic test (e.g., Xpert MTB/RIF) or system (e.g., the QA/CQI system for Xpert MTB/RIF) and is essential to inform decision-making. Performance indicators should include testing site performance indicators, clinical indicators and programmatic indicators, including those that measure test results, supplies, test performance, PT results, and QA processes.

9.1 Establish an M&E framework for Xpert MTB/RIF testing and for the QA system

The first step is to establish a framework for monitoring and evaluation (M&E) of Xpert MTB/RIF testing and the QA system and includes defining of performance indicators. Table 7 lists GLI-recommended key performance indicators for Xpert MTB/RIF testing as well as general laboratory quality indicators¹⁶ that should be monitored monthly by each testing site. Additional indicators such as the completeness of documentation (e.g., use and completeness of registers, logs, forms) or adherence to SOPs may be assessed during supervisory visits. For some indicators (e.g., proportion of specimens that are rifampicin resistant), targets are setting-specific. Laboratories should monitor indicators and establish local targets and acceptable ranges. Deviations from expected values should be investigated.

Whenever possible, countries should collect disaggregated data according to the population group tested (e.g., HIV positive, MDR-TB risk, extrapulmonary TB). If the quality indicator for error rates exceeds the target value, it should be further disaggregated to identify common error codes, in order to assist with corrective and preventive actions. The GeneXpert platform produces electronic data and a data connectivity solution (Element 5) should be established for remote monitoring of quality indicators.

Activities at a glance

- Establish an M&E framework
- Identify key performance and quality indicators
- Collect & analyse data
- Evaluate progress & identify trends

¹⁶ GLI Practical Guide to TB Laboratory Strengthening. ²⁰¹⁷. Available at <http://stoptb.org/wg/gli/gat.asp>.

Table 7: Key performance indicators that should be monitored monthly by testing sites

Xpert MTB/RIF Testing Quality Indicators	Target
Number of tests performed, by type of test and key population (e.g., HIV+, pediatric, vulnerable population, EPTB)	Full utilization of a 4-module GeneXpert instrument is 12 tests per workday.
Service interruptions (stock-outs, equipment down time, etc.)	No interruptions
Number and proportion of specimens with MTBC detected, rifampicin resistance not detected	Dependent on population tested and country drug-resistance prevalence and patterns
Number and proportion of specimens with MTBC detected, rifampicin resistance detected	Dependent on population tested and country drug-resistance prevalence and patterns
Number and proportion of specimens with MTBC detected rifampicin indeterminate	Dependent on population tested and country drug resistance prevalence and patterns
Number and proportion of specimens with MTBC detected trace, disaggregated by patient group (For Ultra test)	Dependent on population tested and country drug resistance prevalence and patterns
Number and proportion of specimens with MTBC not detected	Dependent on population tested and country drug-resistance prevalence and patterns
Number and proportion of specimens with errors	<3%
Number and proportion of specimens with invalid results	<1%
Number and proportion of specimens with no results	<1%
Proportion of specimens tested with Xpert MTB/RIF for which a result was reported within 24 hrs (i.e., time from receipt of specimen to reporting of results)	>95%. The target turnaround time may be modified by the programme based on testing schedules

In addition to these quality indicators, the testing sites should also be able to provide some of the data needed to assess the quality of the diagnostic cascade (Table 8). Some of the indicators will also need data from clinicians and program personnel, which may be collected routinely or using a once or twice a year survey depending on the country capacity.

Table 8. Key performance indicators that should be monitored to assess the quality of the diagnostic cascade.

Diagnostic Cascade Quality Indicators	Target
Number and percentage of presumptive TB patients tested with Xpert MTB/RIF (End TB Strategy Laboratory Indicator 1) ¹⁷	Dependent on population tested and country prevalence patterns
Percentage of notified new and relapse TB cases tested with a WRD as the initial diagnostic test (Indicator 2)	80% (2020)
Percentage of notified new and relapse TB cases with bacteriological confirmation (Indicator 3)	80% [relapse: 90%] (2020)
Number and proportion of bacteriologically confirmed patients who were initiated on treatment according to the national algorithm	Target is setting specific
Percentage of testing sites using a WRD at which a data connectivity system has been established that transmits results electronically to clinicians and to an information management system (Indicator 4)	100% (2020)
Number and proportion of Xpert MTB/RIF test results reported to clinicians using electronic systems	Target is setting specific
Number and proportion of TB patients detected by Xpert MTB/RIF that were reported to the TB control program, TB or MDR TB treatment focal person	Target is setting specific
Percentage of notified bacteriologically confirmed TB cases with DST results for rifampicin (Indicator 7)	100% (2020)
Percentage of notified rifampicin-resistant TB cases with DST results for fluoroquinolones and second-line injectable agents (Indicator 8)	100% (2020)
Number and proportion of patients with RIF-resistant TB identified by Xpert MTB/RIF testing referred for second-line DST	100%
Proportion of specimens collected for Xpert MTB/RIF testing for which a result was received within the specified target time (i.e., time from collection of a specimen to receipt of results)	>95%. The 'specified time' should be determined for each laboratory taking into account testing schedules and specimen transport schedules
Proportion of specimens referred for DST for which a result was received within the specified target time (i.e., time from referral of a specimen to receipt of results)	>95%. The 'specified time' should be determined for each test required (e.g., molecular DST or liquid culture DST) and the collection schedule used

Performance indicators for a QA system are designed to assess the performance of each of the key features of a QA system including coverage and use of standardized procedures (i.e., SOPs), document control, quality indicator monitoring, internal quality controls, external quality assessment, proficiency testing, regular on-site supervision, and timely feedback, corrective actions and follow-up in all of the facilities in the diagnostic network. Table 9 provides a suggested minimum list of indicators to be monitored to evaluate the performance and quality of the QA/CQI system for Xpert MTB/RIF testing. The data for these indicators should be collected monthly by the supervisory laboratories. District or supervisory laboratories may compile and analyse the data from their jurisdictions. The data should also be submitted to the national level for aggregation and analysis. The analyses should be done once or twice a year. Indicators calculated using aggregate data (e.g., of testing sites labs reporting key performance indicators (KPI)s monthly) are useful to monitor overall performance, but to facilitate detecting problems and initiating corrective actions, it may be necessary to disaggregate the data by region or supervisory laboratory.

¹⁷ The indicator number in parentheses refers to the number of the global indicators in the WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy.

Table 9. Key indicators for the QA/CQI system that should be monitored at the supervisory or national level

Diagnostic Cascade Quality Indicators	Target
Percentage of diagnostic testing sites that are covered by a functional national system of performance indicator monitoring and external quality assessment (EQA) (Indicator 9 of Framework ¹⁸)	100% (2020)
No. and % of testing sites enrolled in a PT programme	100%
No. and % of enrolled testing sites participating in a PT programme	100%
No and % of testing sites participating in a proficiency testing (PT) programme that successfully passed	100%
No and % of testing sites covered by a system of supportive supervision	100%
No. and % of testing sites that have had supervisory visits in the past year	100%
No. and % of testing sites that monitor and evaluate key performance indicators at least monthly	100%
No. and % of testing sites reporting KPIs monthly to supervisory laboratory	100%
No. and % of testing sites with standardized, competency-based job descriptions for all positions	100%
No. and % of testing sites that have internal quality controls in place for Xpert MTB/RIF	100%
No. and % of testing sites that have a document control system in place	100%
No. and % of testing sites that have all of (and adhere to) the necessary SOPs in place	100%
Number and % of testing sites with complete quality documentation	100%

Countries should review the proposed quality indicators in line with their country guidelines and priorities. The development of the indicators, as well as data collection and analysis, will require a strong collaborative effort led by NTP, including laboratory services and stakeholders involved in the programme.

A full M&E framework includes data collection tools and countries should review their existing tools to determine which data are already being collected and which existing tools need to be revised to enable collection of additional required data. Where necessary, additional data collection tools may be required. The frequency of data collection should consider the feasibility and resources required for collecting data and providing feedback, and the schedule of existing meetings at which data may be reviewed. Adequate frequency of data collection is needed to ensure any non-conformities or lack of progress towards targets can be acted upon in a timely manner, and that operational changes can be applied.

Programmes should establish a baseline for all performance indicators, bearing in mind that this may only be possible for some indicators after development and implementation of new data collection tools. Targets should be set for each indicator; this may be an absolute number or a proportion of sites meeting a defined criterion. The national level should review progress towards meeting targets at least on annual basis. The programme should critically evaluate reasons for not meeting targets, put in place corrective actions and set targets for the next year.

¹⁸ This is indicator 9 of the WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy. 2016. World Health Organization. Available at <http://www.who.int/tb/publications/labindicators/en/>

9.2 Assign responsibilities for data collection, reporting and analysis

All testing sites should collect and analyse testing data on at least a monthly basis, using a standardised format. Targets should be set for all indicators monitored (usually by the national programme following consideration of GLI guidance), and any unexplained change in quality indicators, such as increase in error rates, a change in MTBC positivity rate or RIF-resistance rate, or a significant change in volume of tests conducted, should be documented and investigated. A standard set of quality indicators should be used for all sites conducting a particular test to allow for comparison. Quality indicators should be reviewed by the laboratory manager and quality officer and must always be linked to corrective actions if any unexpected results or trends are observed. Documentation of corrective actions and subsequent improvement and normalization of laboratory indicators following the corrective actions are critical.

A system should be in place for centralized reporting of monthly quality indicators to the supervisory laboratory, regional QA officer (if applicable), NTRL or NTP. The appropriate QA officers or manager or data units should review and analyze the reported data. For Xpert MTB/RIF testing, the use of diagnostics connectivity solutions (Element 5) will allow for real-time remote monitoring of sites within a network and provide the capacity to easily and accurately stratify data as needed for analysis of performance.

After reviewing existing tools and making necessary revisions to capture the information required for performance indicators, countries should allocate responsibility for data collection, compilation (e.g., by region and nationally) and analysis of results. This can be recorded in the M&E framework document.

Data for most indicators will be collected by laboratory staff at each testing site, with support from advanced users or supervisory staff. These data will need to be compiled into a regional and/or national level data set for all sites.

Responsibilities for data collection, a system for sending data to regional and/or national level, and responsibility for data analysis and reporting should be clearly defined. Individuals responsible, and not just institutions, should be named and provided with appropriate training and tools to undertake the applicable activities. Mechanisms for feedback of data and reports, including recommendations for action items, should be established and clearly communicated to all involved.

Where possible, use existing cadres, e.g., advanced users, and incorporate data collection for M&E into existing supervision and technical support activities.

The M&E programme is the overall responsibility of the NTP, led by the programme manager, with other programmes and institutions critically involved, including National AIDS Control programme, Department of Laboratory Services, MOH, and health facilities. All M&E reports should be prepared and provided to the NTP manager for review, finalization and approval, prior to being disseminated to stakeholders.

9.3 Collect, compile and analyse data

Based on the M&E framework, data collection tools should be developed for data collection at different levels, from testing site data, district and regional patient-related data (e.g., treatment initiation) to national level data (e.g., training and PT programme). Examples of data collection and analysis forms for key performance indicators are available as Microsoft Word documents in the Supporting Documents/forms and templates. The data collection and analysis forms are also available in an Excel format that can automatically calculate the indicators when the required data are entered.

How do I collect, compile and analyse data?

- Identify who will collect the data (e.g., users, regional TB coordinators, National QA Unit, GeneXpert advanced users)
- Assign responsibility for developing data collection tools, for example, to the National QA officer or M&E manager
- Develop data collection tools and incorporate these into existing tools where possible (e.g., supervisory visit checklists)
- Schedule training for data collectors at all levels (site level, regional level, super users, national level, programme)
- Establish and communicate deadlines for reporting of data, based on data collection frequency, timing of review meetings and monitor adherence of data collectors to the schedule
- Compile a performance indicator report on quarterly, biannual and annual basis
- Prioritize the introduction of remote monitoring to assist with collection of instrument data on test performance

Basic analysis of performance indicators compared with the targets should be conducted locally (e.g., at each testing site) and these data used for local decision-making. That is, where possible the testing site staff should analyse their data to detect problems (e.g., high error rates), conduct a root cause analysis and initiate corrective actions. Such a local review and follow up should not wait for regional or national analysis to take place. In some cases (e.g., unexpected high rates of RIF resistance), assistance from the supervisory site will be needed to analyse the problems and develop and initiate corrective actions. Remote connectivity systems enable basic automated analyses and alerts which will facilitate this local analysis and use of data for action. Data may be exported for more in-depth or specialized analysis such as the analysis of individual indicators and groups of indicators (e.g., those relating to quality) at the regional or national level.

9.4 Evaluate progress and identify trends

QA and quality improvement are a continuous and cyclical process. QA activities should be phased in until all testing sites have been covered in all areas. This will require continual sharing of best practices, lessons learned and planning. Furthermore, expansion of testing services to additional sites, either by strengthening of referral networks or by installing new instruments, should be planned in a rational manner, with due attention paid to new services meeting required quality standards from the outset.

