Xpert® MTB/RIF test Rollout and Implementation Plan

UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH AND SOCIAL WELFARE

NATIONAL TUBERCULOSIS AN LEPROSY PROGRAMME

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FIRST EDITION

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FOREWORD

The adoption of the Xpert® MTB/RIF test Rollout and Implementation Plan by the Ministry of Health and Social Welfare (MoHSW) marks a big step forward because it underscores the programmes commitment to providing the latest technology in rapid testing for tuberculosis (TB) in Tanzania. Emphasis in this publication is on the use of the Xpert MTB/RIF test to diagnose TB and multi-drug resistant TB (MDR-TB) across the tiered healthcare system. The publication provides guidance on the rollout of the Xpert MTB/RIF test, and in collaboration with World Health Organisation and partners, provides best-practise for its use as a rapid diagnostic test for TB & MDR-TB.

Tuberculosis closely follows HIV and malaria as a major cause of morbidity and mortality in Tanzania, especially among adults. The trends of TB cases have increased from 11,753 in 1983 to 63,151 in 2014, which is more than a fivefold increase. The increase in case notifications over the last two decades is largely attributable to the HIV epidemic and population increase.

It is therefore paramount that the MoHSW and the health sector in general strengthen efforts in the care and control of TB to reduce unnecessary suffering and loss of life, especially among young people. Key to reducing transmission is the early diagnosis of TB & MDR-TB. Standardization of approaches in the diagnosis and clinical care of TB patients in both the private and public health sectors and ensuring consistent provision of high-quality services by all health care providers are essential to prevent MDR TB. TB is targeted for control in the Essential Health Package, which means every district should incorporate them into their comprehensive council health plans.

The Ministry of Health and Social Welfare and the government are committed to intensifying efforts to prevent and control TB, as well as care for those affected by it, in collaboration with development partners and other stakeholders. I take this opportunity to express my sincere appreciation and gratitude to all of our partners for their contribution to the development of this manual and for the continuing financial and technical support.

It is my sincere hope that all health workers will find this manual useful in their daily work and that the information contained herein will stimulate a renewal of the spirit of commitment and dedication to improve the quality of services provided for the people of Tanzania.

Prof. Mohammad Bakari Kambi
Chief Medical Officer

ACKNOWLEDGEMENTS

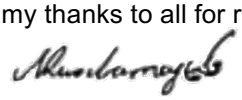
The National Tuberculosis and Leprosy Programme (NTLP) of the Ministry of Health and Social Welfare (MOHSW) of Tanzania developed this first-ever National GeneXpert Rollout and Implementation Plan in close collaboration with PATH, Foundation for Innovative New Diagnostics (FIND) and other implementing partners. The development of this plan involved extensive, meticulous work; many people were consulted and offered advice and support. Sincere thanks go to Ms. B. Doulla and Dr. B. Mutayoba from the National Tuberculosis and Leprosy Program (NTLP), who identified the critical need for improved coordination and planning of the introduction of GeneXpert in Tanzania and who initiated and prepared the first draft. The NTLP led the development of this document through a collaborative process involving the members of the Laboratory Technical Working Group (TWG). We would also like to thank the TWG members, as their inputs were crucial to the completion of this document.

The MOHSW acknowledges the United States Agency for International Development (USAID) for technical support under its TB IQC TO 2015 through PATH (Contract No. GHN-1-00-09-00006) and Centers for Disease Control and Prevention (CDC) under Cooperative agreement No. 3U2GPS002746 to FIND.

Special appreciation goes to A. Kingalu, S. Mfaume, E. Luhanga, Dr. Z. Mkomwa, Dr. V. Mahamba, C. Kagoma, T. Adepoyibi, A. Ascorra, Dr. A. Trollip and Dr. H. Albert who thoroughly and critically reviewed the rollout plan and provided vital feedback and relevant inputs used to improve the document. More thanks are extended to all the NTLP staff for their tireless efforts in overseeing the whole process.

Sincere appreciation goes to Dr. V. Harris for her endless technical support and guidance on the GeneXpert implementation in Tanzania.

It is not possible to mention each and every individual who contributed to this rollout plan, but I extend my thanks to all for reviewing and finalizing the document.



Dr. Neema Rusibamayila

Director of Preventive Services

ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
ART	Anti-retroviral Therapy
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CTC	Counselling and Testing Centre
CTRL	Central Tuberculosis Reference Laboratory
DLT	District laboratory technologist
DST	Drug sensitivity test
DTLC	District tuberculosis and leprosy coordinator
EQA	External quality assessment/assurance
FIND	Foundation for Innovative New Diagnostics
GLI	Global Laboratory Initiative
HIV	Human immunodeficiency virus
LED FM	Light-emitting diode fluorescence microscopy
LPA	Line probe assay
MDR-TB	Multidrug-resistant tuberculosis
MOHSW	Ministry of Health and Social Welfare
MOU	Memorandum of Understanding
MTB	*Mycobacterium tuberculosis*
NIMR	National Institute for Medical Research
NTLP	National Tuberculosis and Leprosy Programme
PEPFAR	US President's Emergency Plan for AIDS Relief
PLHIV	People living with HIV/AIDS
QO	Quality Officer
RIF	Rifampicin
RLT	Regional laboratory technologist
RTLC	Regional tuberculosis and leprosy coordinator
SOP	Standard Operating Procedure
SRL	Supranational Reference Laboratory
SWOT	Strengths, weaknesses, opportunities, and threats
TB	Tuberculosis
TWG	Technical Working Group
USAID	US Agency for International Development
WHO	World Health Organization
XDR-TB	Extensively Drug-resistant Tuberculosis

FIGURES

TABLES

OBJECTIVES

The overall objective of this implementation plan is to define the strategy for implementation of the Xpert MTB/RIF test for rapid detection of tuberculosis (TB) and rifampicin (RIF) resistance in Tanzania, within the context of the National Tuberculosis and Leprosy Programme (NTLP) strategic plan and other national health guidelines. It is intended to serve as the main guiding document for national, regional and local programme managers, clinicians, coordinators, laboratory staff and other health workers; national and regional reference laboratories; local and international implementing partners; and donors involved in TB control.

The objectives for Xpert MTB/RIF test implementation in Tanzania are as follows:

1. To utilise the Xpert MTB/RIF test to improve detection of TB and multidrug-resistant tuberculosis (MDR-TB);
2. To rollout the Xpert MTB/RIF test so that there is at least one GeneXpert instrument per region (up to the district level). The target is to place 100 GeneXpert instruments in Tanzania by 2017.

This plan seeks to provide a roadmap for internal and external support for Xpert MTB/RIF test rollout and implementation. The following Tanzania national policy documents currently exist and this implementation plan fits within the overall policy framework provided by these documents.

- National TB Laboratory Strategic Plan (2015–2020)
- Manual for the Management of Tuberculosis and Leprosy
- National policy guidelines for collaborative TB/HIV activities

BACKGROUND

MDR-TB and HIV-associated TB are global priorities for tuberculosis control. MDR-TB is an increasing concern globally and directly threatens disease-control efforts in many countries. According to the World Health Organization (WHO), 136,000 of 300,000 estimated new cases of MDR-TB worldwide were diagnosed and notified in 2013 [1], and misdiagnosis can lead to nosocomial and community transmission, amplification of drug resistance, and thousands of deaths [2]. Further concern arises regarding MDR-TB due to the emergence of extensively drug-resistant TB (XDR-TB) and rapid mortality in MDR-TB and XDR-TB cases with HIV co-infection. Difficulty in diagnosing TB among HIV-infected persons using traditional diagnostics (smear microscopy and chest X-ray) is one of the factors responsible for the trend of missed or late TB diagnosis [3]. For example, microscopy alone detects only about 45% of liquid-culture-confirmed TB cases among HIV-infected persons [4]. Even among those HIV-infected cases correctly diagnosed with TB using smear microscopy, TB disease is usually diagnosed at an advanced stage [5]. Adding chest X-ray for diagnosis of smear-negative TB can increase sensitivity of the TB case-finding algorithm among HIV-infected persons to about 62%, [6] but this is dependent on X-ray availability and clinician expertise [7]. These diagnostic limitations have highlighted the urgency for rapid diagnostic methods, especially in resource-limited settings.

The Xpert® MTB/RIF test for the GeneXpert® platform (Cepheid Inc., Sunnyvale, CA, USA) is a fully automated nested real-time polymerase chain reaction (PCR) system. It detects MTB complex DNA, as well as MTB with rifampicin resistance-conferring mutations, by identifying mutations in the *rpoB* gene in sputum and other sample types (*i.e.* pleural, lymph node aspirate or tissue, cerebrospinal fluid, gastric fluid and tissue other than lymph node). By fully integrating and automating all processes

required for real-time PCR-based molecular testing, the Xpert MTB/RIF test represents a simple and robust molecular test suitable for use in resource-limited settings, where TB burden is highest, and is able to provide results directly from sputum within 90 minutes. The Xpert MTB/RIF test can be used outside of central reference laboratories, and is ideal when placed at district and even sub-district levels.

The introduction and scale-up of new tools for the diagnosis of TB has the potential to make a huge difference in the lives of people in Tanzania and around the world. To apply these tools most effectively, policy makers need the information to make the right decisions about which new tools to implement and where in their national diagnostic algorithms to apply them. Given the difficulties involved in this process, tools such as discrete event simulation models (one of which was used in Tanzania) could play a significant part in improving and informing these decisions.

The importance of a technological breakthrough such as the Xpert MTB/RIF test for countries with high rates of TB/HIV co-infection such as Tanzania—which has a co-infection rate of 37% [3]—cannot be overstated. In Tanzania, WHO estimated that of the 530 MDR-TB cases among notified TB cases in 2013, 86 were from retreatment cases [3]. This represents a substantial under-diagnosis of MDR-TB cases in the country, contributing to poor patient outcomes and further spread of the disease.

In adults thought to have TB, with or without HIV infection, the Xpert MTB/RIF test is sensitive and specific. Compared with smear microscopy, the Xpert MTB/RIF test substantially increases TB detection among culture-confirmed cases. In a recent meta-analysis [8], as an initial test replacing smear microscopy, the Xpert MTB/RIF test pooled sensitivity was found to be 89% [95% Confidence Interval (CI) 85% to 92%] and pooled specificity 99% (95% CI 98% to 99%), (22 studies, 8998 participants: 2953 confirmed TB, 6045 non-TB). For people with HIV infection, the Xpert MTB/RIF test pooled sensitivity was 79% (95% CI 70% to 86%; 7 studies, 1789 participants), and for people without HIV infection, it was 86% (95% CI 76% to 92%; 7 studies, 1470 participants). For rifampicin resistance detection, the Xpert MTB/RIF test pooled sensitivity was 95% (95% CI 90% to 97%; 17 studies, 555 rifampicin resistance positives) and pooled specificity was 98% (95% CI 97% to 99%; 24 studies, 2411 rifampicin resistance negatives).

The Xpert MTB/RIF test has the potential to revolutionise TB diagnostic capability for clinicians managing the disease, and to transform the usual lengthy pathway to diagnosis and treatment for those with MDR-TB. However, the epidemiological context and the organisation of the TB-specific health system strongly determine the actual impact of the Xpert MTB/RIF test on case detection and/or time-to-diagnosis, and therefore need to be taken into consideration for strategic planning. It is also important to ensure adequate coordination for the sustainable introduction and rollout of the GeneXpert technology. For these reasons, this implementation plan has been developed as a subset of the *National TB Laboratory Strategic Plan* (2015–2020) to provide a roadmap for Xpert MTB/RIF test implementation in Tanzania.

SITUATIONAL ANALYSIS

EPIDEMIOLOGICAL DATA

Tuberculosis is still a major public health problem in the country: Tanzania is ranked 18th among 22 high-burden countries globally that account for 80% of the global TB burden. The first national TB prevalence survey was successfully completed in November 2012 and the preliminary results showed a prevalence of 295 cases per 100,000 people, which is much higher than the routine notification of 142 cases per 100,000 people. The preliminary survey results can be further interpreted to infer a low

case detection rate of 42% to 54%, with the disease burden found to be concentrated in rural settings and in older age groups. In addition, the trends of TB cases have increased from 11,753 in 1983 to 63,862 in 2012, which is more than a fivefold increase [9]. The increase in case notification over the last two decades is largely attributable to the HIV epidemic and population increase.