Data should be collected and initially reviewed at the local testing site level. Trends that require intervention (e.g., increase in proportion of unsuccessful results [errors, no results, invalid results, and interrupted runs], increase in service interruption) must be communicated, appropriate corrective actions must be undertaken and impact of the interventions reviewed. Furthermore, analysis of regional or national level data will identify trends that extend beyond individual sites (e.g., reagent batch issues, PT, or equipment maintenance).

Measuring of impact performance indicators will highlight areas for improvement around translating rapid diagnostic results into rapid initiation of appropriate care and treatment, and ultimately improved patient outcomes.

The NTP needs to work with stakeholders to develop annual goals so that they are understood and embraced by everyone contributing to Xpert MTB/RIF QA, and so that partner activities are aligned with NTP priority needs and the overall implementation framework. At least one annual review of all performance indicator data should be conducted at the national level, under the leadership of NTP, with laboratory and clinical experts and with the participation of all relevant stakeholders.

How do I evaluate progress towards targets?

- Review the performance indicators compared with annual and 5-year targets
- Prioritize, plan and budget for future activities
- Review and revise implementation strategies, if needed, to meet the goals
- Engage stakeholders in the review and re-programming

Element 10. Strengthen the clinical-laboratory interface and the diagnostic cascade

A comprehensive system to ensure the quality of laboratory testing must address all the relevant parts of the diagnostic cascade, not just what happens in the laboratory. Published literature on a variety of laboratory tests highlights that factors that have the largest impact on quality of diagnostic services occur in the pre-pre-analytical phase (choice of test, etc.) and post-post-analytical (interpretation of results and patient management). Indeed, data from South Africa¹⁹ suggests that even in a well-managed laboratory network, gaps still exist in ensuring rapid referral of all diagnosed patients to treatment.

At the national and supervisory level, efforts should concentrate on training, developing SOPs and systems. Guidance on technical aspects of collecting quality specimens and reporting accurate results are described in Element 10 of Part 2 below.

How do I strengthen the clinical-laboratory interface?

- Provide training to laboratorians, nurses, clinicians and other healthcare workers on the aspects of the diagnostic cascade that affect the quality of TB testing
- Ensure that national testing algorithms are followed and that the correct test is ordered for each presumptive TB patient
- Develop SOPs for collecting quality samples and promptly submitting them to the testing site along with a properly completed test requisition form
- Develop SOPs and forms to ensure that accurate results are reported to clinicians, TB control officers, and TB and MDR TB treatment focal persons and include information on the interpretation of the test results
- Develop systems to support the flow of information between clinicians, program staff and laboratorians and establish procedures for regular meetings of staff to discuss issues, troubleshoot problems and strengthen the clinical-laboratory interface
- Monitor the performance of the diagnostic cascade (see Element 9)

Activities at a glance

- Provide training on the diagnostic cascade to all laboratorians and healthcare workers
- Develop SOPs for the clinical-laboratory interface
- Develop systems to support the flow of information between clinicians, program staff, and laboratorians
- Monitor the performance of the diagnostic cascade

¹⁹ Naidoo et al. 2017. The South African Tuberculosis Care Cascade: Estimated Losses and Methodological Challenges. *J Infect Dis* 216 (suppl_7): S702-S713, <https://doi.org/10.1093/infdis/jix335>

Part 2: QA for Xpert MTB/RIF Testing Sites

Background

This section of the guide focuses on the QA activities at the testing site that are essential to the provision and documentation of quality testing. For laboratories that are pursuing accreditation to IS15189 standards, the QA activities described here are closely related to the twelve Quality System Essentials (QSEs) that direct and control an organization with regard to quality from the basis of a quality management system (QMS). The reader is referred to the WHO Laboratory Quality Management System: Handbook (2011)²⁰ for an in-depth discussion of QMS and QSEs. Table 10 shows the relationship of the QA activities described in this section with the QSEs.

Standards and key activities for assuring quality

Quality standards are goals toward which efforts and resources to assure quality Xpert MTB/RIF testing should be directed. Standards that were developed to measure the performance of the TB diagnostic network form the basis of the standards for the Xpert MTB/RIF QA system. The TB diagnostic network standards are based on standards developed by the Global Laboratory Initiative (GLI) for ensuring the quality of AFB smear microscopy²¹, by the African Society of Laboratory Medicine (ASLM) and Association of Public Health Laboratories (APHL) for evaluating diagnostic networks²², and by USAID and partners for evaluating TB diagnostic networks in Nigeria and India²³. The standards, associated key QA activities, and corresponding sections of this guide are described in Table 10.

The national and supervisory levels are responsible for the processes and systems needed to ensure quality testing in all facilities and includes developing national policies and procedures; monitoring and evaluating performance indicators; conducting external quality assessment and proficiency testing programs; and providing supportive supervision. At the individual testing site, the QA system focuses on the processes and procedures to ensure the quality and reliability of each test performed in the laboratory and a well-functioning laboratory-clinical interface to ensure efficient referral for testing, prompt reporting and linkage to care of diagnosed patients.

²⁰ WHO Laboratory Quality Management System: handbook. 2011. (<http://www.who.int/ihr/publications/lqms/en/>)

²¹ TB Microscopy Network Accreditation. An assessment tool. Global Laboratory Initiative. 2013. http://www.stoptb.org/wg/gli/assets/documents/TBMicroscopy_Network_Accreditation_Web.pdf

²² Ondoa, P. et al. A new matrix for scoring the functionality of national laboratory networks in Africa: introducing the LABNET scorecard. African Journal of Laboratory Medicine, 5, Oct. 2016. <http://www.ajlmonline.org/index.php/ajlm/article/view/498/712>

²³ Albert, H. Essential standards for a TB diagnostic network. ASLM 2016.

Table 10: Diagnostic Network Standards and Key Quality Assurance Activities

GLI Standard	Key QA Activities
Structures and policies are in place that enable continuous, country-wide availability of free, quality assured diagnosis according to the national guidelines.	<p>Governance (Element 1)²⁴</p> <ul style="list-style-type: none"> • Appoint, train, and empower quality officers <p>Planning (Element 2)</p> <ul style="list-style-type: none"> • Participate in a situational analysis and development of a prioritized action plan.
A minimum package of tests and quality standards is defined for each level of the TB diagnostic network.	<p>Quality assurance documentation (Element 3)</p> <ul style="list-style-type: none"> • Use standardized documents and forms for sample request and results recording and reporting at all testing sites
Adequate numbers of competent, well-trained and motivated technical and managerial staff are available at all levels of the diagnostic network.	<p>Training and certification (Element 4)</p> <ul style="list-style-type: none"> • Train at least two users from each site and assess competency • Train sufficient advanced users to provide supervision and advanced troubleshooting
Inter-operable and inter-connected electronic recording and reporting systems are in place that generate reliable data that are monitored and analysed in real time.	<p>Data connectivity and remote monitoring (Element 5)</p> <ul style="list-style-type: none"> • Utilize remote monitoring systems to collect and analyse data relating to performance indicators, QA and procurement
Testing is performed in a manner and in facilities that ensure safety for the staff, the customers, the community and the environment.	<p>A safe and functional testing site (Element 6)</p> <ul style="list-style-type: none"> • Ensure that the site is not hazardous for the staff, patient or environment • Ensure that a good working environment is available
Testing is performed with state-of-the-art and well-maintained equipment and an uninterrupted supply of quality reagents and consumables.	<p>Supply chain (Element 7)</p> <ul style="list-style-type: none"> • Ensure uninterrupted supply of Xpert MTB/RIF supplies and reagents • Perform new lot testing on new batches of reagents <p>Equipment servicing and maintenance (Element 7)</p> <ul style="list-style-type: none"> • Ensure that all GeneXpert instruments undergo routine maintenance and calibration • Verify all instruments as fit for use at installation, after service or calibration, or after moving instruments
Continuous quality improvement targets all facilities within the network and includes quality indicator monitoring, external quality assurance, and regular on-site supervision.	<p>Proficiency Testing (PT) (Element 8)</p> <ul style="list-style-type: none"> • Enroll in a PT programme • Investigate incorrect PT results and take corrective actions <p>Site supervision (Element 8)</p> <ul style="list-style-type: none"> • Receive on-site supervisory visits on a regular basis (at least yearly) by competent personnel <p>Monitoring and evaluation (Element 9)</p> <ul style="list-style-type: none"> • Collect, analyse and report performance indicator data monthly
An efficient diagnostic-clinical interface allows for appropriate diagnostic tests to be ordered and performed and ensures the timely linkage of diagnosed patients to appropriate care and treatment	<p>Strengthen the clinical-laboratory interface and the diagnostic cascade (Element 10)</p> <ul style="list-style-type: none"> • Ensure that national testing algorithms are followed and that the correct test is ordered for each patient • Ensure that quality specimens are collected, properly labelled, correctly stored, and promptly transported to the testing site • Enforce the use of standardized test requisition forms • Report accurate results to clinicians and TB and MDR TB treatment focal persons and include information on the interpretation of the test result • Monitor the performance of the diagnostic cascade

²⁴ The element numbers correspond to the numbers of the sections of this guide that describe the activities needed to accomplish the standard.

Pillars of a Quality Assurance System



At the Xpert MTB/RIF testing sites, the key steps in quality assurance include:

1. **Governance:** Appoint, train and empower a quality officer. The quality officer should report to the head of the laboratory and must have the authority to implement and enforce the quality assurance programme. Quality assurance or quality improvement officers should also be appointed at participating clinical sites to oversee the quality of the clinical and diagnostic services.
2. **Planning:** Develop a costed prioritized action plan for phased implementation of the required QA activities that aligns with national and regional plans. Adequately budget the activities and set a time line for implementation and monitor progress.
3. **Quality procedures and documentation:** Enforce adherence to SOPs, use standardized requisition, recording and reporting forms, and maintain documents and records.
4. **Ensure GeneXpert users are trained:** Train all GeneXpert users in the operation of the GeneXpert instrument, performance of the Xpert MTB/RIF test, and quality assurance activities and assess and document their competency.
5. **Diagnostics connectivity and remote monitoring:** Establish and maintain a remote monitoring system to collect and analyse data relating to performance indicators, QA and procurement.
6. **Make the testing site safe and functional:** Ensure the environment is clean, secure, temperature-controlled and has adequate uninterrupted power.
7. **Equipment and supplies:**
 - a. **Maintenance and calibration of the GeneXpert instrument:** Verify that the GeneXpert instrument is functioning properly.
 - b. **Regularly maintain and calibrate** the instrument according to the manufacturer’s recommendations.
 - c. **Ensure adequate supplies & reagents:** Implement a process to ensure an adequate, uninterrupted supply of quality-assured reagents.
8. **Participate in an EQA programme:** The EQA program should include proficiency testing, on-site evaluations, and supportive supervision; analyse EQA results; take corrective action if needed and document follow-up.
9. **Monitor performance of Xpert MTB/RIF testing and the QA system:** Regularly monitor, analyse, and report performance indicators.
10. **Clinical-Laboratory interface:** strengthen the clinical-laboratory interface to ensure that national testing algorithms are followed, the correct test is ordered for each patient, quality samples are collected and submitted to the laboratory, accurate results are reported to the clinician, results are correctly interpreted and patients are promptly placed on appropriate therapy.

Detailed guidance is provided in the subsequent sections for each of the individual elements. Note: The elements are described in a logical order to ensure implementation of a functioning QA system, but the order is not meant to be a prescriptive step-by-step order (i.e., complete element 1 before element 2, etc.). As part of the strategic planning process (see Part 1, Element 2), countries will prioritize the activities and develop a phased implementation plan and time line. Such plans should focus on providing the appropriate structures (e.g., quality teams, data monitoring units), support (e.g., training, supportive supervision, constructive feedback) and monitoring and evaluation processes (e.g., collection and regular analysis of key performance data) needed to implement a functioning continuous quality improvement process. For example, implementing a proficiency testing program without implementing a corresponding system of timely feedback, corrective actions and supervisory visits will greatly limit the usefulness and impact of the proficiency testing program on the quality of testing.

The following sections in this guide describe practical steps for the implementation of a system for ensuring the quality of Xpert MTB/RIF testing at the testing site level. (Part 1 provided guidance for the national and supervisory levels). This part is divided into sections, each dealing with one of the QA elements (Table 10) required for assuring a quality Xpert MTB/RIF test result. Links to additional resources are provided at the end of the guide. Hyperlinks to tools and job aids to assist with the implementation of QA activities are provided. These templates can be customized as required.

Element 1. Governance

The governance structure of Xpert MTB/RIF QA activities at the testing site is an extension of the governance structure at the national level (see Part 1, Section 1) and requires clearly defined roles and responsibilities.

At smaller facilities, the laboratory manager will be responsible for overseeing QA activities. At larger facilities, there may be a Health Facility Quality Committee (HFQC) which provides oversight and coordination for QA activities at the facility and provides regular progress reports to the supervisory levels. If so, the Xpert MTB/RIF testing site may be able to rely on the HFQC for oversight of Xpert MTB/RIF QA. In this case, it will be essential that the Xpert MTB/RIF testing site is represented on the HFQC to ensure adequate communication and translation of policy into action. In addition, the person responsible for the Xpert MTB/RIF testing should be trained in basic QA procedures and report to the HFQC.

Activities at a glance

- Establish a governance structure
- Appoint, train, and empower a QA officer

Table 11. Example of a testing site governance structure with defined roles and responsibilities

Position	Roles and responsibilities
Health Facility Quality Committee (if applicable)	<ul style="list-style-type: none"> • Ensure accountability, leadership and governance at health facility level • Provide oversight and coordination for QA and CQI activities at the institution • Provide regular progress reports to the regional QA structure • Translate policy into practice
Laboratory manager	<ul style="list-style-type: none"> • Oversee and enforce TB QA policies and procedures at the testing site • Appoint a QA officer • Supervise collection of data and analysis of quality and performance indicators • Troubleshoot problems and initiate corrective actions
Quality assurance officer	<ul style="list-style-type: none"> • Oversee and direct the execution of the Xpert MTB/RIF QA processes and procedures at the testing site • Oversee implementation of corrective actions • Participate in the collection of data and analysis of quality and performance indicators • Report directly to the testing site and laboratory manager
Xpert user	<ul style="list-style-type: none"> • Adhere to all QA policies and procedures • Assist with the collection of data, troubleshooting, and corrective actions

What you need to do

Steps in establishing a governance structure at the testing site include:

- Develop an organogram of the governance structure that clearly defines relationships and lines of supervision
- Assign roles and responsibilities and develop terms of reference
- Establish lines of communication and reporting within the governance structure of the testing site and the national and regional QA networks.
- Map out the flow of information and identify points of contact.

A key step is for each Xpert MTB/RIF testing site to appoint a quality officer (full-time or part-time) or assign the duties of a quality officer to an existing staff member. The quality officer would be responsible for overseeing and directing the Xpert MTB/RIF QA processes at the testing site and reporting directly to the testing site and laboratory manager. In many laboratories, the QA officer might be responsible for QA of all testing done at the site.

Quality assurance or quality improvement officers should also be appointed at participating clinical sites and empowered to oversee the quality of the clinical and diagnostic services.

Element 2. Planning

The planning process should include 1) a situational analysis to determine the current status of testing and quality practices and the implementation of Xpert MTB/RIF QA activities at the testing site, 2) development of a costed prioritized action plan for phased implementation of the required QA activities with targets and a time line and 3) allocation of an adequate budget for QA activities.

What you need to do

2.1. Situational analysis

A situational analysis is needed to determine which Xpert MTB/RIF QA activities are currently implemented at the testing site and their impact on quality of diagnosis and to identify the gaps in providing quality assured Xpert MTB/RIF results. The situational analysis will most likely be done by the National QA Officer or the supervisory laboratory QA Officer using the Situational Analysis Checklist and ACTS . The situational analysis report will describe gaps identified, recommendations for how to implement quality assurance activities and propose a time line for implementation. An excerpt from an example situational analysis checklist, with commonly observed outcomes and recommendations is provided.

The testing site staff should review the Situational Analysis Checklist and collect all of the documents (e.g., policies, procedures, SOPs, test requisition forms, result reporting forms, logbooks, registers, etc.) needed for the assessment.

The testing site manager or laboratory manager should review the situational analysis report and work with the supervisory laboratory personnel to develop an action plan including time lines to address the recommendations.

2.2. Budget

- Working with the state, region and facility officials, the testing site should assist with the development of a budget that addresses both the implementation of recommendations from the situational analysis and the implementation and continuance of the QA activities thereafter. A GeneXpert costing tool is available on the FIND website: <https://www.finddx.org/implementation-resources/#tb> planning and resources (both financial and human).

Table 12: Budgetary considerations for QA activities

QA activity	Budgetary considerations
Generate QA documentation	<ul style="list-style-type: none"> Preparing and printing of standardized sample request and results reporting forms, SOPs, etc. Preparing and printing of standardized logbooks
Maintain and service equipment	<ul style="list-style-type: none"> Site upgrades, calibration kits and warranty costs
Training & certification	<ul style="list-style-type: none"> Costs associated with training including travel, accommodation, materials, etc.
Onsite supervisory visits	<ul style="list-style-type: none"> Costs associated with hosting an on-site visit and preparing documents
PT testing	<ul style="list-style-type: none"> Costs associated with testing PT panels Costs associated with procuring PT panels, if done at site level
Strengthen the supply chain	<ul style="list-style-type: none"> Material cost per test, including but not limited to Xpert MTB/RIF test reagents, consumables, sample collection items, printing paper, etc.
Remote monitoring	<ul style="list-style-type: none"> Costs associated with installing and maintaining a remote monitoring system

Activities at a glance	
<input type="checkbox"/>	Participate in a situational analysis
<input type="checkbox"/>	Assist with the development of an action plan
<input type="checkbox"/>	Assist with the development of a QA budget

Element 3. Quality procedures and documentation

Without accurate and complete documentation, the quality of Xpert MTB/RIF test results may be compromised. Standardized documents, forms and SOPs (developed at the national level) should be available and adhered to at the testing sites and participating clinical sites. The documents must address activities throughout the diagnostic cascade including documentation for clinical activities (e.g., specimen collection and referral) and laboratory activities. Documents and records must be up-to-date, accurate and readily accessible. A document control system is needed to ensure regular review of quality management documents (e.g., SOPs) and to ensure the correctness of the documentation that support laboratory testing, which in turn increases quality assurance.

What you need to do

Each testing site will need to receive and tailor the required QA-related documents by adding site specific information, creating and implementing a document control system, and ensuring that all users read and understand the documents. The priority for each site should be to implement standard SOPs, including training of staff on the use of the SOP.

Activities at a glance

- Receive documents from supervisory or national level
- Customize documents by adding testing site-specific information
- Implement a document control system
- Ensure users read & understand the QA documents

Activity	How do I achieve this?
Generate QA-related documentation	<ul style="list-style-type: none"> Obtain the required documents (should be available from NTRL, see Part 1) Review the documents, customize as needed for the testing site (e.g., insert site specific contacts), but do not alter the test procedure Sign and date the document to indicate review and approval Print and disseminate the approved documents Post job aids at the testing bench Provide training in the use of the documentation Ensure all staff have read documents and signed as proof of reading Make sure obsolete versions of SOPs are removed and the most recent version is accessible to all staff
Ensure users read and understand the QA documents	<ul style="list-style-type: none"> Have each user review all documents annually Provide training on the documents Have each user indicate that they have read and understood by signing in the place provided on the form
Create a document control system	<ul style="list-style-type: none"> Obtain the SOP for Document Control Create a Document Retention List: determine the storage time and location for all documents used Make a document control log and document revision form Add a front page to each quality document used in the laboratory to track versions Create folders for storing SOPs at a convenient location for staff to have access to the SOPs when needed Develop personnel files for all staff members to document their knowledge of the correct documents Roll out the document control system

Table 13: SOPs, forms, and documents that must be available at the testing sites

Resource	Description
National TB Diagnostic Algorithm	Describes a step-by-step protocol for diagnosis of TB at healthcare facilities
Specimen collection and transport SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedures to be followed to ensure collection of good quality specimens and safe, rapid transport of specimens
Document Control SOP http://www.gliquality.org/activities/2/33	Describes the procedures to ensure that the correct documentation (e.g., SOP) is used for laboratory testing
Xpert MTB/RIF test SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedures for performing the Xpert MTB/RIF test
Xpert MTB/RIF Ultra SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedures for performing the Xpert MTB/RIF Ultra test
Test requisition form	Form for requesting Xpert MTB/RIF testing
Laboratory test registers	Register for recording patient, specimen, and test information
GeneXpert maintenance Log	Form for recording GeneXpert maintenance tasks
Temperature monitoring Log https://www.finddx.org/implementation-resources/#tb	Form for recording daily temperature monitoring in testing and kit storage areas
Non-conformity and corrective action log http://www.finddx.org/tb/	Form for capturing non-conformities and corrective actions
Waste management SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedure of safely disposing consumables and Xpert MTB/RIF reagents (may be included in a Biosafety SOP)
Spill management SOP https://www.finddx.org/implementation-resources/#tb	Describes the procedure to follow in the event of a biohazard spill at a testing site (may be included in a Biosafety SOP)
Xpert MTB/RIF WHO reporting codes http://www.who.int/tb/publications/definitions/en/	Describes the standard WHO reporting codes for reporting Xpert MTB/RIF test results
Xpert MTB/RIF performance indicator reporting form	Form for capturing Xpert MTB/RIF performance indicator data
Xpert MTB/RIF test reporting form http://www.who.int/tb/publications/definitions/en/	Form for reporting Xpert MTB/RIF test results to clinicians
Proficiency Testing (PT) SOP	Describes the general procedure for testing PT samples, resulting, reporting, and corrective action for unacceptable results
PT failure investigation and corrective action form	Form for documenting the results of the investigation of PT failures and remedial action taken

Element 4. Training, competency assessment and certification

GeneXpert users must be trained in the operation of the GeneXpert instrument, correct performance of the Xpert MTB/RIF test and carrying out the associated QA activities. Advanced users receive additional training that assists in the implementation of the Xpert MTB/RIF test. Clinicians and other clinical staff must be trained on the diagnostic algorithm, ordering tests, collecting specimens, submitting samples and interpreting results. The competency of all users must be regularly assessed. Failure to adequately train and assess users can impact quality:

- Poorly trained staff may perform the Xpert MTB/RIF test incorrectly and report out inaccurate results
- Poorly trained staff are less productive than well-trained competent staff
- Failure to adhere to SOPs leads to inconsistent requesting, testing and reporting of Xpert MTB/RIF test results leading to possible errors and confusion for clinicians
- Poor quality results cause clients, patients and clinicians to be dissatisfied and could lead to a lack of confidence in the quality of the service
- Lack of trained advanced users may delay troubleshooting and corrective actions at the testing sites

Activities at a glance

- Train users in the operation of the GeneXpert instrument, Xpert MTB/RIF test and QA activities
- Assess users for competency

What you need to do

4.1. Provide training for Xpert MTB/RIF users, advanced users, and clinicians

Training and certification activities and procedures must be clearly developed, documented and executed in line with international standards. A standardized Xpert MTB/RIF training programme should be available from the NTP or NTRL and include training curricula for trainers, users, advanced users and clinicians. Standardized training material is available from the Global Laboratory Initiative²⁵ including training packages on the Xpert MTB/RIF test and on programmatic aspects of diagnostic laboratory strengthening.

- Using a standardized curriculum, users must be trained in operating the GeneXpert instrument and performing of the Xpert MTB/RIF test and the associated QA activities. Users must pass a competency assessment before beginning testing.
- Advanced users must be trained to co-ordinate Xpert MTB/RIF test QA activities such as supervisory visits, competency assessments and troubleshooting. Advanced users are selected from the group of certified users by trainers based on their aptitude and temperament to perform advanced GeneXpert functions. Advanced users are certified as competent following a competency assessment.
- Clinical trainings should be conducted as part of the continuous medical education of healthcare and clinical staff to ensure an understanding of the uses for the test and its limitations, and to provide updated information. Testing site managers may be required to sensitize staff from referring sites on the Xpert MTB/RIF assay and provide training on ordering of tests, completing request forms and interpreting test results.

²⁵ <http://www.stoptb.org/wg/gli/trainingpackages.asp>

User (and advanced user) trainings are often coordinated and conducted centrally (e.g., by NTRL), regionally or at site level. The activities of the testing site managers typically include:

- selecting staff for training
- assessing (or delegating the assessment to users that have achieved a competency level of 4 or 5) and 3) documenting the competency of each user (see below)
- scheduling refresher training with competency assessment below level 3
- preparing staff duty roster to ensure regular rotation of trained users on the Xpert MTB/RIF testing bench

4.2. Conduct and document competency assessments

Competency in a procedure must be measured and documented²⁶. Competency assessments are based on the staff's actual skills and knowledge. Competency assessments for users are performed both at the end of the training and at the testing site according to the testing site's training plan (e.g., twice a year)²⁷. Advanced users should be assessed at the end of the GeneXpert advanced user training and regularly (usually annually or bi-annually) thereafter. Competent users are issued with a certificate and competency documented in their personnel file.

²⁶ The competency assessor must be competent in the procedure to identify deviations from the SOP.

²⁷ Competency assessments may be performed more frequently under special circumstances (e.g., following refresher training courses). Testing sites may wish to include competency assessments at the beginning of an Xpert MTB/RIF test user rotation, if the time between rotations exceeds three months.