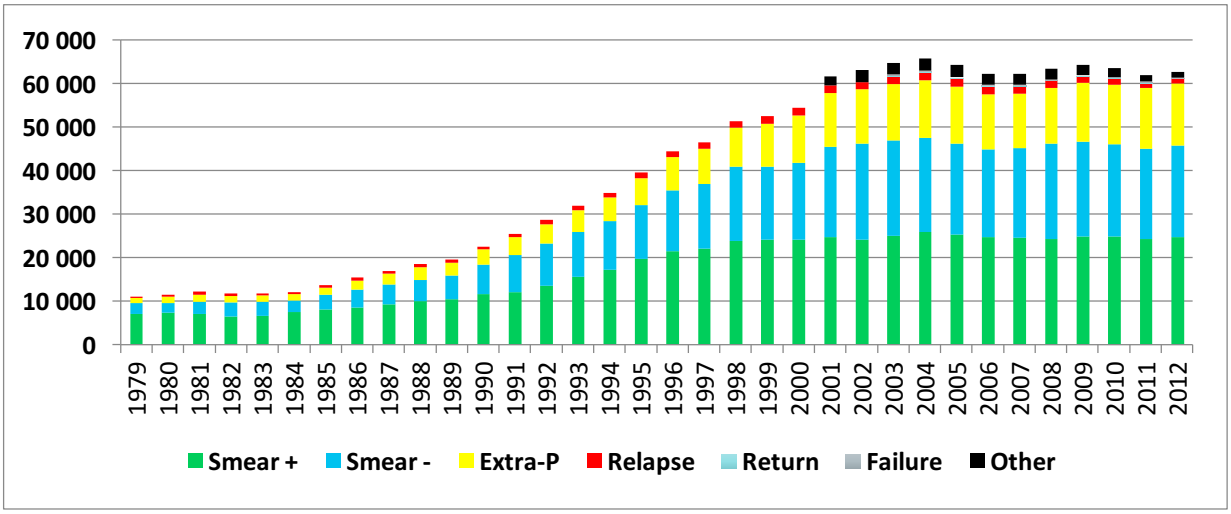


Figure 1. The increase in TB case notifications from 1979 to 2012 [9]

More recent data from Tanzania in 2013 shows that 65,732 TB cases of all forms (new and retreatment) were notified by the programme, an increase from 2012, according to the WHO Global Tuberculosis Report. [3] Among the new pulmonary TB cases in 2013, 24,565 were bacteriologically confirmed and 23,371 were clinically diagnosed. The number of new extra-pulmonary TB cases was 15,016. [3]

Table 1. Tanzanian TB profile from WHO global TB database, 2013[1]

Estimates of TB burden 2013		
	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	6 (3.4-8.2)	12 (7-17)
Mortality (HIV+TB only)	6.1 (4.8-7.5)	12 (9.8-15)
Prevalence (includes HIV+TB)	85 (45-140)	172 (92-277)
Incidence (includes HIV+TB)	81 (77-84)	164 (157-170)
Incidence (HIV+TB only)	30 (29-31)	61 (58-63)
Case detection, all forms (%)	79 (77-83)	

Estimates of MDR-TB burden 2013		
	NEW	**RETREATMENT**
% of TB cases with MDR-TB	1.1 (0.5-2)	3.1 (0.9-7.9)
MDR-TB cases among notified pulmonary cases	530 (240-960)	86 (25-220)

TB case notifications 2013		
	NEW	**RELAPSE**
Pulmonary, bacteriologically confirmed	24 565	1 101

[1] Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries. Available at: http://www.who.int/tb/country/data/profiles/en [3]

Estimates of TB burden 2013		
	NUMBER (thousands)	RATE (per 100 000 population)
Pulmonary, clinically diagnosed	23 371	
Extrapulmonary	15 016	
Total new and relapse	**64 053**	
Previously treated, excluding relapses	1 679	
Total cases notified	**65 732**	

Among 62 952 new cases: 6 658 (11%) cases aged under 15 years; male:female ratio: 1.4

Reported cases of RR-/MDR-TB 2013			
	NEW	**RETREATMENT**	**TOTAL**
Cases tested for RR-/MDR-TB	1 192 (5%)	728 (26%)	2 020
Laboratory-confirmed RR-/MDR-TB cases			64
Patients started on MDR-TB treatment			28

TB/HIV 2013		
	NUMBER	**(%)**
TB patients with known HIV status	54 504	(83)
HIV-positive TB patients	20 320	(37)
HIV-positive TB patients on co-trimoxazole preventative therapy	19 835	(98)
HIV-positive TB patients on antiretroviral therapy	14 864	(73)
HIV-positive people screened for TB	457 901	
HIV-positive people provided with IPT	166	

Treatment success rate (%)	
New and relapse cases registered in 2012	90
Previously treated cases, excluding relapse, registered in 2012	80
HIV-positive TB cases, all types, registered in 2012	77
RR-/MDR-TB cases started on second-line treatment in 2011	75
XDR-TB cases started on second-line treatment in 2011	

The HIV prevalence in Tanzania was 5.1% (urban 7.2% and 4.3% rural) [9] in 2012 among people aged 15-49 years old, down from 5.8% in 2007. A recent review of the NTLP identified the following gaps in diagnosis of TB and MDR-TB in the country:

- Diagnostic gaps and delays;
- Under-diagnosis of childhood TB;
- Lack of service provision at designated diagnostic centres;
- Lack of quality assurance of TB diagnostic testing;
- Low level of drug susceptibility testing (DST) among previously treated TB cases (>90% did not receive DST testing);
- Low usage of the GeneXpert instrument capacity;
- Lack of linkage to care in rifampicin-resistant TB cases identified by the Xpert MTB/RIF test;
- Lack of antiretroviral therapy (ART) initiation in TB-HIV co-infected cases

LABORATORY SERVICES

Though significant improvements have been made in recent years, the laboratory network in Tanzania still faces many challenges. The primary issues were captured in the strengths, weaknesses, opportunities, and threats (SWOT) analysis (Annex A) conducted as part of the development of the *National TB Laboratory Strategic Plan*. The plan calls for the establishment of zonal laboratories, which will mark a significant shift in the structure of laboratory services in Tanzania, with implications for the Xpert MTB/RIF test rollout. Importantly, an identified threat related to laboratory services due to the fact that the NTLP is a donor dependent programme, which poses a threat to sustainability.

Sputum smear microscopy is the main TB diagnostic tool used in the country and is available at a total of 945 facilities (diagnostic centres) at the district/sub-district level. Xpert MTB/RIF test is currently being implemented at 67 sites in 23 provinces/regions (Table 2). The rollout of Xpert MTB/RIF test highlights the existing need for strong testing site networks, robust quality assurance systems, and adequate culture and drug susceptibility testing capacity at the Central Tuberculosis Reference Laboratory (CTRL).

Table 2. Summary of TB testing facilities in Tanzania[2]

TB test[3]	**Number of facilities test is available**
Sputum smear microscopy (diagnostics centres)	Available at [945] diagnostic centres, district/ sub-district levels. TOTAL for clinical use: [941] TOTAL for research use only: [4]
TB culture: Solid culture	Available at 8 Laboratories: CTRL, Kibong'oto, Kilimanjaro Christian Medical Centre, Dodoma Regional Hospital, Ifakara Health Institute, Public Health Laboratory (Ivo de Carneri), Mbeya Hospital and Mbeya Medical Research Center TOTAL for clinical use: [5] TOTAL for research use only: [3]
TB culture: Liquid culture	Available at 4 Laboratories: CTRL, Mbeya Referral Hospital, Mbeya Medical Research Centre and Ifakara Health Institute. TOTAL for clinical use: [2] TOTAL for research use only: [2]
Drug sensitivity testing	Available at 2 Laboratories: CTRL, Mbeya Referral Hospital TOTAL for clinical use: [2]
Rapid detection of TB or drug resistant TB (Xpert MTB/RIF test)	Available at 67 sites in 23 regions:

[2] NTLP internal data, March 2015

[3] Testing categories are defined as follows: Smear microscopy (Ziehl Neelsen, fluorescence microscopy-conventional vs. LED, direct vs. concentrated); TB culture: Solid culture medium, liquid culture medium. DST (first line DST by conventional methods, *e.g.* direct or indirect test; solid or liquid culture medium, drugs tested, concentration of drugs tested; proportion, absolute concentration or resistance ratio method; second line DST by conventional methods, *e.g.* solid culture medium, drugs tested, concentration of the drugs; rapid detection of TB or drug resistant TB. *e.g.* Xpert MTB/RIF test

TB test[3]	Number of facilities test is available
	62 x 4 module GeneXpert instruments, 1 x 6 modules GeneXpert instruments and 4 x 8 module GeneXpert instruments

GROUPS ELIGIBLE TO RECEIVE XPERT MTB/RIF TESTING

Policy and objectives:

- The NTLP will implement Xpert MTB/RIF testing for all presumptive TB and presumptive MDR-TB cases in Tanzania in adults and children, irrespective of HIV status;
- The NTLP will roll out GeneXpert instruments in a phased manner to enable equitable access to testing in all regions of the country.

In the five years since WHO endorsed Xpert MTB/RIF, there has been substantial global momentum to introduce the technology into many high-burden countries around the world. The MOHSW adopted the WHO recommendations for the use of Xpert MTB/RIF in the diagnosis of HIV-associated TB and MDR-TB. WHO recommends the following policy on the use of Xpert MTB/RIF to diagnose pulmonary TB and rifampicin resistance in adults and children [10]:

- Xpert MTB/RIF should be used, rather than conventional microscopy, culture and drug sensitivity test (DST), as the initial diagnostic test in adults suspected of having MDR-TB or HIV-associated TB (strong recommendation, high-quality evidence);
- Xpert MTB/RIF should be used, rather than conventional microscopy, culture and DST, as the initial diagnostic test in children suspected of having MDR-TB or HIV-associated TB (strong recommendation, very low-quality evidence);
- Xpert MTB/RIF may be used, rather than conventional microscopy and culture, as the initial diagnostic test in all adults suspected of having TB (conditional recommendation acknowledging resource implications, high-quality evidence);
- Xpert MTB/RIF may be used, rather than conventional microscopy and culture, as the initial diagnostic test in all children suspected of having TB (conditional recommendation acknowledging resource implications, very low-quality evidence);
- Xpert MTB/RIF may be used as a follow-on test to microscopy in adults suspected of having TB who are not at risk of MDR-TB or HIV-associated TB, especially when further testing of smear-negative samples is necessary (conditional recommendation acknowledging resource implications, high-quality evidence).

NATIONAL TB DIAGNOSTIC ALGORITHM

Policy and objectives:

- The NTLP will sensitize all institutions and implementing partners involved in Xpert MTB/RIF implementation on the national TB diagnostic algorithm;
- The NTLP will provide training and tools required for implementing the national TB diagnostic algorithm;
- The NTLP will confirm all Xpert MTB/RIF test rifampicin resistant cases using culture and DST for 1st and 2nd line and ensure all cases receive appropriate treatment.

The NTLP has developed the national TB diagnostic algorithm (Figure 2 & 3) that will ensure universal access to high quality TB, MDR-TB and HIV-related TB diagnosis. All implementation of Xpert MTB/RIF testing in the country should be done in accordance with the national TB diagnostic algorithm, and in close conjunction with the NTLP manual [11]. All testing sites offering Xpert MTB/RIF testing will follow the national TB diagnostic algorithm. All implementing partners must commit to following the algorithm.

The MOHSW has determined that Xpert MTB/RIF testing will be implemented as the initial diagnostic test in all presumptive TB and presumptive MDR-TB cases in adults and children. This includes:

- **All new TB cases presenting with presumptive TB**, irrespective of HIV status, *i.e.* PLHIV and those with negative and unknown HIV status

- **Presumptive MDR-TB**. The NTLP manual defines the following patient groups as being at high risk for MDR-TB:

    - Cases that have failed, relapsed, or returned after loss to follow-up and that were on a TB retreatment regimen (formerly chronic TB cases);
    - Failure of the first-line regimen (sputum smear positive cases at month five during the course of the standard treatment regimen for new TB cases);
    - Relapses and returns after loss to follow-up from standard treatment for new smear positive cases at month 3 of retreatment;
    - Symptomatic close contacts of a known MDR-TB patient.