Level	Competencies required	How do I achieve this?
Users	<ul style="list-style-type: none"> • Operating and understanding basic maintenance of the GeneXpert instrument • Performing the Xpert MTB/RIF test • Recording & reporting results using standard registers & tools • Carrying out and documenting all required QA activities. 	<ul style="list-style-type: none"> • Users must be trained using the standardized curriculum <ul style="list-style-type: none"> – Through training, users must acquire the necessary skills to be certified competent in the Xpert MTB/RIF test procedure
Advanced users	<ul style="list-style-type: none"> • In addition to the recommendations for users, advanced users must be competent in supervisory visits, competency assessments, troubleshooting & advanced maintenance procedures 	<ul style="list-style-type: none"> • Advanced users must be trained using the standardized curriculum <ul style="list-style-type: none"> – Through training, advanced users must acquire the necessary skills for troubleshooting, supervision & performing competency assessments
Testing site managers	<ul style="list-style-type: none"> • Providing supervision & coaching to users, analysing quality assurance data, troubleshooting & implementing corrective action • Managing site cartridge supplies • Communicating with supervisory laboratory, suppliers, and service providers 	<ul style="list-style-type: none"> • Testing site managers should have a basic understanding of the GeneXpert instrument and Xpert MTB/RIF test <ul style="list-style-type: none"> – Testing site managers must receive training in QA data analysis & procurement
Clinicians	<ul style="list-style-type: none"> • Adhering to national testing algorithm • Ordering of the appropriate test for a patient • Completely filling in the correct test requisition form • Collecting & submitting specimens for testing 	<ul style="list-style-type: none"> • Clinicians must receive training in application of the national testing algorithm
Health screeners	<ul style="list-style-type: none"> • Identifying patients that are eligible for Xpert MTB/RIF testing • Referring patients for Xpert MTB/RIF testing • Collecting and submitting specimens for testing 	<ul style="list-style-type: none"> • Health screeners must receive training in the national testing algorithm & identifying patients eligible for Xpert MTB/RIF testing

Element 5. Diagnostics connectivity and remote monitoring

Diagnostics connectivity refers to the ability to connect diagnostic test devices that produce results in a digital format, such as GeneXpert instruments. Connected devices can transmit data automatically to 1) clinicians and patients which allows for faster patient follow-up, 2) laboratory information management systems or electronic registers, reducing staff time and the chance of transcription errors and 3) the NTP to assist with surveillance of trends on disease or resistance patterns.

In addition, these systems offer the ability to manage inventory, conduct QA and remotely monitoring performance:

- Software can track consumption and inventory to avoid stock outs and expiring cartridges as well as potentially identify cartridge lots or instruments (modules) with poor performance and abnormal error rates.
- Software can rapidly and automatically calculate many of the key performance indicators and greatly facilitate the monitoring and evaluating processes.
- With remote monitoring, designated persons can get an overview of the facilities, devices and commodities in their network. For, example, the head of a supervisory laboratory can easily see how many tests are being performed and where and which sites are underperforming or experiencing abnormal results or errors, which may highlight a need for corrective action.

Because of the promise to improve recording, reporting and monitoring of data and performance indicators, diagnostics connectivity solutions, especially for Xpert MTB/RIF testing, are the way of the future and countries should give high priority to investing in developing and maintain such systems and in training personnel to operate the systems and to use the data generated for decision making.

Diagnostics connectivity solutions typically comprise: 1) a connectable diagnostic device that produces electronic data, 2) a software platform that receives and interprets data and 3) a means to transmit data from the device to the software platform and to a server. Systems have been developed by Cepheid, USA (C360), SystemOne (GxAlert™/Aspect™), Savics (DataToCare™) and Blue Frontier (Connected Diagnostics Platform). The systems connect GeneXpert instruments to central in-country servers or cloud-based servers via the internet or SMS. Instrument data can be accessed via web-based dashboards. The software can usually be configured so that subsets of data can be securely made available to those that need access to them. Security protocols also protect the privacy of the patient.

Activities at a glance

- Work with national level to determine which diagnostic connectivity system will be used
- Obtain & install all needed hardware & equipment
- Identify and train users
- Implement SOPs
- Establish lines of communication

The decision to implement a diagnostics connectivity solution will likely be made at the national level. The testing site staff will need to work with the national and supervisory levels to operationalize the system at the testing site. Important considerations at the site level are:

- What hardware and software will need to be installed and maintained at the testing site?
- Will internet or cellular service be used and what is the quality and reliability of the service?
- Who will have access to the data at the site?
- What training will be required for testing site staff to access the system?
- How will data be secured?
- How, and at what frequency, is the system backed-up?
- What is the availability of information technology support on-site or remotely and what are the computer skills of the users?
- What are the associated costs of implementing and maintaining a remote monitoring system (e.g., internet access charges, information technology support, software licenses)?

Details of diagnostics connectivity solutions may be found in the **GLI Quick Guide to TB Diagnostics Connectivity Solutions**²⁸.

How do I establish a data connectivity solution?

- Work with national level to
 - determine which diagnostic connectivity system and communication system will be used
 - obtain and install all needed hardware and equipment, e.g., routers, modems, server, or SIM cards
 - set up the connectivity solution
- Determine which staff members will have access to the system and to which data or features
- Have all users participate in implementation workshops and trainings that include data collection, data use and management, and day-to-day operations of connectivity solution
- Implement SOPs for access, reporting, data entry, data security and data back-up
- Arrange for on-site or remote information technology support
- Establish lines of communication with the national, regional or local units that will remotely monitor data

²⁸ GLI Quick Guide to TB Diagnostics Connectivity Solutions. GLI. 2016. <http://stoptb.org/wg/gli/gat.asp>.

Element 6. A safe and functional testing site

In a functional testing site, the GeneXpert instrument will be properly positioned on a vibration-free workbench in a clean, secure location and there will be an uninterrupted supply of power and appropriate working and storage temperatures. In a safe environment, WHO biosafety recommendations for conducting the Xpert MTB/RIF test will be followed with adequate ventilation (although the instrument should not be placed directly under an air-conditioning unit), appropriate personal protective equipment (PPE) will be used and biological waste will be disposed of safely and in accordance with regulations. Failure to provide a safe and functional work environment can impact the quality of testing in several ways including:

- An unsafe testing site is a hazard to staff, patients, the community and the environment
- In a poorly maintained or dirty testing site, specimens may become contaminated or cross-contaminated leading to inaccurate or incorrect results
- In an unsecure testing site, test results may be delayed if there is equipment failure or theft
- Testing sites that do not maintain uninterrupted power, optimal working temperature, and a clean environment can have equipment failures and high error rates that delay reporting and waste cartridges

What you need to do

6.1. Create and maintain a functional working environment

The working environment should consider placement and security of the GeneXpert instrument, power supply and operating conditions.

Activities at a glance

- Place the GeneXpert correctly
- Secure the GeneXpert instrument from theft
- Ensure an uninterrupted power supply
- Ensure an optimal working temperature
- Perform a risk assessment
- Ensure sufficient ventilation for testing procedures
- Provide suitable PPE and train staff in its correct use
- Discard waste as recommended
- Use appropriate disinfectant and prepare correctly

Considerations & Activities	How do I achieve this?
The GeneXpert is a precision instrument designed for operation indoors. The GeneXpert must be protected from dust.	<ul style="list-style-type: none"> Place the instrument in a sheltered environment, preferably on a stable bench with at least 5 cm of clearance on either side. Do not place the instrument close to the vents of other instruments or air-handling units. Remove clutter and enable clear access to the computer and module units. Do not place the instrument in a thoroughfare where it may easily be bumped.
Security measures and access control to the testing site are required to prevent theft of the GeneXpert instrument or the computer.	<ul style="list-style-type: none"> Access to testing areas should be restricted to authorized staff. Unaccompanied visitors should not be allowed in testing areas. Provide security measures of security locks, security bars and doors, if possible. Do not allow security measures to impair general safety nor be in violation of local regulations for escape routes in the case of fire or other emergencies. Secure instruments and the computer by a Kensington security lock or similar theft deterrents.
Uninterrupted power is needed to support the instrument in the event of a power interruption.	<ul style="list-style-type: none"> Use an uninterrupted power supply (UPS) to support the instrument in the event of a power interruption for at least the test duration (2 hours). Refer to the guidance document to determine appropriate selection of UPS.
The optimal operating temperature for the GeneXpert instrument is 15-30°C. The relative humidity must be between 10%-95% (non-condensing). Xpert MTB/RIF test reagents must be stored at 2-28°C	<ul style="list-style-type: none"> Depending on the local setting sites may require air conditioning units to be installed in the testing site and/or storage area. Storage of reagents (Element 7: Equipment and Supplies)

6.2. Create and maintain a safe working environment

The main occupational biosafety risks at a testing site are related to the inhalation of aerosols containing TB bacilli. The risk of infectious aerosol generation depends on:

- Type of procedure (e.g., splitting samples, vortexing, centrifugation)
- Frequency of testing and the testing site's workload
- Consistency of the material and its predisposition to aerosolize (e.g., viscous versus non-viscous liquids)
- Number of TB bacilli in the material or specimen (e.g., smear positive samples versus smear negative samples)

WHO has adopted an approach that assesses the risks associated with different technical procedures performed in different types of TB laboratories. **WHO's Tuberculosis laboratory biosafety manual (2012)**²⁹ describes the minimum requirements for facilities and the safe working practices that can be adopted following a risk assessment.

²⁹ Tuberculosis Laboratory Biosafety Manual. WHO. 2011. (http://www.who.int/tb/publications/2012/tb_biosafety/en/)

Biosafety

When used with unprocessed sputum specimens, the Xpert MTB/RIF test is a low-risk procedure and requires the same level of precaution as for performing direct AFB sputum-smear microscopy. When appropriate microbiological techniques are used, direct smear testing and processing of specimens for the Xpert MTB/RIF assay may both be carried out on an open bench in an adequately ventilated area. The bench used to process specimens for these procedures should be separate from areas where specimens are received and from areas where paperwork is completed and telephones are used. Appropriate PPE must be used (see below).

In the *WHO's Tuberculosis Laboratory Biosafety Manual*²⁹, adequate ventilation is described as directional airflow with 6–12 air exchanges per hour. For low-risk procedures such as Xpert MTB/RIF(2012), natural ventilation should be sufficient providing that air flows away from the technician and across the work area along with potentially infectious materials, then away from occupied areas of the room and to outside the laboratory. When the climate or use of air conditioning prevents the use of natural ventilation (e.g., from open windows), mechanical ventilation systems may be needed to provide an inward flow of air without recirculation in the room, or the use of ventilated workstations or certified biosafety cabinets may be needed to ensure a safe working environment. Note that the use of separate rooms may allow for adequate (natural) ventilation in the area where specimens are processed and cartridges are loaded and the use of air conditioning in the areas where the GeneXpert instrument is located and where temperature-sensitive supplies and reagents are stored. As needed, consult with a biosafety expert for a thorough analysis and recommendations.

Splitting or processing of specimens (e.g., NaLC-NaOH digestion and decontamination) are considered moderate-risk activities for generating infectious aerosols and must be performed within a certified Biological Safety Cabinet (BSC) and appropriate PPE must be used (see below).

Testing sites should conduct a risk assessment to determine whether additional safety precautions are required, such as when performing the Xpert MTB/RIF test in settings with a high burden of MDR-TB or when laboratory personnel are at increased risk of acquiring TB.

Personal Protective Equipment (PPE)

PPE minimizes the risk of exposure to aerosols, splashes and accidental inoculation. PPE includes laboratory coats and gowns, gloves and respirators:

- Wearing gloves is recommended. However; it may give technicians a false sense of safety; regular and thorough hand washing is essential. Gloves must be changed if they become contaminated or compromised.
- Surgical masks are not respirators, and do not protect the wearer against inhaling infectious aerosols. Surgical masks must not be worn in TB laboratories or testing sites.
- WHO does not recommend the use of respirators for sites only performing the Xpert MTB/RIF test and smear microscopy (i.e., low-risk testing sites) in adequately ventilated laboratories. The use of respirators does not replace the requirement for adequate ventilation. However, respirators must be used in medium- and high-risk testing sites; when recommended by countries or facilities; when testing samples from patients with high risk of MDR-TB; when splitting samples or when testing decontaminated and concentrated samples.

²⁹ Tuberculosis Laboratory Biosafety Manual. WHO. 2011. (http://www.who.int/tb/publications/2012/tb_biosafety/en/)

Waste management

Waste management procedures must comply with all pertinent local and national requirements and regulations. All materials associated with the Xpert MTB/RIF test should be treated as if they are biohazardous. All potentially infectious materials (except sharps) should be placed in properly labelled disposable biohazard bags. The biohazard bags containing the contaminated material should be sealed before being promptly transported for autoclaving or incineration. Transfer pipettes should be decontaminated using an appropriate disinfectant prior to disposal (e.g., place used pipettes in a one-liter plastic beaker containing 10% bleach solution and allow at least one-hour contact time before discarding pipettes into biohazard plastic bags).

Correctly prepare disinfectants

The optimal working concentrations for common disinfectants used at testing sites are:

- Bleach: 0.5% final concentration of chlorine in water (e.g., mix 10 ml of 5% bleach solution with 90 ml water), except for disinfecting transfer pipettes (see above).
- Alcohol: 70% solution
- Peracetic acid: 2% in water

Bleach and peracetic acid must be prepared daily. The working concentration of the bleach solution is usually prepared by dilution of concentrated household bleach, which may vary between 3% and 5%. Laboratories must determine the appropriate dilution factor based on the household bleach concentration. Laboratories must adhere to the manufacturer's recommendation regarding expiry dates and label prepared disinfectants with name, concentration, date prepared and expiry date.

Element 7. Equipment and supplies

7.1. Maintenance and calibration of the GeneXpert instrument

The GeneXpert is a precision instrument that requires regular maintenance to ensure that it provides accurate and precise results. The instrument is purchased with a 24-month limited warranty. Extended warranties can be purchased to cover the period after the warranty expires. Maintenance contracts and service level agreements are also available to ensure regular maintenance and service. The GeneXpert instrument must be verified as functioning properly before testing any clinical specimens. The GeneXpert instrument must be recalibrated according to the manufacturer's recommendations. Failure to maintain the GeneXpert instrument can affect quality:

- Poorly maintained equipment is prone to failures, which result in delayed reporting, lack of access to services or inaccurate Xpert MTB/RIF test results being reported
- Failure to ensure warranties or maintenance agreements are adhered to can be costly if modules fail

What you need to do

7.1.1. Perform instrument verification

Each module in the GeneXpert instrument should be evaluated as being “fit for purpose” through verification with known positive and/or negative material prior to commencing testing of clinical specimens. At least a single verification test should be performed per module upon instrument installation and following calibration or swapping of instrument modules. Verification panels are routinely distributed by Cepheid with each new instrument and with re-calibrated modules. Additional verification panels may be required if instruments are moved and would need to be ordered. These verification panels consist of a card containing five dried culture spots (DCS) of a known concentration of whole inactivated RIF-susceptible MTBC. DCS samples should be processed according to instructions and one sample tested per module. All results are expected to be “MTB detected, RIF resistance not detected.”

- If an invalid/error/no result is obtained on any module, repeat the test in that module using the extra DCS sample provided.
- Instrument verification results should be reported to NTRL or the appropriate person responsible for overseeing testing in the country and Cepheid should be contacted immediately in order to assist with any issues encountered during verification process.
- The GeneXpert verification records must be kept at the testing site throughout the lifetime of the instrument.

Activities at a glance

- Maintain all testing site equipment in a good working condition
- Perform preventative maintenance
- Monitor instrument performance and perform on-request maintenance as required
- Ensure warranties and service contracts are in place and adhered to
- Forecast how many cartridges will be used and monitor Xpert MTB/RIF cartridge consumption
- Implement a stock control system to manage Xpert MTB/RIF stock
- Store Xpert MTB/RIF cartridges in accordance with manufacturer's recommendation

7.1.2. Maintain a functional GeneXpert Instrument

The GeneXpert is a precision instrument that requires regular preventative maintenance and ad hoc servicing and maintenance.

Preventative maintenance should be performed on regular basis by the end-user to ensure good performance of the GeneXpert instrument. Step-by-step procedures are described in the **GeneXpert User Manual**. Preventative maintenance should be recorded on the GeneXpert Maintenance Log. Maintenance records must be reviewed by the testing site manager at least monthly and during supervisory visits and instrument-related problems followed-up.

On-request maintenance should be performed in specific situations upon request by Cepheid Technical Support. It allows the checking or the re-setting of the instrument in case of malfunctioning. On-request maintenance is recorded in the GeneXpert Maintenance Log.

7.1.3. Maintain warranty coverage

All GeneXpert systems, with the exception of the GeneXpert Infinity product line, come with a 24-month warranty on service and parts. Three and five-year warranty extensions can be purchased. Warranties typically cover instrument or module repair and/or replacement. All shipment costs are included. Not included are travel costs for all onsite interventions. Guidance on extended warranties can be accessed from the FIND website (<https://www.finddx.org/find-negotiated-product-pricing/>). Programmes should contact Cepheid or their Authorized Service Provider for details of the extended warranties and quotes for the cost of the warranties and covered services. Alternatives to an extended warranty are maintenance contracts and service level agreements.

7.1.4. Arrange for module repair and replacement

If a module failure is suspected, the testing site must initiate efforts to have the module repaired or replaced. This may require supplying the Installation Qualification (IQ) report and the error report to the GeneXpert Focal person in country or directly to Cepheid depending on the country's processes and procedures. Cepheid will inform the testing site if the module needs replacing. The GeneXpert Focal Person or implementing partner (if applicable) must be informed and copied on all correspondence if Cepheid is contacted directly. Module replacement may take a few days to several months depending on the reason for replacement, the partners involved (if applicable), the warranty and the location of the instrument. An adequate budget for module repair and replacement must be available and promptly disbursed when needed.

How do I ensure well-functioning GeneXpert instruments?

- Evaluate each module in the GeneXpert instrument for being “fit for purpose” through verification with known positive and/or negative material prior to commencing testing of clinical specimens, after service or calibration, or after moving instruments
- Perform routine maintenance according to the recommended daily, weekly and monthly schedules. Records of maintenance must be kept
- Ensure GeneXpert instruments are recalibrated according to the manufacturer's recommendations
- Monitor performance of each module (e.g., failed runs) and record in a maintenance log. Use the capabilities of the diagnostic connectivity system to monitor the performance of GeneXpert instruments and individual modules
- Obtain servicing and repair of instruments from authorized service providers according to national policies, procedures and SOPs
- Purchase extended warranties or service contracts for each GeneXpert instrument

What you need to do

7.2. Ensure adequate supplies & reagents

A robust inventory system is required to monitor Xpert MTB/RIF cartridge consumption. Accurately forecasting Xpert MTB/RIF test supply needs reduces the risk of an interruption in service due to shortage of reagents. Failure to maintain an adequate, uninterrupted supply of quality-assured reagents can affect quality because 1) stock-outs result in delayed testing and delayed reporting of results and 2) use of poor quality or expired reagents can result in high error rates and inaccurate test results.

7.2.1. Manage Xpert reagent stock

Inventory management is the process of ordering, receiving and storing supplies to provide an uninterrupted Xpert MTB/RIF test service.

1. A first step is to forecast how many Xpert MTB/RIF cartridges will be used in the period (e.g., one month). To accurately forecast how many cartridges to purchase, the testing site must be aware of its average usage, the lead time for delivery and the capacity for cold storage.

The average usage of Xpert MTB/RIF reagents can be calculated by reviewing the number of tests performed per month. Lead time is defined as time between placing an order and receiving it at the testing site. The lead time needs to consider the time taken to clear customs, and the transport time to the testing site level.

Calculating how much to order:

a = number of Xpert MTB/RIF tests performed (e.g, 210 tests)

b = number of months (e.g, 3 months)

c = average usage per month ($a \div b$) (e.g, $210 \div 3 = 70$ tests per month)

d = lead time (e.g, 4 months)

e = stock in-hand (e.g, 140 cartridges)

f = recommended buffer stock (2 months average usage = 140 tests)

Minimum Xpert MTB/RIF cartridges to order for a four-month lead time:

$$(c \times d) - e + f = (70 \times 4) - 80 + 140 = 340 \text{ cartridges}$$

2. Monitor Xpert MTB/RIF cartridge consumption by using a supply management system (e.g., stock cards or an electronic equivalent). Minimum order levels and lead times must be calculated and documented on stock cards. Rotation of stock using “First-in, First-out” (FIFO) and First Expired, First Out (FEFO) principles ensures that out of date reagents are not used. Forecasts should be reviewed and updated from time to time based on actual consumption. Significant variations away from the average monthly consumption should be accounted for to ensure uninterrupted supply of reagents.
3. Label all supplies and reagents with date received, the date first opened and new expiry date when opened; where possible, limit stocks to a six-month supply.

7.2.2. Quality control of new batches of cartridges and reagents

New lot testing, also known as lot-to-lot verification, is performed on new batches of cartridges and reagents. New lot testing usually consists of testing a sample of the new cartridges and comparing the results to existing lot of cartridges with known performance:

- Conditions during transport & storage of cartridges may affect their performance.
- Cartridge test failures may indicate that the new batch of cartridges are not fit for use.

New lot testing is preferably performed at the central (e.g. NTRL) or regional level, thereby ensuring that cartridges with test failures are not distributed and reducing the burden of testing and number of cartridges used.

On occasion, new lot testing at the testing site may be needed to monitor conditions during transport and storage of cartridges in-country or to meet ISO 15189 requirements for accreditation. In this case, the use of positive and negative controls (e.g., PT samples, sputum or simulated samples of known reactivity) is recommended for incoming QC of new batches of reagents. The results from positive and negative controls must be recorded, and unexpected results must be recorded, investigated and monitored for trends over time. QC records must have documented review by the testing site manager and retained onsite for a period according to local or national policy. See Supporting Documents/forms and templates for New lot testing SOP template.

7.2.3. Properly store cartridges and reagents

Adverse environmental conditions, outdated reagents, improper reagent shipment and improper reagent storage are all possible sources of error that can invalidate the Xpert MTB/RIF test results. Xpert MTB/RIF cartridges and reagents must be stored at 2-28°C. Expired reagents or cartridges must not be used.

How do I ensure the quantity and quality of supplies?

- Manage supply of Xpert MTB/RIF cartridges (forecast needs and order in a timely manner) to provide an uninterrupted Xpert MTB/RIF testing service
- Conduct new lot testing on each new batch of cartridges as needed
- Properly store Xpert MTB/RIF cartridges and monitor expiration dates

Element 8. Participate in an EQA programme

Testing sites should participate in an EQA program that includes proficiency testing, on-site evaluations and supportive supervision. The Xpert MTB/RIF Proficiency Testing (PT) programme is an important tool for communicating with and motivating staff. Used correctly, the PT programme can be used to identify and resolve problems in Xpert MTB/RIF testing. On-site evaluations and supportive supervision can facilitate evaluation of the quality of testing, analyse QA results, identify problems, provide corrective actions and document improvements. Failure to enroll in a comprehensive EQA program, is a missed opportunity to identify and correct problems that affect the quality of testing.

What you need to do

8.1. Participate in a system of supportive supervision and on-site evaluations

On-site supportive supervisory visits for assessments and training are especially critical during early stages of implementing a new test or procedure as they provide motivation and support to staff. On-site supervisory visits are also good opportunities to provide refresher training, mentoring, troubleshooting advice and technical updates. Strong relationships with GeneXpert users encourage rapid reporting of any problems and enables rapid troubleshooting, re-training and corrective actions. In addition to providing constructive feedback on performance, supportive supervision provides updates on technical guidelines and procedures, opportunities for training and assistance with reviews of quality indicators and results of PT and development of corrective actions.

Given the large benefit of supportive supervision on the quality of laboratory testing, testing sites should proactively seek out opportunities to participate in a system of supportive supervision by contacting supervisory laboratories, QA assurance focal points at the regional or national level, the TB programme officers or Xpert implementing partners.

In most settings, the NTRL or supervisory laboratory will be responsible for planning and conducting the on-site evaluations. The supervisory visits should be planned at regular intervals with schedules communicated to sites in advance. The on-site evaluations should use standardized checklists and include discussions with GeneXpert users, testing site management, review of Xpert MTB/RIF test site documentation and observation of testing site operations. Any problems identified during the assessment should be discussed immediately with facility staff and a plan established for addressing problems. The testing site should receive interim feedback immediately after the supervisory assessment and subsequently a full supervision report. The testing site should undertake and document any recommended corrective actions in a timely manner.

Activities at a glance

- Enroll the testing site in an Xpert MTB/RIF PT programme
- Perform PT testing as required. Receive and analyse PT reports.
- Troubleshoot unexpected PT results and identify corrective actions
- Participate in a system of supportive supervision and on-site evaluations

How do I participate in a site supervisory programme (Testing Site)?

- Schedule supervisory visits according to national policy
- Prepare necessary documents for supervisory visits
- Undertake and document any recommended corrective actions

8.2. Testing PT panels

The objective of PT is to ensure inter-testing site comparability of results. The Xpert MTB/RIF test results reported by each testing site are compared to the reference laboratory Xpert MTB/RIF test result. All testing sites should enroll in an Xpert MTB/RIF PT programme. The GeneXpert Focal Person or the QA Unit can facilitate participation in the PT program.

The National program will decide which PT panels to use. A variety of PT panels using different sample matrices were evaluated by Scott, et al in 2014 and found to be equivalent. Included in this evaluation were artificial sputum (WHO/GLI), dried tube specimens (CDC), dried culture spots (National Health Laboratory Service (NHLS), South Africa) and two commercial suppliers (lyophilized samples and liquid samples). Currently, PT panels are available from CDC (for selected countries and sites), Smartspot Quality (South Africa) and INSTAND Germany (MMQCI). Alternatively, a country may elect to prepare and use its own PT panels, see SOP templates in the Supporting Documents/forms and templates. PT panels should preferably be tested quarterly.

The PT programme assesses pre-analytical, analytical, and post-analytical processes occurring at the testing site, and not necessarily each GeneXpert module. PT panels should preferably be tested quarterly. Module functionality should be verified using the Xpert Check.