SITES WITH NO ONSITE GENEXPERT INSTRUMENT

Pulmonary TB is diagnosed by smear microscopy at sites where there is no GeneXpert instrument. Two expectorated sputum samples will be collected in accordance with NTLP recommendations (MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013) viz. two sputum specimens (spot, and next morning). Since sputum samples may be referred for Xpert MTB/RIF testing, the samples must be of good quality and meet the criteria for Xpert MTB/RIF testing, *i.e*. a sputum sample should contain no particles and be more than 1ml (although 2-4ml is recommended to allow repeat Xpert MTB/RIF testing or referral if needed).

If one or both sputum samples are smear positive, the presumptive TB patient will be initiated on first line treatment. Presumptive MDR-TB patients will be treated based on the risk of MDR-TB, as follows:

- High MDR-TB risk patients (retreatment cases, defaulters, relapses, non-converters (smear positive at month five) & MDR-TB contacts) will be treated with the first-line retreatment regimen (2SRHZE/1HRZE/5RHE) (MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013). One sputum sample, the better of the two samples (smear positive [preferably], >1ml, good quality [no particles]) from high MDR-TB risk patients will be referred for Xpert MTB/RIF testing. The patient treatment will be reviewed based on the Xpert MTB/RIF test result.
- Low MDR-TB risk patients will be treated with the first line regimen (2RHZE/4RH) (MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013).

If both sputum samples are negative, presumptive TB & presumptive MDR-TB patients will be assessed clinically, and a Chest X-ray performed (if available):

- If there is a strong clinical or radiological suspicion of TB, these patients will be treated for TB with the first line regimen (2RHZE/4RH) (MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013). One sputum sample (the better of the two samples (smear positive [preferably], >1ml, good quality [no particles]) from PLHIV, children and high MDR-TB risk patients (retreatment cases, defaulters, relapses, non-converters (smear positive at month five) & MDR-TB contacts) will be referred for Xpert MTB/RIF testing. The patient treatment will be reviewed based on the Xpert MTB/RIF test result.
- If there is no clinical or radiological suspicion of TB, consider a diagnosis other than pulmonary TB.

SITES WITH ONSITE GENEXPERT INSTRUMENT

Pulmonary TB is diagnosed by the Xpert MTB/RIF test at sites that have onsite access to a GeneXpert instrument. One expectorate sputum sample will be collected in accordance with NTLP recommendations (MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013) viz. one sputum specimen collected at spot and sent for Xpert MTB/RIF testing within 24 hours of collection. The samples must be of good quality and meet the criteria for Xpert MTB/RIF testing*, i.e*. a sputum sample should contain no particles and be more than 1ml (although 2-4ml is recommended to allow repeat Xpert MTB/RIF testing):

Presumptive TB & presumptive MDR-TB patients who are reported as ‘MTB not detected’ by the Xpert MTB/RIF test will be followed up clinically and radiologically. If there is a strong clinical or radiological suspicion of TB, these patients will be treated for TB with the first line regimen (2RHZE/4RH)[11]. If there is no clinical or radiological suspicion of TB, consider a diagnosis other than pulmonary TB.

- Presumptive TB & presumptive MDR-TB patients that are 'MTB detected rifampicin susceptible' will be started on first-line TB treatment (2RHZE/4RH);
- Presumptive TB & presumptive MDR-TB patients that are 'MTB detected rifampicin resistant' will be followed-up based on the risk of MDR-TB:

    - High MDR-TB risk patients (retreatment cases, defaulters, relapses, non-converters (smear positive at month five) & MDR-TB contacts) will be referred to an MDR-TB treatment initiation centre and treated with the second line regimen (MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013). A new sputum sample will be collected for referral for culture and DST[4] (
    - Table 3). The patient treatment will be reviewed based on the culture and DST test result.
    - Low MDR-TB risk patients will have the Xpert MTB/RIF test repeated on a new sputum sample.

- The Xpert MTB/RIF test is repeated if the result is 'error', 'invalid' or 'no result'.
- Presumptive TB cases & presumptive MDR-TB patients that are 'MTB detected rifampicin indeterminate' will be started on first-line TB treatment (2RHZE/4RH). The Xpert MTB/RIF test will be repeated.

REPEAT XPERT MTB/RIF TESTING

The Xpert MTB/RIF test is repeated at the same testing facility using a freshly collected (new) sputum sample if:

1. The Xpert MTB/RIF test result is 'error', 'invalid' or 'no result';
2. The Xpert MTB/RIF test result is 'MTB detected rifampicin indeterminate';
3. The Xpert MTB/RIF test result is 'MTB detected rifampicin resistant', and the patient is considered at low risk of MDR-TB.

If a new sample is requested, the original result is written in the register and the clinical facility is given the returned request form with a comment explaining and requesting a new sample from the patient. Follow-up of presumptive TB & presumptive MDR-TB patients is based on the result from the repeat Xpert MTB/RIF test:

- 'MTB not detected'- the patient will be assessed clinically & radiologically (if available) for TB. If there is a strong clinical or radiological suspicion of TB, these patients will be treated for TB with the first line regimen (2RHZE/4RH)[11]. If there is no clinical or radiological suspicion of TB, consider a diagnosis other than pulmonary TB. Clinicians should consider performing another Xpert MTB/RIF test from a new sputum sample.
- 'MTB detected rifampicin resistant'- the patient will be referred to an MDR-TB treatment initiation centre and treated with the second line regimen (MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013);
- 'MTB detected rifampicin susceptible'- the will be treated with the first line regimen (2RHZE/4RH) and a new sputum sample will be collected for referral for culture and DST. The patient treatment will be reviewed based on the culture and DST test result.

MONITORING TREATMENT

The adoption of the Xpert MTB/RIF test does not eliminate the need for conventional TB microscopy, culture and DST. Microscopy or culture, or both, remain necessary for treatment monitoring

[4] First and second-line DST using phenotypic and/or genotypic methods

(MOHSW, Manual for the Management of Tuberculosis and Leprosy, NTLP, 2013), since the use of DNA detection (*e.g.* Xpert MTB/RIF test) is not suitable for monitoring treatment.

ZONAL TB REFERRAL LABORATORIES

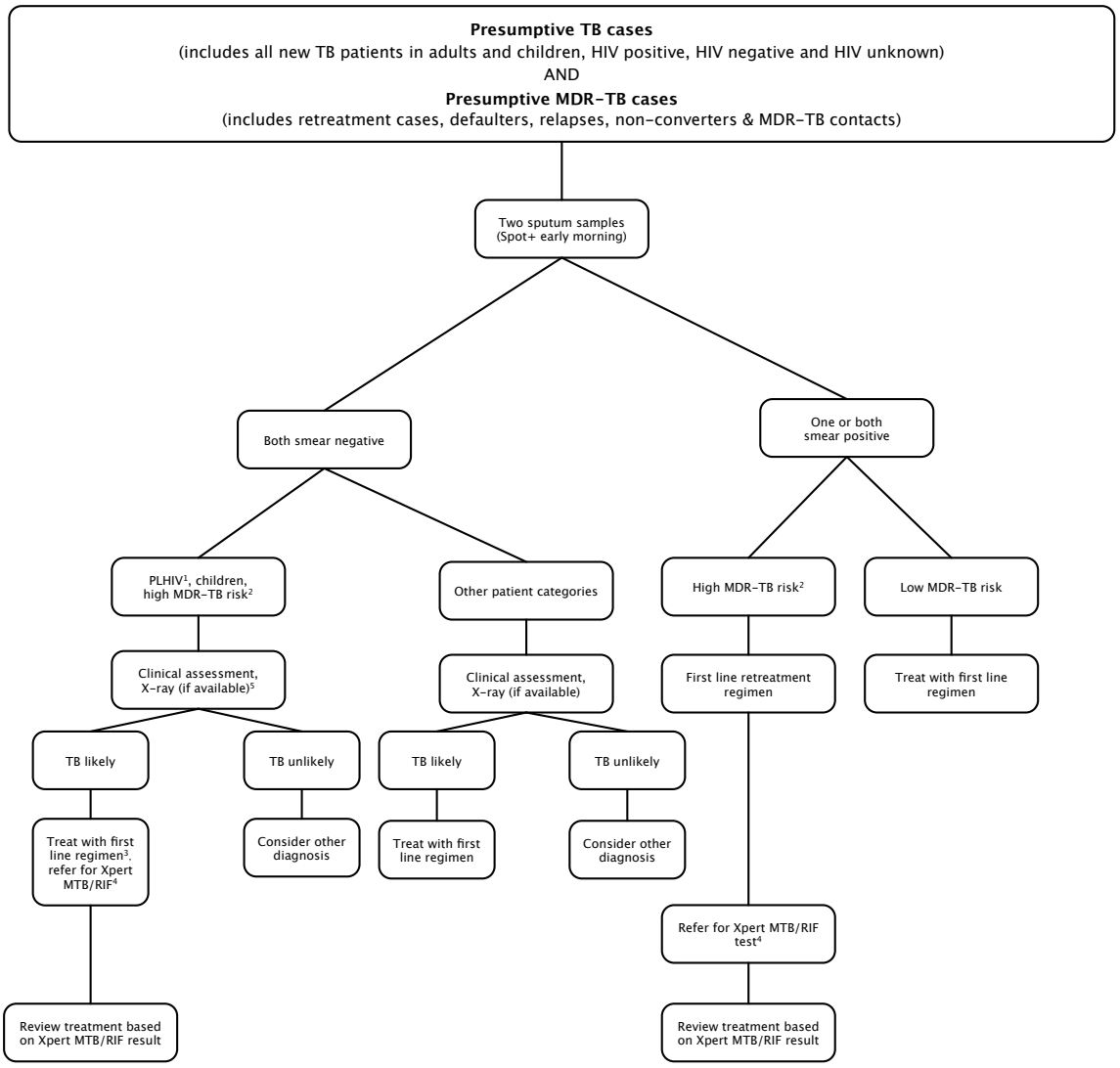
Since Xpert MTB/RIF detects only rifampicin resistance, conventional culture and DST are required to confirm an MDR-TB diagnosis. All cases of rifampicin resistance will be confirmed Zonal TB Referral Laboratories (
Table **3**). Culture and DST (first and second-line DST using phenotypic and/or genotypic methods) will be performed. The Zonal TB Referral Laboratories will release the culture and DST results to the clinician. In addition, rifampicin resistant results will be communicated to the respective RTLC/DTLC and GeneXpert Focal Person for immediate follow up.

The NTLP will work to improve district, regional and national referral systems with the support of implementing partners in order to facilitate sample referral and diagnostic services in remote areas. Samples should be sent following triple packaging guidelines and drivers should be trained in biosafety practices.