Pre-analytical

- Assess that the contact details of the testing site correspond with those on record at the PT programme provider
- Store the PT panels in accordance with the instructions provided with each panel

Analytical

- Follow the instructions for preparing the sample for testing as directed by the PT programme provider
- Perform the Xpert MTB/RIF test as you would a routine patient specimen

Post-analytical

- Record the result of the Xpert MTB/RIF test on the report form provided by the PT programme provider
- Report the results to the PT programme provider and to the GeneXpert Focal Person or QA Unit (if required)
- The PT panel results will be analysed and compared to the expected results. The results will be scored and the outcome reported to the testing site and the QA Unit
- Review the outcome of the PT testing report
- If there are any PT failures, troubleshoot (e.g., using root-cause analysis) and perform corrective actions

How do I participate in a PT programme (Testing Site)?

- Enroll in an Xpert MTB/RIF PT programme in accordance with national policies and procedures
- Perform PT testing as required. Receive and analyse PT reports
- Troubleshoot unexpected PT results and identify corrective actions
- Undertake and document any corrective actions

Element 9. Monitor and analyse Xpert MTB/RIF quality indicators

Testing sites should participate in an EQA program that includes proficiency testing, on-site evaluations, and supportive supervision. The Xpert MTB/RIF Proficiency Testing (PT) programme is an important tool for communicating with and motivating staff. Used correctly, the PT programme can be used to identify and resolve problems in Xpert MTB/RIF testing. On-site evaluations and supportive supervision can facilitate evaluation of the quality of testing, analyse QA results, identify problems, provide corrective actions, and document improvements. Failure to enroll in a comprehensive EQA program, is a missed opportunity to identify and correct problems that affect the quality of testing.

What you need to do

9.1. Identify and implement quality indicator monitoring

In most cases, the NTRL or supervisory laboratory will determine which indicators (See Element 9 of Part 1) are to be monitored, analysed and reported by each Xpert MTB/RIF testing site as well as the thresholds or targets for indicators (e.g., the Xpert MTB/RIF test error rate should be less than < 3%). The testing site manager will need to develop or obtain forms to collect the data for each indicator, train personnel in the importance and use of the indicator data collection forms, implement the routine collection of indicator data and use the data to inform action plans for improvement.

Table 14 lists GLI recommended key performance indicators for Xpert MTB/RIF testing as well as general laboratory quality indicators³⁰ that should be monitored monthly by each testing site. Additional indicators such as the completeness of documentation (e.g., use and completeness of registers, logs, forms) or adherence to SOPs may be assessed during supervisory visits. For some indicators (e.g., proportion of specimens that are rifampicin resistant), targets are setting-specific. Laboratories should monitor indicators and establish local targets and acceptable ranges. Deviations from expected values should be investigated.

Sites should collect disaggregated data according to the population group tested (e.g., HIV positive, MDR-TB risk, extrapulmonary TB). If the quality indicator for error rates exceeds the target value, it should be further disaggregated to identify common error codes, in order to assist with corrective and preventive actions. The GeneXpert platform produces electronic data, and therefore a data connectivity solution should be established to enable remote monitoring of quality indicators (see Element 5).

Activities at a glance

- Implement quality indicator monitoring
- Regularly review quality indicators and troubleshoot unexpected results by identifying corrective actions
- Report quality indicator data to the NTP/MOH

³⁰ GLI Practical Guide to TB Laboratory Strengthening. 2017. Available at <http://stoptb.org/wg/gli/gat.asp>.

Table 14. Key performance indicators that should be monitored monthly by testing sites

Xpert MTB/RIF Testing Quality Indicator	Target
Number of tests performed, by type of test and key population (e.g., HIV+, previously treated)	Full utilization of a 4-module GeneXpert instrument is 12 tests per workday.
Service interruptions (stock-outs, equipment down time, etc.)	No interruptions
Number and proportion of specimens with MTBC detected, rifampicin resistance not detected	Dependent on population tested and country drug-resistance prevalence and patterns
Number and proportion of specimens with MTBC detected, rifampicin resistance detected	Dependent on population tested and country drug-resistance prevalence and patterns
Number and proportion of specimens with MTBC detected rifampicin indeterminate	Dependent on population tested and country drug resistance prevalence and patterns
Number and proportion of specimens with MTB detected trace, disaggregated by patient group (For Ultra test)	Dependent on population tested and country drug resistance prevalence and patterns
Number and proportion of specimens with MTBC not detected	Dependent on population tested and country drug-resistance prevalence and patterns
Number and proportion of specimens with errors	<3%
Number and proportion of specimens with invalid results	<1%
Number and proportion of specimens with no results	<1%
Proportion of specimens tested with Xpert MTB/RIF for which a result was reported within 24 hrs (i.e., time from receipt of specimen to reporting of results)	>95%. The target turnaround time may be modified by the programme based on testing schedules

In addition to the indicators of the quality and performance of the Xpert MTB/RIF testing, sites may be requested by the NTP to collect and report data for additional indicators needed to assess the quality of the diagnostic cascade or to assess aspects of laboratory strengthening under the End TB Strategy. The national or supervisory level will determine the frequency of collection of these data (e.g., once or twice a year).

Table 15. Key performance indicators to monitor the quality of the diagnostic cascade

Diagnostic Cascade Quality Indicators	Target
Number and percentage of presumptive TB patients tested with Xpert MTB/RIF (End TB Strategy Laboratory Indicator 1) ³¹	Dependent on population tested and country prevalence patterns
Percentage of notified new and relapse TB cases tested with a WRD as the initial diagnostic test (Indicator 2)	80% (2020)
Percentage of notified new and relapse TB cases with bacteriological confirmation (Indicator 3)	80% [relapse: 90%] (2020)
Number and proportion of bacteriologically confirmed patients who were initiated on treatment according to the national algorithm	Target is setting specific
Percentage of testing sites using a WRD at which a data connectivity system has been established that transmits results electronically to clinicians and to an information management system (Indicator 4)	100% (2020)
Number and proportion of Xpert MTB/RIF test results reported to clinicians using electronic systems	Target is setting specific
Number and proportion of TB patients detected by Xpert MTB/RIF that were reported to the TB control program, TB or MDR TB treatment focal person	Target is setting specific
Percentage of notified bacteriologically confirmed TB cases with DST results for rifampicin (Indicator 7)	100% (2020)
Percentage of notified rifampicin-resistant TB cases with DST results for fluoroquinolones and second-line injectable agents (Indicator 8)	100% (2020)
Number and proportion of patients with RIF-resistant TB identified by Xpert MTB/RIF testing referred for second-line DST	100%
Proportion of specimens collected for Xpert MTB/RIF testing for which a result was received within the specified target time (i.e., time from collection of a specimen to receipt of results)	>95%. The 'specified time' should be determined for each laboratory taking into account testing schedules and specimen transport schedules (e.g., on demand, daily, twice weekly, etc.)
Proportion of specimens referred for DST for which a result was received within the specified target time (i.e., time from referral of a specimen to receipt of results)	>95%. The 'specified time' should be determined for each test required (e.g., molecular DST or liquid culture DST) and the collection schedule used (e.g., on demand, daily, twice weekly, etc.)

³¹ The indicator number in parentheses refers to the number of the global indicators in the WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy. Available at <http://www.who.int/tb/publications/labindicators/en/>

9.2. Regularly review quality indicators and troubleshoot unexpected results by identifying corrective actions

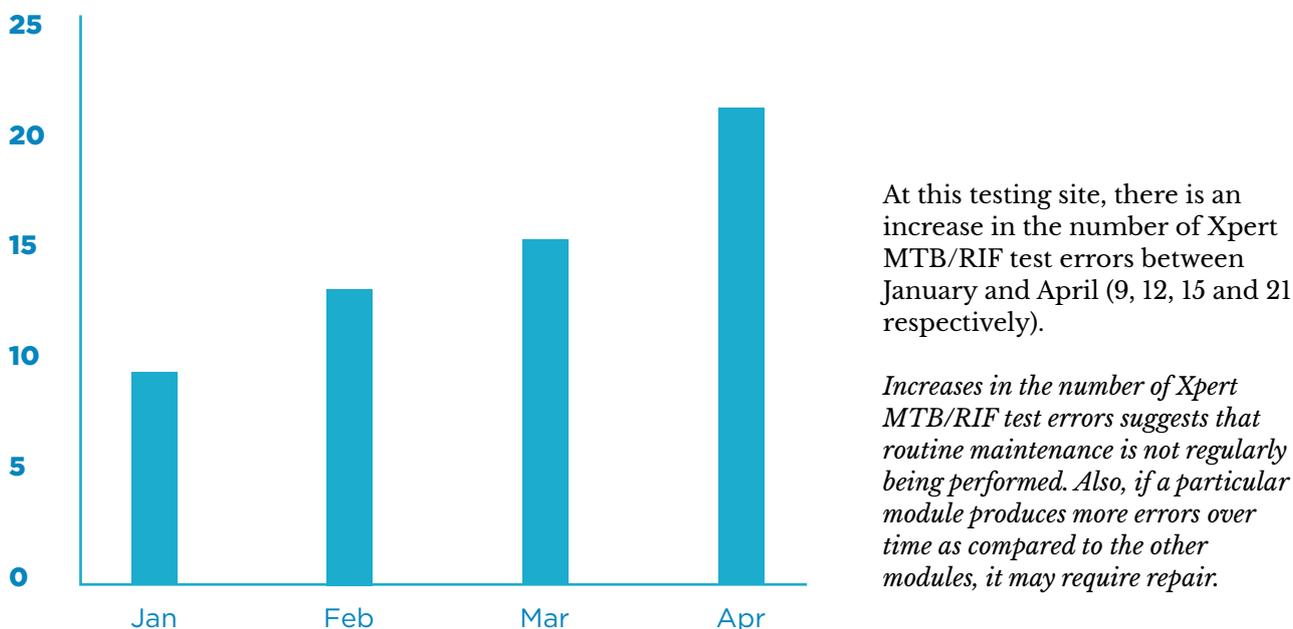
All laboratories should collect and analyse performance data on at least a monthly basis, using a standardised format. Examples of data collection and analysis forms for key performance indicators as Microsoft Word files and in an Excel format that can automatically calculate the indicators when the required data are entered.

Targets should be set for all indicators monitored (usually set by the national or supervisory levels), and any unexplained change in quality indicators, such as increase in error rates, a change in MTB positivity rate or RIF-resistance rate, or a significant change in volume of tests conducted, should be documented and investigated. Indicators should be reviewed by the laboratory manager and must always be linked to corrective actions if any unexpected results or trends are observed. Documentation of corrective actions and subsequent improvement and normalization of laboratory indicators following the corrective actions are critical.

A system should be in place for reporting of monthly quality indicators to the supervisory laboratory, NTR or NTP. These data should also be made available to the supervisory laboratory prior to supervisory visits to facilitate analysis and development of corrective actions if necessary. For Xpert MTB/RIF testing, the use of diagnostics connectivity solutions (Element 5) will allow for real-time remote monitoring of sites within a network and provide the capacity to easily and accurately stratify data as needed for analysis of performance.

An example of Xpert MTB/RIF test performance indicator data collected and analysed at a testing site is shown below:

Figure 4: Performance Indicator - Number of Xpert MTB/RIF Test Errors



What should be done?

Perform a root cause analysis:

- Example 1: the test errors are associated with one module, error code 5007. Solution: the module must be replaced.
- Example 2: the test errors are associated with a particular user. Solution: the user must be retrained.

9.3. Report quality indicator data to the NTP/MO

QA and quality improvement are a continuous and cyclical process. Data should be collected and initially reviewed at the local testing site level. Trends that require intervention (e.g., increase in proportion of unsuccessful results, increase in service interruption) must be communicated, appropriate corrective actions must be undertaken and impact of the interventions reviewed. As far as possible, sites should be empowered to analyse their own data in order to be able to take corrective actions without external assistance. However, more complex issues (e.g., an increase in rifampicin-resistance) may need support from higher levels (e.g., supervisors, advanced GeneXpert users) in order to recommend appropriate actions.

Furthermore, the monthly reports of performance indicators will be collated and analysed at the regional and national levels to identify trends that extend beyond individual sites (e.g., reagent batch issues, PT, or equipment maintenance). The results of these analyses should be communicated to the sites so that they may take corrective action as needed.

Element 10. Strengthen the clinical-laboratory interface and the diagnostic cascade

A comprehensive system to ensure the quality of laboratory testing must address all the relevant parts of the diagnostic cascade, not just what happens in the laboratory. Published literature on a variety of laboratory tests highlights that factors that have the largest impact on quality of diagnostic services occur in the pre-pre-analytical phase (choice of test, etc.) and post-post-analytical (interpretation of results and patient management).

Key steps in strengthening the clinical-laboratory interface and assuring the quality of the diagnostic cascade that the testing site can do include:

- provide training to laboratorians, nurses, clinicians and other healthcare workers on the aspects of the diagnostic cascade that affect the quality of TB testing (e.g., collecting quality specimens)
- collect quality samples and promptly submit to the testing site along with a properly completed test requisition form
- report accurate results to clinicians, TB control officers and TB and MDR TB treatment focal persons and include information on the interpretation of the test results

Activities at a glance

- Provide training on the diagnostic cascade to all laboratorians and healthcare workers
- Collect and test quality samples
- Report accurate results

10.1. Provide training on the diagnostic cascade to laboratorians and health care workers

A standardized training programme should be available from the NTP or NTRL and include training curricula for laboratorians, nurses, clinicians and other healthcare workers on the aspects of the diagnostic cascade that affect the quality of TB testing. Testing sites should keep a log of trained staff and those requiring training and interact with appropriate authorities to have staff trained. All training should be documented, with plans made for regular refresher trainings. Regular meetings can be used to impart information to laboratory and facility staff on updates to procedures and processes.