Table 3. Zonal TB Referral Laboratories

Culture facility	**Location**	**Available TB testing**
Central TB Reference Laboratory	Dar es Salaam	Smear microscopy, Xpert MTB/RIF test, LPA, TB culture (solid & liquid), DST (1st & 2nd line)
Kibong'oto National MDR Laboratory	Kilimanjaro	Smear microscopy, Xpert MTB/RIF test, LPA, TB culture (solid)
Dodoma Regional Referral Laboratory	Dodoma	Smear microscopy, Xpert MTB/RIF test, TB culture (solid)
Mbeya Referral Laboratory	Mbeya	Smear microscopy, Xpert MTB/RIF test, LPA, TB culture (solid & liquid), DST (1st line)
Bugando Laboratory	Mwanza	Smear microscopy, Xpert MTB/RIF test, TB culture (solid)
Pemba Public Health Laboratory	Pemba	Smear microscopy, TB culture (solid)

National TB diagnostic algorithm- no onsite GeneXpert instrument



[1] PLHIV (People living with HIV/AIDS)- Persons who are seriously ill and suspected of having TB regardless of their HIV status, and in those whose HIV status is unknown but who present with strong clinical evidence of HIV infection in settings where there is a high prevalence of HIV or among members of a risk group for HIV

[2] High MDR-TB risk includes retreatment cases, defaulters, relapses, non-converters (smear positive at month five) & MDR-TB contacts

[3] New patients- Treat with first line regimen (2RHZE/4RH); Previously treated patients- Treat with first line retreatment regimen (2SRHZE/1HRZE/5RHE)

[4] Refer the better of the two sputum samples (smear positive [preferably], >1ml, good quality [no particles]) for Xpert MTB/RIF

[5] Children- also use the 'Score Chart for the Diagnosis of TB in Children'

Figure 2. National TB Diagnostic Algorithm for facilities with no onsite GeneXpert instrument

National TB diagnostic algorithm- onsite GeneXpert instrument

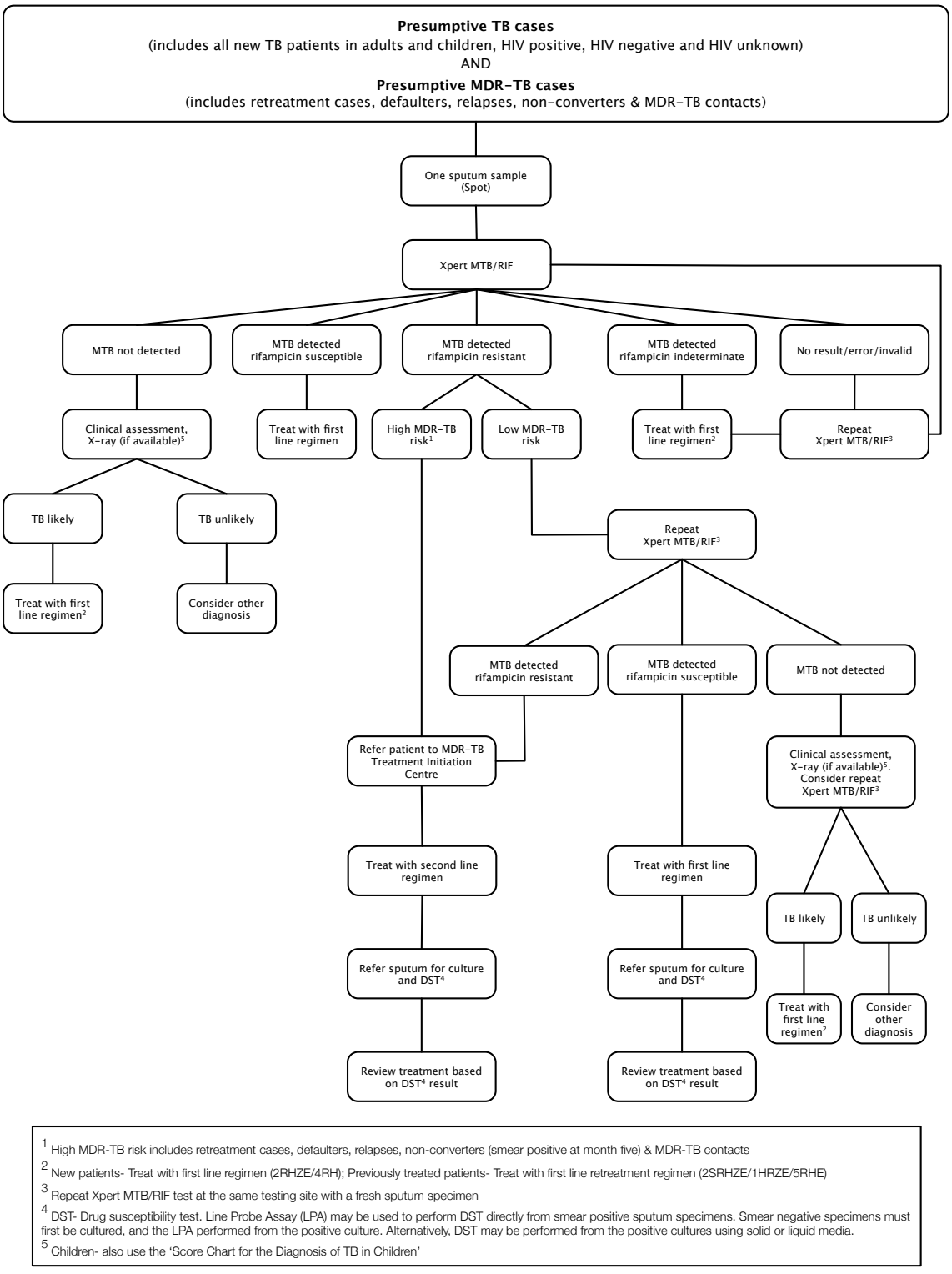


Figure 3. National TB Diagnostic Algorithm for facilities with an onsite GeneXpert instrument

CLINICAL DIAGNOSIS AND TREATMENT

The NTLP is committed to providing clinical care to all patients diagnosed with TB and MDR-TB. The activities at sites with / without onsite Xpert MTB/RIF testing can be summarised as follows (Table 4):

Table 4. Timeline of TB diagnostic and treatment activities at clinical sites

Sites with no onsite GeneXpert instrument	Sites with onsite GeneXpert instrument
Visit 1	
1. Screen patient for TB symptoms 2. Collect one spot sputum sample 3. Provide patient with sputum container (morning sample)	1. Screen patient for TB symptoms 2. Collect one spot sputum sample 3. Refer sample to testing site for Xpert MTB/RIF test
24 hours	48 hours
Visit 2	
1. Collect sputum container from patient (morning sample) 2. Refer both samples to testing site for smear microscopy	1. Interpret Xpert MTB/RIF test result 2. Treat with first-line regimen or Perform clinical assessment and X-ray (if available then treat with first-line regimen or consider other diagnosis or Refer to patients with rifampicin resistant TB to MDR-TB Treatment Initiation Centre or Collect one spot sputum sample for repeat Xpert MTB/RIF test. Ask patient to return in a week for the results of repeat testing
48 hours	48 hours
Visit 3	
1. Interpret smear microscopy results 2. Treat with first-line regimen or Perform clinical assessment and X-ray (if available) then treat with first-line regimen or consider other diagnosis or Ask patient to return in a week for results of repeat testing	1. Interpret Xpert MTB/RIF test result from repeat testing 2. Refer to Treatment Initiation Centre or Treat with first-line regimen and collect one spot sputum sample for culture and DST[5] or Perform clinical assessment and X-ray (if available) then treat with first-line regimen or consider other diagnosis
< 7 days	< 7 days
Visit 4	
1. Review treatment based on Xpert MTB/RIF test result (from referred sample): ○ Continue first-line regimen or ○ Refer to Treatment Initiation Centre	<u>At MDR-TB Treatment Initiation Centre</u> 1. Treat with second-line regimen 2. Collect one spot sputum sample for culture and DST[6]

[5] Review treatment based on culture and DST result- culture and DST results are typically available within three months of sample processing

Clinical facilities with no onsite GeneXpert instrument - At these facilities, patients will be screened for TB symptoms and a spot sputum sample will be collected (Visit 1). The patient information will be recorded in the TB Register. The sputum sample will be stored in the fridge (2-4°C). A sputum container will be given to the patient, and they will be asked to collect an early morning sputum specimen at home, and return to the clinic the following day (Visit 2). The two sputum samples will be referred to the nearest microscopy centre for testing. All samples must be accompanied with the correct NTLP standard sample request form (Annex B). Samples will be transported to the microscopy centre immediately. The patient will be asked to return to the clinical facility in 48 hours for the result and further workup (Visit 3).

At the microscopy centre, smear microscopy will be performed and the result will be reported on the standard reporting forms to the clinical facility straight away. One sputum sample (the better of the two samples (smear positive [preferably], >1ml, good quality [no particles]) from high MDR-TB risk patients will be referred for Xpert MTB/RIF testing to a site with access to the GeneXpert instrument (Figure 2). The testing site performing the Xpert MTB/RIF test will promptly report the result to the clinical facility.

The clinical facility will interpret the results as described in the National TB diagnostic algorithm (Figure 2). Bacteriologically confirmed TB cases will be given a TB number, which will be recorded in the TB register. TB cases will be treated with the first-line regimen in accordance with NTLP recommendations [11]. Smear negative patients will undergo a clinical assessment (and X-ray if available), based on which they will be treated or another diagnosis considered. If the testing site has referred one of the patient's samples for Xpert MTB/RIF testing, the patient needs to return in seven days for these results (Visit 4).

Clinical facilities with onsite GeneXpert instrument - At these facilities, patients will be screened for TB symptoms and a spot sputum sample will be collected and referred to the nearest testing site for Xpert MTB/RIF testing (Visit 1). The patient information will be recorded in the TB Register. All samples will be accompanied with the correct NTLP standard sample request form. Samples will then be transported promptly to the testing site. The patient will be asked to return to the clinical facility in 48 hours for the result and further workup (Visit 2).

At the testing centre, the Xpert MTB/RIF test will be performed and the result will be reported on the standard reporting forms to the clinical facility immediately. Rifampicin resistant results will be reported to the RTLC / DTLC and GeneXpert Focal Person. The testing centre will perform repeat Xpert MTB/RIF testing if indicated (Figure 3).

The clinical facility will interpret the results as described in the National TB diagnostic algorithm (Figure2B). Either the patient will be treated with the first-line regiment, a clinical assessment (and X-ray if available) will be performed, the patient will be referred to a MDR-TB Treatment Initiation Centre, or another spot sputum sample will be collected. If the clinical site has referred one of the patient's samples for repeat Xpert MTB/RIF testing, the patient needs to return in 48 hours for these results (Visit 3). Patients with rifampicin resistant TB will be referred to a MDR-TB Treatment Initiation Centre within seven days of diagnosis.

The clinical facility will interpret the results from the repeat Xpert MTB/RIF testing as described in the National TB diagnostic algorithm (Figure 2). Either the patient will be treated with the first-line regimen and another sample collected for culture and DST, a clinical assessment (and X-ray if available) will be performed, or the patient will be referred to a MDR-TB Treatment Initiation Centre. Rifampicin resistant patients will have treatment initiated at an MDR-TB Treatment Initiation Centre (Visit 4) with the second line regimen in accordance with NTLP recommendations [11]. One sputum sample will be referred to the designated Zonal TB Referral Laboratory for MDR-TB confirmation by

culture and DST. The Zonal TB Referral Laboratories will report the culture and DST results to the Treatment Initiation Centres without delay. Culture and DST results are typically available within three months of sample referral.

XPERT MTB/RIF TESTING IN CHILDREN

The MOHSW has determined that Xpert MTB/RIF testing will be implemented as the initial diagnostic test in all presumptive TB and presumptive MDR-TB cases in children. Provision for the diagnosis of TB and MDR-TB in children is made in the National TB Diagnostic Algorithm (Figure 2 & Figure 3). An additional recommendation that applies to children is the use of the 'Score Chart for Diagnosis of TB in Children'. The Score Chart is used with a clinical assessment and X-ray (if available) in smear negative or Xpert MTB/RIF test 'MTB not detected' cases[6]. In cases that the child is too young to produce sputum, the use of gastric washings or induced sputum should be considered. Refer to the NTLP recommendations for further information on samples, diagnosis and the treatment of TB in children [11].

XPERT MTB/RIF TESTING AND EPTB

EPTB refers to TB involving organs other than the lung (*e.g.*, pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones and meninges). Where possible, EPTB should be bacteriologically confirmed [11]. WHO recommends the following policy on the use of Xpert MTB/RIF to diagnose extra-pulmonary TB (EPTB [10]:

- Cerebrospinal fluid (CSF): Xpert MTB/RIF should be used in preference to smear microscopy and culture as the initial diagnostic test in testing CSF specimens from patients suspected of having TB meningitis. CSF samples must be >0.1ml to be tested by Xpert MTB/RIF;
- Lymph node and other tissues: Xpert MTB/RIF may be used as a replacement test for usual practice (including smear microscopy, culture, and/or histopathology) for testing of specific non-respiratory specimens (lymph nodes or other tissue) from patients suspected of having EPTB.

These recommendations do not apply to samples of stool, urine or blood, given the lack of data on the utility of Xpert MTB/RIF for these specimens. Clinical facilities with no onsite GeneXpert instrument will refer all EPTB samples to the Zonal TB Referral Laboratories for culture.

CURRENT LOCATION OF GENEXPERT INSTRUMENTS

The first GeneXpert instrument was introduced in Tanzania in 2009 for research purposes. Initial rollout for routine patient testing began in 2010. Between 2010 and 2014, GeneXpert instruments have been placed in 67 sites in 23 regions:

- 62 sites have 1 GeneXpert instrument with 4 modules
- 1 site has 1 GeneXpert instrument with 6 modules
- 4 sites have 2 GeneXpert instruments with 8 modules

The complete list (at the time of writing) illustrating instrument placement, implementing partners, and number of modules per instrument can be found in Annex C. Active testing sites, as well as planned locations, are illustrated in Figure 4.

[6] Note: Bacteriological confirmation of TB is achievable in only about 30% to 40% of childhood TB cases and alternative diagnostic criteria should be applied in case of negative Xpert MTB/RIF test results

Since being introduced, GeneXpert instruments (for routine clinical services) have performed a total of 72,792 Xpert MTB/RIF tests; with 11,906 TB positive results and 637 rifampicin-resistant results being reported (Xpert MTB/RIF tracking tool 8th March 2015).

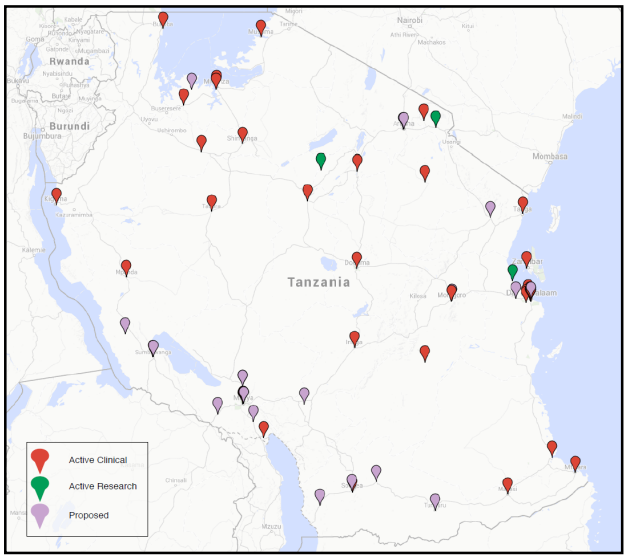


Figure 4. Current location of GeneXpert instruments in Tanzania (March 2015)

IMPLEMENTATION PHASES

XPERT MTB/RIF EXPANSION PLAN

Policy and objectives:

- The NTLP commits itself to the phased implementation of GeneXpert instruments to make testing accessible to those in need
- The NTLP, with support of its partners, commits to equip 100 facilities with GeneXpert instruments at district level by 2017.

The *National Laboratory TB Strategic Plan* states the intention to have one GeneXpert instrument per district by 2018—a total of 162. The target is to have 100 GeneXpert sites in Tanzania by 2017. It further states that district level placement is to be achieved through the provision of instruments at each district hospital. This plan calls for the rollout to occur in three stages. Annex D provides a full list of the districts proposed in the systematic placement of GeneXpert instruments. In summary:

- Stage 1 districts (50 districts): 2013–2014
- Stage 2 districts (54 districts): 2015–2016
- Stage 3 districts (58 districts): 2017–2018

Selection of the districts included in each stage was determined by the experts of the TWG and approved by the TB Program Manager. To determine acceptable sites for GeneXpert instrument placement in Tanzania, the NTLP manager, in collaboration with CTRL and the director of diagnostic services and the GeneXpert Focal Person, will consider epidemiological data on TB, current Xpert

MTB/RIF testing centres, and Xpert MTB/RIF testing capacity. When proposing sites for GeneXpert instrument(s) placement, introducing parties are encouraged to prioritise:

- Clinical and testing sites with high TB and HIV burden priority (*e.g.* annual TB diagnosis per facility of >500 or cases currently enrolled in HIV chronic care >1000);
- Clinical and testing sites with adequate infrastructure and that are conveniently located for sample referral linkages, site supervision and data collection activities;
- Clinical and testing sites that currently provide care and treatment services for TB and MDR-TB cases.

Sites with low sample volume can be linked to the closest facility with a GeneXpert instrument by establishing a robust and functional referral system for sputum samples.

To determine the number of GeneXpert instruments required, an analysis was conducted using the provisional methodology recommended by WHO (Annex E) and WHO Tanzania data (Table 1).

MAXIMUM PROJECTED NEED OF XPERT MTB/RIF TESTS FOR PLHIV

The maximum projected need for Xpert tests was calculated using the WHO Planning and Budgeting Tool (http://www.who.int/tb/dots/planning_budgeting_tool/download/en/) and was based on the following assumptions (Table 5):

- All PLHIV are screened 4 times a year, during each clinical encounter
- 15% of HIV positive people in care at a clinic screened and found to have presumptive TB (*i.e.* eligible for Xpert MTB/RIF testing)
- 100% coverage of Xpert MTB/RIF testing for those to be tested

Table 5. Planning and Budgeting tool – ideal scenario

4.1.3 Decrease the burden of TB in people living with HIV/AIDS[7]	
Annual projected number of HIV positive (adult and children) in care at a clinic, pre-ART and ART	457901
% of HIV positive (adult and children) in care at a clinic that are screened	100%
Average number of times screening is performed each year for a single person living with HIV	4
% of HIV positive (adult and children) in care at a clinic screened and found to have presumptive TB at screening	15%
% coverage of testing with Xpert for the 15% HIV positive presumed to have TB at each screening	100%
Estimated number of HIV positive patients tested with Xpert MTB/RIF	274741

- An estimated **274,741 PLHIV require testing by Xpert MTB/RIF**.
- At maximum instrument testing capacity (3000 tests per annum), this would require 91 GeneXpert 4-module instruments.
- If the GeneXpert instrument testing capacity is decreased, more instruments are required. If we assume 80% testing capacity, **114 GeneXpert 4-module instruments** would be required.
- Correct placement of instruments at high volume counselling and testing centre (CTC) sites, to enable 100% coverage of testing for target HIV-infected population would be critical to meet the targeted testing strategy.
- 457,901 PLHIV were screened for TB in 2103 (assume this is verbal symptom screen).

[7] These figures only include PLHIV being screened for TB, and do not include estimates of non HIV-infected or people who are presumptive MDR-TB cases.

- Therefore, compared with the above calculation (in which 1,831,607 individuals were screened), a fourfold increase in the number of Xpert MTB/RIF tests performed would be required to reach maximum coverage and testing of PLHIV.

ESTIMATED CURRENT SCENARIO

- An alternative calculation was made based on the following assumptions, which may be more realistic in the interim and reflect more closely the current status of screening and access to Xpert testing (Table 6):

    - All PLHIV are screened twice a year
    - 15% of HIV positive people in care at a clinic screened and found to have presumptive TB (*i.e.* eligible for Xpert MTB/RIF testing)
    - 20% coverage of Xpert MTB/RIF testing for those to be tested
    - An estimated **27,474 PLHIV would be tested by Xpert**.
    - This represents **88% of the total number of Xpert tests performed in 2014**, as reported in the Xpert MTB/RIF Tracking tool.
    - Depending on the proportion of actual tests performed that were done on PLHIV compared with non-HIV infected and presumptive MDR-TB cases, this calculation may overestimate the current coverage of testing or overestimate the extent of screening performed.

Table 6. Planning and Budgeting tool – estimated current scenario

4.1.3 Decrease the burden of TB in people living with HIV/AIDS[8]	
Annual projected number of HIV positive (adult and children) in care at a clinic, pre-ART and ART	457901
% of HIV positive (adult and children) in care at a clinic that are screened	100%
Average number of times screening is performed each year for a single person living with HIV	2
% of HIV positive (adult and children) in care at a clinic screened and found to have presumptive TB at screening	15%
% coverage of testing with Xpert for the 15% HIV positive presumed to have TB at each screening	20%
Estimated number of HIV positive patients tested with Xpert	274741

TOTAL PROJECTED NEED OF XPERT MTB/RIF TESTS IN TANZANIA

- Tanzania data report 37% of TB patients are co-infected with HIV (Table 1).
- In order to calculate the total number of projected Xpert MTB/RIF tests, we would need to estimate the proportion of presumptive TB cases who are tested with Xpert MTB/RIF due to being HIV co-infected and those who are HIV-negative or tested due to MDR-TB risk.
- If we assume 50% of presumptive TB cases requiring testing are PLHIV[9], then the total number of Xpert MTB/RIF tests required would be **549,482, requiring 228 instruments running at 80%** capacity.

Different scenarios with alternative assumptions can be explored using the above methodology. Estimations will be updated subsequently based on availability of additional country data to inform the assumptions, placement and utilization of GeneXpert in the country.

[8] These figures only include PLHIV being screened for TB, and do not include estimates of non HIV-infected or people who are presumptive MDR-TB cases.
[9] The assumption of 50% presumptive TB cases being PLHIV requires validation, as this greatly impacts on the final projection

XPERT MTB/RIF AND HIV

There is close association between TB and HIV infection. HIV fuels progression to active disease in PLHIV who are already infected with TB. Similarly, TB is the major cause of mortality among PLHIV. The intertwined relationship between TB and HIV suggests that neither of the epidemics can be controlled effectively without regard for the other. They must be tackled simultaneously to decrease morbidity, mortality, and transmission of TB while avoiding the emergence of drug resistance [12].

Since the release of the first publication on the performance of the Xpert MTB/RIF test for the diagnosis of active tuberculosis [4], results from all over the world, including studies in the Tanzanian setting [13] [14], have shown that the sensitivity of the test is not reduced in individuals infected with HIV. In 2010, the WHO endorsed the use of the Xpert MTB/RIF test as a frontline diagnostic for individuals suspected of having tuberculosis and HIV co-infections. The Xpert MTB/RIF test, with a sensitivity in HIV positive, smear negative patients of 75 to 98%, has persistently and convincingly outperformed smear microscopy and has shown results on a par with solid culture. The sensitivity of the Xpert MTB/RIF test improves with additional tests performed, thus highlighting the fact that an HIV infected individual with a negative Xpert MTB/RIF test will need to be further investigated and managed, *e.g.* retest an additional sample and consider the clinical and radiological findings.
NTLP policy is that all PLHIV and persons newly diagnosed with HIV infection will receive screening for TB symptoms and signs at all sites providing HIV/AIDS services and will receive information about available TB services. It is therefore imperative that GeneXpert instruments be placed in proximity to HIV CTC sites as well as clinical sites that provide ART and HIV support and care.

ROLES AND RESPONSIBILITIES

Policy and objectives:

- The NTLP will be responsible for setting policy and guidelines for Xpert MTB/RIF implementation and for coordination of all stakeholders;
- The NTLP will establish coordinating committees and mechanisms for collaboration among the NTLP and other stakeholders at the national, regional, and district levels;
- The NTLP will establish the position of Xpert Focal Person to coordinate operational implementation activities.

NTLP

TECHNICAL WORKING GROUP (TWG)

- Review and appraise implementation of strategic and annual plans for the Xpert MTB/RIF test at all levels.
- Receive and appraise periodic technical and financial progress reports.
- Oversee implementation of operational research, monitoring, and evaluation in order to develop sound, evidence-based best practices in TB diagnostics.
- Advise on adoption of new national/international/global initiatives on TB diagnostics including Xpert MTB/RIF test implementation.
- Participate in national and international initiatives on TB diagnostics, TB activities and Xpert MTB/RIF test implementation.
- Report to the national TB/HIV coordinating committee on the progress of implementing TB activities, including the Xpert MTB/RIF testing in the country.

NTLP MANAGER

- Make programmatic decisions pertaining to Xpert MTB/RIF test implementation, including decisions regarding GeneXpert instrument placement.
- Delegate a GeneXpert Focal Person responsible for coordination of Xpert MTB/RIF test implementation activities.
- Provide support to the GeneXpert Focal Person.
- Coordinate implementing partners and the TB programme, and promote information sharing, including procurement and funding.
- Oversee the GeneXpert instrument handover process.

CTRL, GENEXPERT FOCAL PERSON

- Liaise with the NTLP manager, director of diagnostic services, head of CTRL, TWG, implementing partners, district TB and leprosy coordinators (DTLC), and regional TB and leprosy coordinators (RTLCs) regards Xpert MTB/RIF implementation.
- Advise the NTLP manager on the progress of Xpert MTB/RIF implementation as required.
- With the support of the regional GeneXpert Focal Points: collate countrywide quality indicators, undertake remote and onsite troubleshooting, liaise with the manufacturer, and coordinate stock management.
- Organise training for new sites, re-training and onsite training as required.
- Organise GeneXpert Focal Points and co-ordinate supervisory visits.