- The GLI standardized curriculum for Xpert MTB/RIF users and advanced users contains modules that address the diagnostic cascade.
- Clinical trainings should be conducted as part of the continuous medical education of healthcare and clinical staff. Testing site managers may be required to provide training to familiarise staff from referring sites on the uses and limitations of the Xpert MTB/RIF assay and provide training on ordering of tests, completion of request forms and interpretation of test results. This will help ensure that national testing algorithms are followed, the correct test is ordered for each patient, quality samples are collected and submitted to the laboratory, accurate results are reported to the clinician, results are correctly interpreted and patients are promptly placed on appropriate therapy.

10.2. Test quality samples

A good quality specimen is required to produce a quality Xpert MTB/RIF test result. Specimens must be properly collected, labelled, stored and promptly transported to the testing site. Standardized test requisition forms must be used and completely filled out with all the required information. Failure to obtain and use good quality specimens can affect quality because

- Specimens may be rejected because of poor quality, inadequate volume or improper labelling which may lead to recalling patients to obtain a good quality specimen which may lead to a delay in diagnosis
- The use of poor quality specimens may lead to high error rates and wastage of cartridges and supplies
- Incomplete or incorrect labelling may lead to inaccurate, misdirected or delayed reporting.

What you need to do

10.2.1. Collect good quality sputum samples

Good quality specimens are essential to achieve good quality test results. Sputum specimens must:

- Have adequate volume. A minimum of 1ml of sputum is required for the Xpert MTB/RIF test.
- Be of good quality. A sputum specimen must be from the lungs, not from the nose and mouth. If the sputum is too bloody or contains too much pus, or food particles, it may cause an invalid Xpert MTB/RIF test result.

The Xpert MTB/RIF test can also be used for the detection of MTBC in certain non-respiratory specimens (e.g., cerebrospinal fluid, lymph nodes and other tissues), which are usually collected in higher level facilities. SOPs for processing these samples can be found in the *Xpert MTB/RIF implementation manual - Technical and operational 'how-to': practical considerations*³². Clinicians should refer to accepted local and international standards for the collection of these samples. Specific requirements for non-respiratory specimens are:

- For cerebrospinal fluid, a minimum volume of 0.1ml is required for the Xpert MTB/RIF test.
- Lymph nodes and other tissues must be processed in a BSC given the risk of producing aerosols while grinding and homogenizing samples.

Sputum must be collected in a durable, screw top, plastic container. Ensure that SOPs on how to collect good quality sputum samples are available on site and that patients are instructed in providing good quality specimens. *The Laboratory Diagnosis of Tuberculosis by Sputum Microscopy - The GLI Handbook*³³ contains useful guidance on collecting sputum samples for the diagnosis of TB.

Activities at a glance

- Inform healthcare workers on the sample requirements for Xpert MTB/RIF testing
- Ensure patients are instructed in good sputum collection technique
- Ensure complete and accurate labelling of specimen containers and request forms
- Establish clear policies and procedures for sample rejection

³² Xpert MTB/RIF implementation manual - Technical and operational 'how-to': practical considerations. http://who.int/tb/publications/xpert_implem_manual/en/

³³ Laboratory Diagnosis of Tuberculosis by Sputum Microscopy - The GLI Handbook. GLI. 2013. <http://www.stoptb.org/wg/gli/gat.asp>

10.2.2. Store and transport specimens

If specimens are not collected on site, it may be necessary to store specimens at the collection site until they can be transported to the Xpert MTB/RIF testing site. Procedures and considerations for storing and transporting TB specimens may be found in the *GLI Guide for TB Specimen Referral Systems and Integrated networks*³⁴.

Process and Considerations	How do I achieve this?
<p>Storage</p> <ul style="list-style-type: none"> • If there is a delay in sending sputum samples to the testing site, they should be stored at 2-8°C prior to transport • Samples may be stored at 2-8°C for a maximum of 10 days prior to testing • Samples may be stored at a maximum of 35°C for up to 3 days, and then refrigerated at 2-8°C for a combined maximum duration of 10 days 	<ul style="list-style-type: none"> • After specimen collection, store the sputum container in a fridge/cooler box (do NOT freeze) until collection for transport to the testing site • For Xpert MTB/RIF testing, bacteria in the sputum specimens can be inactivated and then stored and transported at ambient temperature or at 2-8°C³⁵. • Protect the sputum container against heat and sunlight and place the container in a plastic bag to prevent contamination • Keep a record of sputum collection at the clinical facility, and the date of transport to the testing site
<p>Specimen transport</p> <ul style="list-style-type: none"> • Sputum samples should be transported to the testing site as soon as possible, preferably on the day of collection 	<ul style="list-style-type: none"> • Samples must be transported in such a way as to prevent spillage or leakage while in transit. • Triple packaging must be used. • Drivers of vehicles transporting sputum should be educated regarding safety procedures and have access to a spill kit in case of a spill or leakage • A specimen transport log should be used to track specimen transport
<p>Specimen receipt</p> <ul style="list-style-type: none"> • Sputum samples must be promptly processed at the testing site 	<ul style="list-style-type: none"> • Upon receipt of samples, ensure that the request forms are completed and that the samples are correctly labelled • Record the date and time that specimens arrive at the testing site. The testing site should monitor specimen transport times to troubleshoot delays if they occur • The testing site must evaluate and record the quality and volume of sputum samples. Report back to referring facilities in case of poor quality specimens or incomplete labelling

10.2.3. Sample rejection

Testing sites should have a policy for rejecting samples for Xpert MTB/RIF testing. The policy must be communicated to clinicians and healthcare workers requesting Xpert MTB/RIF testing. Records should be kept of the number of rejected samples. If a sample is rejected, the testing site must attempt to collect another sample. Reasons for rejecting samples include:

- The sample is incorrectly labelled or is received without the necessary requisition forms - these samples may not correctly identify the patient;
- The sample has leaked in transit - these samples are a risk to testing site personnel;
- In case of sputum, the volume is less than 1ml or the sputum is too bloody and/or contains too much pus - these samples may give erroneous results.

³⁴ Guide to TB Specimen Referral Systems and Integrated Networks. GLI. 2017. <http://www.stoptb.org/wg/gli/gat.asp>

³⁵ Technical Expert Group Meeting Report: Commercial sample transport products. Geneva, World Health Organization. 2017. (WHO/HTM/TB/2017.19). http://www.who.int/tb/areas-of-work/laboratory/policy_statements/

10.3. Report accurate results

The Xpert MTB/RIF test results produce reports indicating whether the sample contains MTBC and whether MTBC is resistant to RIF. Test results must be reported as soon as possible to allow rapid treatment initiation. Standardized test report forms must be used that contain all the required information on the test result and interpretation. Inaccurate reporting of results can lead to under- or over-diagnosis of TB or drug resistance, leading to negative impact on patients and the community. The lack of standardization of reporting may lead to confusion and incorrect interpretation of results.

What you need to do

10.3.1. Monitor performance of internal quality controls

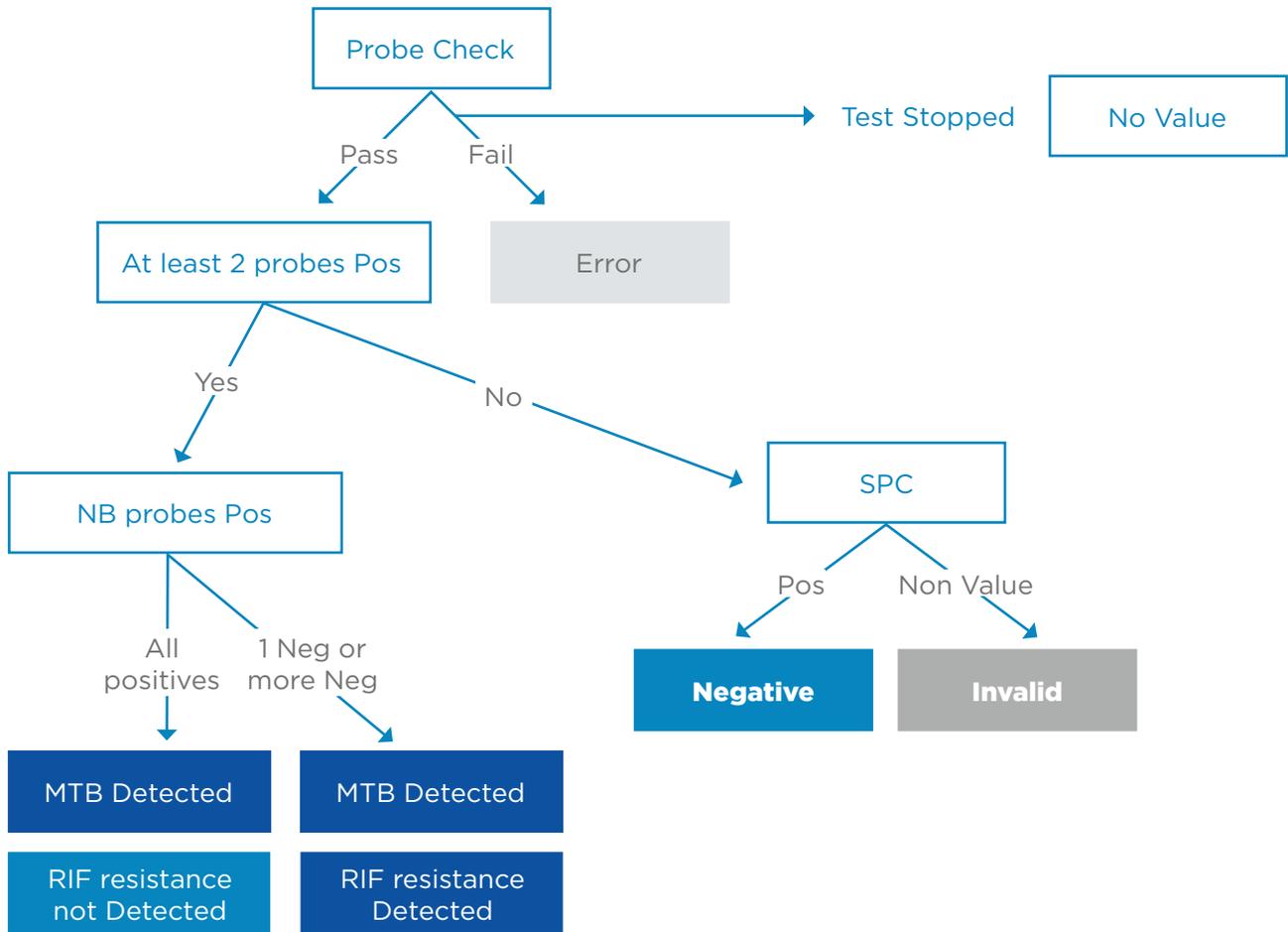
Internal quality controls should be monitored for all tests to ensure a quality result. Each Xpert MTB/RIF cartridge contains a Sample Processing Control (SPC, non-infectious lyophilized spores of *Bacillus globigii*) that verifies that proper lysis of MTBC has occurred, verifies adequate processing of the specimen, and detects specimen-associated PCR inhibitor³⁶. The SPC must be positive in a sample where “MTB Not detected” and can be either positive or negative if “MTB Detected”. If the control is negative in a “negative” sample, the test is “Invalid”.

Each Xpert MTB/RIF test cartridge also contains Probe Check Control (PCC). The PCC is a check undertaken by the system before the start of the PCR reaction and measures the fluorescence signal from the probes to monitor bead rehydration, reaction-tube filling, probe integrity and fluorescent dye stability. If the PCC is not passed, the test is stopped, and an “Error” result is obtained.

Activities at a glance

- Inform healthcare workers on the sample requirements for Xpert MTB/RIF testing
- Ensure patients are instructed in good sputum collection technique
- Ensure complete and accurate labelling of specimen containers and request forms
- Establish clear policies and procedures for sample rejection

³⁶ GeneXpert Dx Systems Operator Manual. <ftp://hbdc:Crasa7Uc@ftp.caplaser.net/>



Note that the use of external positive and negative controls with each Xpert MTB/RIF test run is not feasible as each module (and each cartridge) is a single instrument. Xpert MTB/RIF test internal controls are sufficient.

10.3.2. Report results

When performing the Xpert MTB/RIF test, the GeneXpert instrument reports whether the sample contains MTBC (through the detection of DNA from MTBC) and whether MTBC is resistant to RIF (through the detection of mutation in the *rpoB* hot-spot region). The MTB/RIF assay reports results as MTB not detected; MTB detected RIF resistance not detected; MTB detected RIF indeterminate; MTB detected RIF resistance detected, or error/no result/invalid. The MTB/RIF Ultra assay uses the same semi-quantitative categories used in the Xpert MTB/RIF assay (MTB detected high, medium, low, and very low) and adds a new semi-quantitative category, 'MTB detected trace'. There is no information on rifampicin resistance or susceptibility for samples with an MTB detected trace result.