ZONAL TB REFERRAL LABORATORIES

- Conduct TB bacteriology testing. Submit samples to CTRL for DST and species identification tests.
- Plan, train, supervise, and carry out regular quality control of GeneXpert testing activities within their zone.
- Participates in supervision of Xpert MTB/RIF testing in the zone and training of testing site workers involved in Xpert MTB/RIF, in collaboration with the RTLC.
- Undertake remote and onsite troubleshooting, liaise with the GeneXpert Focal Person, and coordinate stock management within the zone.
- Initiates, coordinates, and collaborates in routine testing and operational research of relevant TB and leprosy control activities.

RTLC AND REGIONAL LABORATORY TECHNOLOGISTS

- Support DTLCs, district laboratory technologists (DLT) and GeneXpert users to collate reports regarding unusual errors from district staff, and report to GeneXpert Focal Person.
- Manage stock at the regional level.
- Collate and monitor quality indicator data from the testing sites and alert the GeneXpert Focal Points if needed.
- Include GeneXpert oversight into testing site and clinical supervisory visits.
- Provide support to the GeneXpert Focal Person and respond to requests from CTRL.
- Train clinical staff using clinical training program on the use of Xpert MTB/RIF diagnostics and results interpretation.
- Ensure all cases are initiated into correct treatment in a timely fashion and TB numbers are entered into the TB Laboratory Register.
- Immediately report all rifampicin resistance detected to the MDR Focal Person at the NTLP.

DTLP & DLT

- Stock management at the district level.
- Troubleshoot GeneXpert-related issues, report unusual errors from facility staff to RTLCs and regional laboratory technologists (RLTs).
- Include GeneXpert oversight into testing site and clinical supervisory visits.

- Support GeneXpert Focal Person, RTLCs and RLTs as required, and respond to requests;
- Assist the RTLC and NTLP to train and retrain clinical staff using clinical training program on the use of Xpert MTB/RIF diagnostics and results interpretation.
- Ensure all cases are initiated into correct treatment in a timely fashion and TB numbers are entered into the TB Laboratory Register.
- Immediately report all rifampicin resistance detected to the MDR Focal Person at the NTLP.

GENEXPERT FOCAL POINTS (SUPER-USERS)[10]

- Under direction of the GeneXpert Focal Person, carry out site supervisory visits on a regular basis.
- Provide onsite training.
- Perform facility-level test management and ordering under supervision of Laboratory Manager.
- Perform daily testing using the GeneXpert instrument, perform regular maintenance and communicate challenges to the DLT.
- Immediately report all rifampicin resistance detected to the DLT & RTLC.
- Troubleshoot GeneXpert-related issues, report unusual errors to the GeneXpert Focal Points or GeneXpert Focal Person and RTLC.
- Provide monthly quality indicator reports to the GeneXpert Focal Person.

CLINICIANS & HEALTH CARE WORKERS

- Diagnose TB & MDR-TB presumptive cases in accordance with the National TB Diagnostic Algorithm.
- Treat TB, and refer MDR-TB cases as directed in the Manual for Management of Tuberculosis [11].
- Refer rifampicin resistant cases to the MDR-Unit as directed in the TB diagnostic algorithm;
- Record and report monthly quality indicator data to RTLC and/or DTLC.

IMPLEMENTING PARTNERS

- Consult with the NTLP regards placement of GeneXpert instruments and provide a plan for placement and handover.
- Formalise agreement with the MOHSW and commit to the objectives of the National Strategic Plan.
- Support the NTLP in the rollout of Xpert MTB/RIF testing by providing quality indicator data and regular reports on testing site operations.
- Meet regularly with the NTLP, share their experiences and contribute to improving access to healthcare in Tanzania.

Phased implementation of the Xpert MTB/RIF test requires cooperation between the NTLP, CTRL and implementing partners. Within NTLP/CTRL, assignment of staff responsible for implementation is necessary to reduce confusion regarding the responsibilities and duties at all levels in relation to Xpert MTB/RIF test implementation. The existing lines of responsibility for the NTLP are extended to include Xpert MTB/RIF test operations. All relevant staff should be sensitised regarding their roles and responsibilities.

[10] The job description for the GeneXpert Focal Points will be included in their contracts with their letter of appointment. Their performance will be monitored regularly.

STAKEHOLDER COORDINATION

Stakeholders include donors (Global Fund, WHO, USAID, CDC, US Department of Defense, World Bank, Global Drug Facility) and implementing partners (Annex C).

The following guidelines ensure that all stakeholders contributing to Xpert MTB/RIF implementation follow the national guidelines and their activities are standardised and coordinated by NTLP:

1. All introducing parties (implementing partners and donors) seeking to place a GeneXpert instrument in Tanzania will hold an initial consultation with the National TB Manager before arranging placement.
2. The introducing party will provide the NTLP with a proposal for placement of the GeneXpert instrument(s). The proposal will contain information:
    a. Duration of support to be provided by the introducing party. Implementing partners are encouraged to provide a minimum of two years support);
    b. Quantification of the resources being provided by the introducing party regarding reagents, calibration, warranty, maintenance, training (*e.g.* technical / clinical), and technical support;
    c. Transition plan, including how the GeneXpert instrument(s) will be supported after the handover date.
3. The NTLP manager, in collaboration with CTRL and the director of diagnostic services and the Xpert focal person, will advise on instrument placement based on the coverage gaps and the strategic objectives of the NTLP.
4. The NTLP manager, in collaboration with CTRL and director for diagnostic services, will consult with the DTLCs and/or RTLCs regarding clinical and testing site readiness and options for providing continued support beyond the end date of the support that will be provided by the introducing party. Based on the outcomes of these consultations, alternative-testing sites may be proposed to the partners or donors.
5. Agreement between NTLP and the introducing parties regarding instrument placement will be reached.
6. A Memorandum of Understanding (MOU) between the MOHSW and introducing parties will be signed. The MOU binds the introducing party to following the NTLP guidelines for GeneXpert instrument use, as well as the handing over of a fully functional GeneXpert instrument to the NTLP.
7. Following placement of a GeneXpert instrument(s), introducing parties will provide NTLP with the following:
    a. Monthly quality indicators reported according to National TB guidelines (see below);
    b. Annual calibration certificates;
    c. Annual progress report outlining testing site activities;
    d. *Ad hoc* reports using the NTLP supervision and troubleshooting checklist with additional narrative, if there is any material changes that may affect sustainability of testing after hand-over.
8. Introducing partners shall coordinate their procurement of GeneXpert instruments & reagents with the NTLP.
9. NTLP shall schedule an annual meeting with the introducing partners to discuss matters of mutual interest.
10. Introducing partners shall advise the NTLP of transfer a minimum of six months before the intended handover of the GeneXpert instrument (see GeneXpert Instrument Handover).

IMPLEMENTATION ROADMAP

As Tanzania scales up the use of the Xpert MTB/RIF test for case detection, there is an urgent need for standardised processes and tools to assist in better monitoring and evaluation (M&E) of Xpert MTB/RIF test implementation. NTLP has implemented a standardised comprehensive M&E framework that includes all programmatic and testing site aspects of Xpert MTB/RIF test implementation (Figure 5). The M&E framework, represented diagrammatically below, adopts a phased approach; from site selection and readiness, installation of equipment, training and competency assessment, site monitoring visits, to handover of GeneXpert instruments from partners/donors to the NTLP.

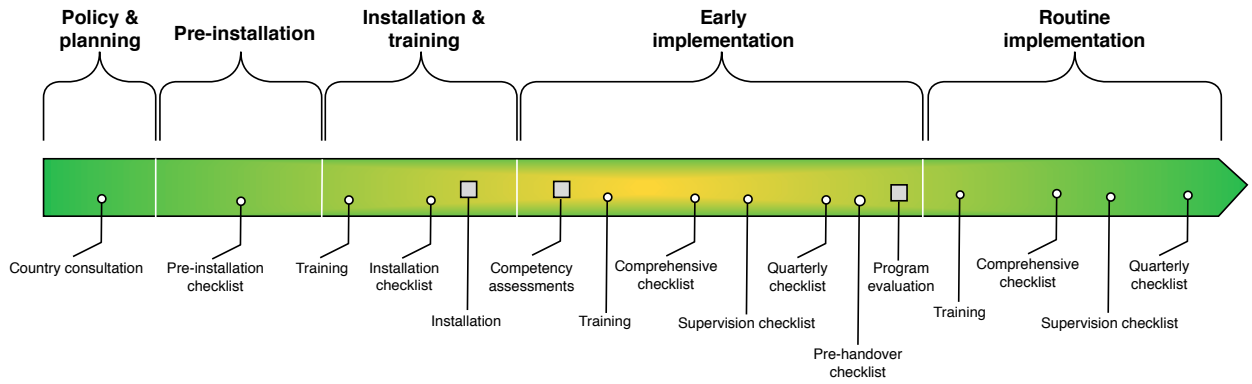


Figure 5. Roadmap to Xpert MTB/RIF test implementation in Tanzania

The roadmap represents implementation at national and site level:

- Implementation of the Xpert MTB/RIF test can be considered to be in one of the five roll-out phases; individual testing sites may vary in their stage of implementation. As some sites may implement routine testing, others may be being assessed for suitability of instrument placement.
- The role of implementing partners in Xpert MTB/RIF test implementation is a crucial. Making use of the M&E framework ensures that implementation roles are clearly identified and that NTLP has the key coordinating role and can plan for the capacity to sustain implementation after GeneXpert instrument handover from partners.
- Some operational activities are synchronous and can be initiated in different phases, or may extend beyond 'phase completion'. The M&E framework is therefore only a guide to implementation and may be customized depending on regional circumstances.
- While there is significant emphasis on the implementation of the Xpert MTB/RIF test at the laboratory, implementation also includes initiation of clinical sites.

PHASE1: POLICY & PLANNING

Policy and objectives:

- The NTLP will work with partners from all relevant sectors in planning, implementing, monitoring, and evaluating TB activities to ensure the most effective response to the TB epidemic;
- The NTLP will organize and guide utilization of multi-sectorial and multidisciplinary expertise to structure, finance, deliver, and manage TB control activities;
- The NTLP will work closely with other departments within MOHSW, *e.g.* NACP, and other government agencies to further the objectives of the *National TB Laboratory Strategic Plan*;
- The NTLP will coordinate placement of GeneXpert instruments at appropriate locations to meet the objectives of providing TB diagnostic services to all presumptive TB cases;
- The NTLP will implement a referral system to provide access to Xpert MTB/RIF testing in remote regions of Tanzania.

The implementation of the Xpert MTB/RIF test is led by the NTLP and is facilitated by cooperation between the NTLP/CTRL, TWG and implementing partners. In-country coordination is essential to optimize the use of resources, streamline activities, and ensure that sound technical advice is delivered and appropriate approaches are used. It is also fundamental to ensure that there is collaboration among national TB programme, HIV/AIDS programme, and public or private laboratory services.

It is essential that the implementation of the Xpert MTB/RIF test be coordinated at the country level. Technical agencies and donors need to work within the framework of the NTLP and National AIDS Control Programme to assist in implementing Xpert MTB/RIF testing. An increase in the number of cases of TB and MDR-TB detected will require an increase in the capacity for patient management and provision of anti-TB drugs. It is necessary to ensure that cases of MDR-TB are accurately reported and forecast in order to guarantee an uninterrupted supply of quality assured treatment. In addition, sustained and prolonged technical assistance is required to rapidly increase the capacity to deliver care for MDR-TB cases.

PHASE 2: PRE-INSTALLATION

Policy and objectives:

- The NTLP will ensure that all sites meet minimum required criteria, including infrastructure, uninterrupted power and personnel prior to installation of GeneXpert instruments to enable effective and safe operation.

The pre-installation phase initiates the operational process for Xpert MTB/RIF test implementation. Standardized checklists are used to assess that testing site & clinical sites are prepared for GeneXpert instrument installation (Annex F). It is the responsibility of the GeneXpert Focal Person to arrange, conduct and report the outcomes from the pre-installation assessments to the NTLP. The GeneXpert Focal Person coordinates the site assessments with the DTLC/RTLC. The DTLC/RTLC will contact the clinical site managers, schedule the visit and make the necessary arrangements for transport and accommodation.

PRE-INSTALLATION SITE VISIT AND CHECKLIST

Clinical site assessments are performed by the GeneXpert Focal Person, implementing partner technical advisor and/or RTLC using standardised checklists (Annex F). Pre-installation clinical site assessments will be performed at least three months before the projected installation date. Clinical site assessment can be logistically challenging due to the number of clinical sites that need to be assessed. The Clinical Checklist can be used to assesses the preparedness for Xpert MTB/RIF implementation, and should determine awareness of implementation, identify potential staff training needs, as well as determine the capacity to treat TB and refer MDR-TB cases.

Testing site (laboratory) assessments are performed by the GeneXpert Focal Person and/or the implementing partner technical advisor and/or GeneXpert Focal Points using standardised checklists (Annex F). Pre-installation testing site assessments will be performed at least three months before the projected installation date. The Testing Site Pre-Installation Checklist assesses the preparedness for Xpert MTB/RIF implementation, and should determine whether there is adequate infrastructure and systems to support GeneXpert instrument placement and identify potential staff for training (Annex G). The data gathered by completion of the Pre-Installation Checklist will be used to update the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation). Testing sites that meet the pre-requisite criteria may move to the installation phase. Sites that do not meet the pre-requisite criteria may require support to meet the standard.

When reporting the outcomes of the pre-installation assessments to the NTLP, the implementing partner technical advisor, RTLC and/or the GeneXpert Focal Person must provide a brief narrative report along with details of the work required to make upgrades. The NTLP and implementing partner will agree on who is responsible for upgrading the facility, and the timeframe for the upgrade. The GeneXpert Focal Person will delegate responsibility for overseeing the upgrading of facilities to the RTLC or Laboratory Manager. The GeneXpert Focal Person may arrange a follow-up visit when the work is complete, or may delegate this responsibility to the RTLC. A written confirmation that the upgrade has been completed must be received prior to GeneXpert instrument installation. Each facility that did not meet the pre-requisite standard must be re-assessed for readiness prior to installation. The GeneXpert instruments may be relocated to another testing site if the installation criteria cannot be met.

PHASE 3: INSTALLATION AND TRAINING

Policy and objectives:

- The NTLP, in coordination with implementing partners will train a cadre of testing site users and clinical staff for Xpert MTB/RIF implementation;
- The NTLP will designate appropriate staff to act as supervisors (RTLCs) and GeneXpert Focal Points, whose responsibility it is to provide supervision and technical support to testing sites;
- The NTLP aims to have 2 trained certified users per site and at least one trained focal point per region;
- The NTLP will train all RTLCs on Xpert MTB/RIF testing using standard program by the end of 2015.

The installation phase begins with the delivery of the instruments to the testing sites. Installation of GeneXpert instruments can be performed by trained individuals (GeneXpert Focal Points) or by implementing partners if they have been pre-approved to perform installations by the NTLP and are willing to follow NTLP guidelines for installation. The installation dates must be coordinated between the NTLP/CTRL, implementing partners, and the testing sites. To facilitate scheduling, implementing partners will provide at least three months' notice to the NTLP/CTRL regards proposed installation

dates. Installation dates must take into account that GeneXpert instruments can be delayed at customs. The GeneXpert Focal Person or the implementing partner will finalize installation dates once the GeneXpert instrument(s) have been released by customs. Installation dates will take into account travel time to sites (and between sites if consecutive installations are to take place). The GeneXpert Focal Person (or a delegated person) and the implementing partner technical advisor should be present during installation.

INSTALLATION SITE VISIT AND CHECKLIST

During installation, the GeneXpert Focal Person/GeneXpert Focal Point or the implementing partner technical advisor should follow and complete the Installation Checklist (Annex F). The Installation Checklist is used to ensure the GeneXpert instrument is installed in accordance with predefined standards and that all the relevant documentation is in place. The checklist is also used to collect relevant GeneXpert instrument data that will be uploaded to the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation). The RTLC/ DTLC Medical Officer in charge, Laboratory manager and Xpert users will receive a copy of the checklist with a list of non-conformances. They are responsible for implementing all additional materials and correcting the non-conformances within three months of receiving the list.

A brief narrative report must be submitted to the NTLP for each installed site or group of installed sites.

PHASE 4: EARLY IMPLEMENTATION

Policy and objectives:

- The NTLP, in coordination with implementing partners will conduct regular visits and coordinate additional support to sites during early implementation to ensure Xpert MTB/RIF testing is successfully established as part of routine operations.

During installation, 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 samples. Within three months of installation and staff training, the GeneXpert Focal Person and/or designated GeneXpert Focal Point will oversee the evaluation of the testing site by the relevant supervisors utilizing a standardized checklist to ensure staff have implemented as instructed during training and installation (Annex F). This includes but is not limited to the implementation of all SOPs and reporting materials. Problems will be identified and retraining carried out where necessary. The data gathered by completion of the checklists will be used to update the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation).

Samples submitted by the clinical sites will be tested using the Xpert MTB/RIF test. The testing site reports the Xpert MTB/RIF test results to the clinicians, and cases identified with having TB & MDR-TB cases are treated or referred to the MDR-TB Initiation Centre (RTLC is responsible for the transfer of cases to the MDR-TB Unit). In the early stages of implementation, the GeneXpert Focal Person, GeneXpert Focal Points and the implementing partner technical advisors will work closely with testing sites to ensure quality of results:

- Testing sites must be mentored and regular supervisory visits must be arranged;
- Additional training for supervisors/advanced users in troubleshooting and on-site supervision must be arranged;
- Testing sites must establish a system for instrument calibration;
- Testing sites must enrol in an EQA Programme;
- Testing sites must establish a system for regular maintenance, calibration and servicing of instruments;
- Xpert MTB/RIF test results must be monitored by establishing a system of monthly reporting and review of testing site quality indicators.

The DTLC & RTLC will work closely with clinical sites to ensure:

- Clinicians are following the Xpert MTB/RIF test TB diagnostic algorithm;
- TB cases are receiving the correct treatment and being initiated on treatment in a timely fashion;
- Cases identified as “MTB detected rifampicin indeterminate” are followed up
- Cases identified as RR-TB are referred to the MDR-TB Unit;
- Clinical sites are recording and reporting case detection.

EARLY IMPLEMENTATION PROGRAMME EVALUATION

A Programme Evaluation at the end of the early implementation phase ensures that the processes and systems established are functional and that implementation is able to proceed to routine testing independently of external support. Evaluation protocols should be prepared by implementing partners in close collaboration with NTLP and the GeneXpert Focal Person and submitted for appropriate ethical review. The results of the assessments will be reviewed by the NTLP and TWG. The outcome measures and scope of the evaluation must be pre-determined and should be focused on the impact of Xpert MTB/RIF test implementation on patient important outcomes.

GENEXPERT INSTRUMENT HANDOVER

Handover of instruments, changing roles and/or withdrawal of implementing partners is coordinated by the NTLP and the implementing partner. Handover of GeneXpert instruments to the NTLP/NTRL can be guided by following the requirements in the Pre-Handover Checklist [Annex F). The GeneXpert Focal Person, GeneXpert Focal Point or implementing partner will complete the checklist in the month before the intended handover. The checklist is used to determine the details of when, where and what kind of GeneXpert instrument was installed, what the status of calibration is; and whether all documentation related to the GeneXpert instrument has been supplied to the NTLP/NTRL. The implementing partner is responsible for ensuring that the GeneXpert instrument is in good working order, and that calibration has been performed. The data gathered by completion of the Pre-Handover Checklist will be used to update the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation).

PHASE 5: ROUTINE TESTING

Policy and objectives:

- The NTLP will put in place procedures to maintain quality-assured and uninterrupted services at all testing sites;
- The NTLP will review programmatic data on a regular basis to inform programme operational planning;
- The NTLP will keep abreast of developments in the field and review any new data pertaining to TB diagnosis for possible implementation.

The routine testing phase is the concluding phase of Xpert MTB/RIF test implementation. In the routine testing phase, the NTLP maintains the systems established in the earlier phases. During this phase:

- Regular on-site supervisory visits according to agreed schedules using standardized checklists will be conducted by the GeneXpert Focal Point and/or RTLCs;
- Routine monthly reporting and review of testing site quality indicators will be conducted by the GeneXpert Focal Person Point and NTLP;
- Testing site data will be collated using the Xpert MTB/RIF Tracking Tool;
- Participation and review of results from the Xpert MTB/RIF test EQA Programme will be conducted;
- Regular maintenance, calibration and servicing of instruments will be conducted;
- Follow-up training for testing and clinical sites; and re-training of personnel will be conducted;
- Regular program evaluations to assess the impact of Xpert MTB/RIF test implementation will be conducted.

GENEXPERT INSTRUMENT WARRANTY AND CALIBRATION

GeneXpert instruments purchased from Cepheid have a two-year warranty that begins from the date of shipment of the instrument. The date of shipment should be communicated to the GeneXpert Focal Person and recorded in the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation) to allow for accurate forecasting.
Care will be taken to minimize shipment time by ensuring all documents for tax exemption and customs clearance are in place before shipment is made and by making regular follow up with the shipment and clearance company. Installation should be done as soon as possible to ensure the longest possible warranty coverage. To minimise delays, additional items (*e.g.* UPS) should be place before instrument installation.

A one-year warranty is included in the purchase price of the instrument. The second-year extended warranty is only valid if the GeneXpert instrument was registered on installation and the calibration was completed within one year of the shipment date. Implementing partners are encouraged to buy the extended warranty when procuring GeneXpert instruments. The warranty covers all breakdowns of the GeneXpert instrument, computer and associated items. Within the warranty period, the implementing partner or the GeneXpert Focal Person can report all breakdowns directly to Cepheid technical support. The following details should be included, where possible, in communication with Cepheid technical support:

- The serial number of the instrument
- The serial number of the computer
- Contact person

- The site shipment address
- The IQ report of the instrument
- The system log report for at least the last 3 months
- The last 3 months testing files in .gxx format
- Last calibration report if appropriate

Cepheid will allocate a reference code to the trouble shooting case; this should be followed during all communications with Cepheid about this case. If troubleshooting is unable to solve the problem, Cepheid will ship a new part directly to the shipment address. A qualified authorized person should be contacted in country to make the necessary repairs when the parts arrive. The GeneXpert Focal Person should be kept in copy for all communications with Cepheid.

Calibration should be done once yearly or after 2000 tests (whichever comes first). If a module fails calibration it should not be used for further testing, the module can be isolated in the GeneXpert software. Replacement parts should be ordered from Cepheid as soon as possible. The GeneXpert Focal Person should be informed about all calibrations and the calibration report from Cepheid must be provided within one week of calibration. If modules have failed, a plan for replacing modules should also be submitted and the GeneXpert Focal Person included in all communications in this regard.

RECORDING AND REPORTING

Policy and objectives:

- The NTLP and implementing partners will implement national standardized recording and reporting tools at all clinical and testing sites;
- The NTLP will sensitize all implementing partners to use the nationally approved recording and reporting tools.

The new standardised reporting and reporting formats released by WHO [13] capture GeneXpert information (

Table 7) and will be disseminated to all facilities in Tanzania. These reports include revised quarterly reports, TB Laboratory Registers, patient registers, treatment cards, testing site request forms, presumptive TB registers, and MDR registers. Xpert MTB/RIF test-related information will be integrated into the existing TB reporting structures and protocols.

All testing sites are required to contribute to quarterly reports for the NTLP and CTRL. Xpert MTB/RIF rifampicin resistant results will be reported directly to the GeneXpert Focal Person. The data will be used to update the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation).

Table 7. Tanzanian approved reporting codes [13]

GeneXpert result	WHO reporting code
MTB not detected	N
MTB detected rifampicin resistance not detected*	T
MTB detected rifampicin resistance indeterminate*	TI
MTB detected rifampicin resistance detected*	RR

Error/ No result/ Invalid	I

*All MTB detected results should be written in red ink

PROCUREMENT AND SUPPLY CHAIN MANAGEMENT

Policy and objectives:

- The NTLP, in coordination with implementing partners, will procure quality reagents, items and services economically from reliable sources;
- The NTLP, in coordination with implementing partners, will estimate, position and monitor appropriate levels of stocks based on estimated needs, operational policy, objectives and priorities;
- The NTLP, in coordination with implementing partners, will ensure timely procurement and distribution of supplies to enable uninterrupted testing at all sites following the national algorithm.