If the Xpert MTB/RIF test is invalid, the GeneXpert instrument reports an error, invalid result or no result. There are a number of reasons for an invalid result, including internal control failure due to the presence of PCR inhibitors (pus, blood or food particles present in the sputum specimen) or failure of the instrument due to electrical failure.

Xpert MTB/RIF results must be recorded in a standard format in the register (or equivalent, e.g., Laboratory Management System [LMS]) at the testing site. Xpert MTB/RIF results must be analysed and reviewed on monthly basis to detect changes, which may indicate procedural problems (*Element 9: Monitor and analyse performance indicators*).

The results of the Xpert MTB/RIF test are reported on the approved reporting form. Report Xpert MTB/RIF results within 24 hours after the sputum specimen is received at the testing site to allow rapid treatment initiation. Reports may be sent by Short Message Service (SMS), email or fax and can also be sent as paper copies by courier, according to the arrangement with the referring sites (and national policy). See Element 5 for a discussion of the uses of diagnostics connectivity systems for reporting. Appropriate results reporting systems should be put in place to ensure rapid reporting of results to the referring sites.

The report form should include additional information to assist the clinician in interpreting the results. Details of testing Xpert MTB/RIF testing algorithms and interpretation of results are provided in the GLI Model TB Diagnostic Algorithms³⁷ and the GLI Guide on Planning for country transition to Xpert[®] MTB/RIF Ultra Cartridges³⁸.

Testing sites may need to update registers and reporting forms to comply with national policy.

³⁷ GLI Model TB Diagnostic Algorithms. 2017. http://stoptb.org/wg/gli/assets/documents/GLI_algorithms.pdf

³⁸ GLI Guide on Planning for country transition to Xpert[®] MTB/RIF Ultra Cartridges. 2017. http://www.stoptb.org/wg/gli/assets/documents/GLI_ultra.pdf.

Table 16: WHO recommended format for reporting Xpert MTB/RIF test results

Xpert MTB/RIF test result	WHO reporting code
MTB not detected	N
MTB detected RIF resistance not detected	T
MTB detected – Trace (Ultra test only)	TT
MTB detected RIF indeterminate	TI
MTB detected RIF resistance detected	RR
Error / No result / Invalid	I

10.3.3. Protect data confidentiality

The data stored on the computer/laptop connected to the GeneXpert instrument contains sensitive patient information, (i.e., name, patient ID and test results). Measures must be put in place to prevent unauthorized access of data and data theft. Unauthorized access of data from the computer or laptop (e.g., printing, copying of files to USB or CD) should be prevented by protecting the data (restrict network and system access, enforce user authentication and requiring the use of unique, strong passwords by all system users). Unauthorized access of data via an internet connection should be prevented by the use of firewalls, limiting access to authorized users, maintaining antivirus software, and performing regular system updates.

See the *GLI Quick Guide to TB Diagnostics Connectivity Solutions*³⁹ for a discussion of data confidentiality and security when using a diagnostics connectivity system.

³⁹ GLI Quick Guide to TB Diagnostics Connectivity Solutions. GLI. 2016. <http://stoptb.org/wg/gli/gat.asp>.

Additional Resources

WHO Laboratory Quality Management System: handbook (2011). A comprehensive reference on laboratory quality management systems and quality systems essentials for all stakeholders in health laboratory processes, from management and administration, to bench- work laboratorians. The handbook covers topics that are essential for quality management of a public health or clinical laboratory. (<http://www.who.int/ihr/publications/lqms/en/>)

GLI Training Package on Xpert MTB/RIF. The package consists of slide presentations that can be customized and used to train GeneXpert users in all aspects of Xpert MTB/RIF deployment, including related QA procedures. Topics covered include: Overview of TB and diagnostics, biosafety, specimen collection, procurement, installation, Xpert MTB/RIF technology, results interpretation, reporting, troubleshooting, maintenance, a clinical guide, and quality assurance. (http://stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF.asp)

Xpert MTB/RIF test training for healthcare workers. The training is based on WHO recommendations and provides practical tools for implementing Xpert MTB/RIF testing. (<http://www.finddx.org/tb/>)

GLI Training Package: Programme Modules for Diagnostic Network Strengthening (2018). This modular training package has been developed to guide programme and laboratory managers and their implementation partners on key topics for diagnostic network strengthening. (http://www.stoptb.org/wg/gli/TrainingPackage_Programme.asp)

Roadmap for Xpert MTB/RIF implementation (2017). A schematic representation of the elements that are required to implement quality assurance activities for the Xpert MTB/RIF test. (<http://www.finddx.org/tb/>)

Challenge TB Tools. Extensive library of TB laboratory tools, guidelines and manuals. (<http://www.challengetb.org/library/lab>)

FIND TB laboratory strengthening resources. Free, generic SOPs, documents and forms can be customized for use at testing sites. (<https://www.finddx.org/implementation-resources/#tb>)

GeneXpert Dx Systems Operator Manual. Instructions on how to operate GeneXpert® Dx System. (<ftp://hbbc:Crasa7Uc@ftp.caplaser.net/>)

Xpert MTB/RIF implementation manual - Technical and operational 'how-to': practical considerations (2014). This edition of the implementation manual replaces the first edition and takes into consideration the current body of evidence and operational experiences available, in the context of the updated policy recommendations, including use of Xpert MTB/RIF to diagnose pulmonary TB, paediatric TB, extrapulmonary TB and RIF resistance. (http://who.int/tb/publications/xpert_implem_manual/en/)

WHO Meeting Report of a Technical Expert Consultation: Non-inferiority analysis of Xpert MTB/RIF Ultra compared to Xpert MTB/RIF (2017). The current WHO recommendations for the use of Xpert MTB/RIF now also apply to the use of Ultra as the initial diagnostic test for all adults and children with signs and symptoms of TB and in the testing of selected extrapulmonary specimens (CSF, lymph nodes and tissue specimens). (<http://www.who.int/tb/publications/2017/XpertUltra/en/>)

GLI Guide on Planning for country transition to Xpert® MTB/RIF Ultra Cartridges (2017). Practical guidance for planning and implementing a smooth transition from use of Xpert MTB/RIF to Xpert MTB/RIF Ultra cartridges. Includes advice on how to develop an actionable implementation plan, from country-level to site-level, for adoption of the Xpert MTB/RIF Ultra cartridge. (http://www.stoptb.org/wg/gli/assets/documents/GLI_ultra.pdf)

GLI Model TB Diagnostic Algorithms (2017). Model algorithms that graphically depict the most up-to-date WHO recommendations on use of TB diagnostics and provides guidance on the interpretation of test results and follow-up testing. (http://stoptb.org/wg/gli/assets/documents/GLI_algorithms.pdf)

GLI Quick Guide to TB Diagnostics Connectivity Solutions (2016). An overview of diagnostics connectivity solutions, and what is required to establish one and use it effectively (<http://www.stoptb.org/wg/gli/gat.asp>). Also contains a link to an online table comparing the functionalities of currently available software (<http://tinyurl.com/glicconnectivity>).

GLI Practical Guide to TB Laboratory Strengthening (2017). Practical guidance on implementation of WHO recommendations and international best practices for TB laboratory strengthening. It is an updated version of the GLI Guide for Providing Technical Support to TB Laboratories, providing the latest practical guidance on use of newly recommended diagnostics in model algorithms, as well as guidance in key technical areas, including quality assurance and quality management systems, specimen collection and registration, procurement and supply-chain management, diagnostics connectivity, biosafety, data management, human resources, strategic planning and other topics. (<http://stoptb.org/wg/gli/gat.asp>)

GLI Guide to TB Specimen Referral Systems and Integrated Networks (2017). This guide describes the various phases to create and strengthen specimen referral systems, essential components involved in referral, as well as other considerations for TB programme and laboratory managers, ministry of health officials, and other stakeholders across disease programmes. In addition to describing transport mechanisms and equipment required to safely move specimens, this guide also provides information on logistics, results reporting, data management, monitoring and evaluation, and standard operating procedures that will facilitate and improve specimen referral systems. (<http://www.stoptb.org/wg/gli/gat.asp>)

Laboratory Diagnosis of Tuberculosis by Sputum Microscopy–The GLI Handbook (2013). The handbook contains useful guidance on collecting sputum samples and conducting AFB-smear microscopy for the diagnosis of TB. (<http://www.stoptb.org/wg/gli/gat.asp>)

WHO Definitions and Reporting Framework for Tuberculosis–2013 revision (2014). Revised WHO standard case definitions for TB and drug-resistant TB, the categories used to assign outcomes, and the standard reporting framework for TB. (http://apps.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf?ua=1)

WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy (2016). Collaborative strategy between the WHO Global TB Programme and the GLI core group, that comprises 12 core indicators that measure countries' capacity to detect TB accurately and rapidly using new diagnostics, provide universal DST, and ensure the quality of testing. (<http://www.who.int/tb/publications/labindicators/en/>)

WHO Tuberculosis Laboratory Biosafety Manual (2012). The minimum biosafety measures that should be implemented at the different levels of TB testing laboratories to reduce the risk of a testing site-acquired infection. (http://www.who.int/tb/publications/2012/tb_biosafety/en/)

WHO Laboratory Biosafety Manual (2004). Helpful reference and guide for developing and establishing national codes of practice for securing microbiological assets, ensuring their availability for clinical, research and epidemiological purposes. (http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/)

TB Laboratory Biosafety Training (2014). This free, interactive Biosafety training course addresses the needs of TB laboratories in low- resource settings by providing the tools needed to improve safety in the testing site. (<https://www.finddx.org/online-trainings/>)

Providing Uninterrupted Power for GeneXpert® in Low and Middle Income Settings: A Practical Guide (2017). Practical information on approaches and equipment for ensuring an uninterrupted power supply (UPS) for GeneXpert instruments. (https://www.finddx.org/wp-content/uploads/2018/02/UPS-guide-XpertMTB-RIF_FINAL_07DEC16.pdf)

Tuberculosis Laboratory Maintenance Plan (LMP) for preventive and routine maintenance of laboratory equipment. Expert opinion of the European TB Laboratory Initiative 2017. Provides practical guidance for planning and implementing equipment maintenance in TB laboratories in the WHO European Region. (http://www.euro.who.int/__data/assets/pdf_file/0009/355788/WHO-ELI-TB-Lab-Maintenance-Plan_ENG.PDF)

Guidelines for Managing the Laboratory Supply Chain: Version 2. Arlington, Va.: USAID | DELIVER PROJECT, Task Order 1 2008. General guidance for managing a laboratory's commodities and describes planning, coordination, and the well-recognized cycles of selection, procurement, distribution, and use. (http://deliver.jsi.com/dlvr_content/resources/allpubs/guidelines/GuidManaLabSC_v2.pdf)

List of Supporting Documents/ Forms and templates

Link: www.stoptb.org/wg/gli/xpertqaguide.asp

1. Xpert MTB/RIF Quality Assurance Situational Analysis Checklist
Includes checklist for conducting a situational analysis of the status of Xpert MTB/RIF testing and quality assurance activities. Part A addresses activities at the national and supervisory levels and Part B addresses activities at the testing site level. An example of a portion of a completed situational analysis report is also provided.

Maintenance log template

Provides an example of a form to record maintenance

(<https://www.finddx.org/implementation-resources/?level0=main-accordion-4&level1=secondary-left-accordion-1>)

2. Indicator report forms

Contains forms as customizable MS Word files for collecting data for performance indicators and for calculating the indicators. These forms are also available as Excel files which will automatically calculate the indicators when the required data are entered. Separate forms are provided for Xpert MTB/RIF Testing Quality Indicators (Monthly Report); Diagnostic Cascade Quality Indicators and QA System Process Indicators.

Training

Provides an overview of training materials from the Global Laboratory Initiative for Xpert users, advanced users, and clinicians and nurses. Link for GLI modules: (http://www.stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF_Ultra.asp)

3. Competency assessment for GeneXpert users
Contains forms to perform and document competency assessments. Part A describes competency assessment for GeneXpert users. Part B describes competency assessment for GeneXpert advanced users
4. Assessment Checklist for Testing Sites (ACTS) checklist and User's Guide
Contains the Assessment Checklist for Testing Sites (ACTS) for conducting on-site supervisory visits. A user's manual is also provided.

Xpert MTB/RIF SOP

Contains an example of a standard operating procedure for conducting the Xpert MTB/RIF test.

(<https://www.finddx.org/implementation-resources/?level0=main-accordion-4&level1=secondary-left-accordion-1>)

5. Proficiency testing programme – guidelines and SOPs
Contains guidelines, forms and SOPs for producing proficiency testing panels in-country and conducting an Xpert MTB/RIF Proficiency Testing program.
6. New lot testing SOP
Contains an SOP for quality control of new lots of Xpert cartridges.