FORECASTING

NTLP will incorporate procurement plans for GeneXpert instruments and necessary consumables into its annual forecasting and quantification exercises for all TB laboratory diagnostic supplies and commodities. Cepheid does not provide some of the supplies required for using the Xpert MTB/RIF test. When calculating orders of supplies, past consumption rate, stock on hand, shelf life of the ordered material, lead-time, and storage capacity will be considered in order to assess quantity and frequency of orders.

The Xpert MTB/RIF test implementation plan with forecasted quantities and budget details should be aligned with the *National TB Laboratory Strategic Plan*. Implementing partners should consult with NTLP regards the procurement and placement of GeneXpert instruments; and the supply of reagents through non-NTLP supply chains. Specifications for additional equipment (*e.g.* Uninterrupted Power Solutions) can be obtained from the GeneXpert Focal Person.

PROCUREMENT

There are many different channels by which Xpert MTB/RIF test cartridges are procured and supplied in Tanzania leading to challenges with under- and over-stocking. Distribution of cartridges to sites with GeneXpert instruments requires special consideration, as the cartridges have short shelf life. Hence, the national and regional TB control programmes should coordinate the distribution, from a single, central point.

A national pool, under the oversight of the GeneXpert Focal Person, has been established to supply patient testing sites in the country (clinical research sites are excluded as they operate independently). The monthly indicators (see Monitoring and Evaluation section) will be used to calculate district consumption and appropriate supplies allocated including a buffer stock. The regular TB supply chain should be used for this purpose. Due to transport issues to some sites, it may be necessary to implement a district-level stock buffer to ensure stock-outs do not occur.

STORAGE AND DISTRIBUTION

A framework for the proposed Xpert MTB/RIF supply chain system that will be established is as follows:

1. Sites request regular stock orders from the regional or district warehouse by a set date, namely two weeks before the start of the new quarter. To avoid stock-outs due to delivery delays via the DTLC or RTLC, the testing site should have a minimum of one month's buffer stock on hand. Emergency requests can be made under special circumstances, though frequent emergency orders should be investigated and corrective and preventive actions taken.
2. RTLC/DTLC or a designated representative checks orders against indicators and confirms request.
3. District and regional warehouses should place quarterly stock orders to ensure sufficient stock for all sites. To allow for delivery to warehouses, orders should be made midway through the quarter (February, May, July, and October). A minimum of one month's worth of buffer stock should be kept on hand. Emergency requests can be made under special circumstances, though frequent emergency orders should be investigated.
4. CTRL focal person confirms request by checking orders against indicators.
5. MSD central reagent pool should be carefully monitored both from electronic records and from regular stock counts. Reagents/consumables should be shipped in a timely fashion.
6. NTLP and MSD to work in close collaboration to order reagents from Cepheid twice per year. Ensure buffer stock available at MSD. All partners must coordinate with NTLP and MSD regarding cartridge purchases.

REPORTING

All testing centres must establish a strong, transparent and reliable commodity management systems at the institutional level. A system for regular inventory of cartridges must be in place with updated information on stock levels and expiry dates for all available batches of cartridges. The principle of First-Expiry-First-Out (FEFO) should be strictly followed. In situations where a potential over- or under-stocking occurs at testing sites, the GeneXpert Focal Person should be informed and will work with sites to transfer cartridges to other sites (to avoid expiration of cartridges) or to arrange urgent delivery of cartridges. However, this should be viewed as a last resort, and sites should be assisted to implement an effective stock management system.

The proposed framework will include the RLT/DLT and the pharmacists among the designated representatives to check orders and report errors. Where possible the supply chain for Xpert MTB/RIF should be integrated into the Laboratory Information Management System and the National Logistics Management Systems. The GeneXpert Focal Person will oversee the integration process of the LIS with the NTLP. The NTLP & MSD will procure in line with the approved supply plan (Framework 6).

MAINTENANCE AND TROUBLESHOOTING OF GENEXPERT INSTRUMENTS

Policy and objectives:

- All testing sites will follow standardized procedures for troubleshooting, repair and maintenance of GeneXpert instruments;
- The Xpert focal person is designated as the point of contact for all servicing and repair communications with the manufacturer.

A number of maintenance procedures must be followed regularly (daily, weekly, monthly, and annually) to ensure proper functioning of the GeneXpert instrument, with each task checked during

supervisions (Annex H). GeneXpert Users are responsible for all instrument maintenance. The extent to which users have performed instrument maintenance will be reviewed during supervision and troubleshooting visits. Failure to maintain the GeneXpert instrument can lead to testing errors and instrument breakdowns.

GeneXpert instrument: All testing sites experiencing GeneXpert instrument failure or module failure (*i.e.* high errors on module, red light on the module or stuck cartridge, fan failure, communication problems) will immediately notify the RLT/RTLC/DLT/DTLC/GeneXpert Focal Point and the GeneXpert Focal Person. The GeneXpert Focal Person will contact the site and will begin troubleshooting by telephone, if the problem cannot be solved, the GeneXpert Focal Point for that region will be sent as soon as possible (within two weeks) to provide technical assistance. The Supervision Checklist (Annex F) will be used to document & report the findings of the supervisory visit. The GeneXpert Focal Point will collect the following information for further examination:

- The serial number of the instrument
- The serial number of the computer
- Contact person
- The site shipment address
- The IQ report of the instrument
- The system log report for at least the last 3 months
- The last 3 months testing files in .gxx format

The implementing partner or GeneXpert Focal Person is responsible for communicating with Cepheid and the GeneXpert Focal Person must be copied on all trouble shooting communications. The GeneXpert Focal Person and implementing partners are responsible for following up corrective actions and evaluating their success.

Computer malfunction: All testing sites will have updated antivirus software installed on the GeneXpert computer and the use of memory sticks, other devices, and the installation of other software on that computer is prohibited. The GeneXpert Focal Points are responsible for keeping the anti-virus software up to date. If computer-related problems are experienced, users and / or laboratory managers should bring these to the attention of their facility's information technology department. If the information technology department cannot resolve the malfunctions, the relevant RTLC/DTLC should be contacted, who can liaise with the GeneXpert Focal Person and implementing partners to resolve the problem and/or contact Cepheid.

The following information should be collected where possible for troubleshooting purposes:

- The serial number of the instrument
- The serial number of the computer
- Which windows version is on the computer
- Which software version is on the computer
- Contact person
- The site shipment address
- The IQ report of the instrument
- The system log report for at least the last 3 months
- The last 3 months testing files in .gxx format

The implementing partner or GeneXpert Focal Person is responsible for communicating with Cepheid and the GeneXpert Focal Person must be copied on all trouble shooting communications. The GeneXpert Focal Person and implementing partners are responsible for following up corrective actions and evaluating their success.

Xpert MTB/RIF cartridges: Damage and inappropriate use or storage of cartridges can all lead to high rates of invalid results. Upon obtaining multiple invalid results, the operator should record the batch number. If a pattern is detected (high rates of invalid results linked to a particular batch number), they must report it to their RTLC/DTLC who may consult the GeneXpert Focal Person.

Staff-related errors: The most common GeneXpert instrument & Xpert MTB/RIF test errors are due to incorrect processing of samples. A high error rate (in particular of errors 2008, 5006, and 5007) spread across all modules suggests that operator error may be a cause and onsite re-training of staff may be necessary. RTLCs or GeneXpert Focal Points should compile a list of recommended candidates for re-training, in addition to new personnel. The list should be communicated to the GeneXpert Focal Person to arrange re-training. Preferably, candidates should be mentored on-site to ensure that training is successful.

Troubleshooting at sites (including calibration, electrical problems with the UPS) is documented by the GeneXpert Focal Point using the Supervision Checklist (Annex F). Unresolved issues are escalated to the GeneXpert Focal Person for further investigation / resolution.

An Authorised Service Provider (ASP) is an agency tasked by Cepheid to provide installation, troubleshooting and support to Xpert MTB/RIF testing sites on their behalf. NTLP will establish contracts with the ASP. The terms of reference for the ASP will be clearly defined, and the extent of the services offered by the ASP will be communicated to the GeneXpert Focal Person. All installations and troubleshooting involving the ASP will be coordinated by the GeneXpert Focal Person.

TRAINING AND COMPETENCY ASSESSMENT

A standardised training curriculum, based on the Global Laboratory Initiative (GLI) Xpert MTB/RIF test training package (http://www.stoptb.org/wg/gli/documents.asp?xpand=2), has been customised for training clinical and testing site personnel in Tanzania. All users must be trained using the approved national training curriculum. A cadre of master trainers is utilised from previously trained RTLC (for clinical training) and GeneXpert Focal Points (for Xpert MTB/RIF test users) to provide training in all districts. The master trainers assist the NTLP to cascade clinical and Xpert MTB/RIF test training in a phased manner alongside instrument placement. Training is conducted by implementing partners and the GeneXpert Focal Person. Implementing partners will coordinate and report the outcome of training with the GeneXpert Focal Person. Implementing partners are responsible for the initial training of users at their testing sites, using the standardised training curriculum.

The outcomes of trainings and mentorship are recorded using the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation) and a report must be provided to the NTLP in a standardised narrative format.

TRAINING CURRICULUM

The standardised training curriculum provides training for:

> *GeneXpert Users:* The objective of the user training is to enable testing site personnel to perform the Xpert MTB/RIF test, understand the testing algorithms, interpret Xpert MTB/RIF test results, maintain the GeneXpert instrument, and supply the NTLP with relevant quality indicators. Administrative users are the main site contacts. They are specifically trained to

perform reporting functions. Users who fail to pass both theoretical and practical competency assessments can be followed up and re-assessed before re-training.

GeneXpert Focal points: This training is intended for administrators and senior Xpert MTB/RIF users who have a proven track record and who have been selected to mentor other sites. The objective of the Focal point training is to enable selected testing site personnel to co-ordinate GeneXpert implementation activities such as supervisory visits, competency assessments, troubleshooting, and training and to collect quality indicators in country. After completing the training, GeneXpert Focal Points will be mentored by existing master trainers this may include being supervised during testing site assessments and GeneXpert installations as well as learning to organise and facilitate User training. After GeneXpert Focal Points graduate from the mentorship program, they will be considered master trainers.

Clinical staff: The objective of the Clinical training is to instruct clinicians and healthcare workers in the fundamentals of the GeneXpert technology, introduce the testing and treatment algorithms and to provide guidance on the requesting and interpretation of Xpert MTB/RIF test results. Clinical staff from relevant entities within the GeneXpert facility, TB unit, CTC, as well as out cases, wards, administrative staff and staff from sites who will refer samples to the site, must be included in the training.

RTLCs: The objective of this training is to instruct Regional TB clinicians in the fundamentals of the GeneXpert technology, introduce the testing and treatment algorithms, and provide guidance on the requesting and interpretation of Xpert MTB/RIF test results especially on complicated cases. This training prepares RTLC clinicians to train clinical staff on Xpert MTB/RIF testing and to perform quarterly supervisory visits while supporting GeneXpert Focal Points. RTLCs are also trained in the collection of programmatic quality indicators.

TRAINING IN THE IMPLEMENTATION PHASES

Clinical sites:

- Following installation, the RTLC/DTLC will arrange for the GeneXpert Focal Person/ GeneXpert Focal Points or the implementing partner technical advisor to sensitize clinical staff the utility of the Xpert MTB/RIF test. Sensitization should include an introduction to the National TB Diagnostic Algorithm, sample collection and transport, as well as interpretation and reporting of results.
- It is mandatory that clinicians, TB care nurses, TB and HIV programme officers, and hospital administrators undertake technical training on the Xpert MTB/RIF test use and diagnostic algorithm prior to implementing the Xpert MTB/RIF test service. A three-day training should be conducted for clinical staff using the nationally standardised training material.
- A one-day on-site sensitisation workshop will be conducted for general health care workers from testing and sample referring centres, on the proper implementation of Xpert services, diagnostic algorithms, testing site networking, sample referrals and result feedback mechanisms.

Testing sites:

- Following installation, the RTLC/DTLC will arrange for the GeneXpert Focal Person/ GeneXpert Focal Points or the implementing partner technical advisor or Authorised Service Provider (ASP) to sensitize testing site staff to the operation of the GeneXpert instrument.
- GeneXpert Users will undertake technical training on the Xpert MTB/RIF test use and diagnostic algorithm prior to implementing the Xpert MTB/RIF test service. A five-day training

should be conducted for testing site personnel from Xpert MTB/RIF testing sites, using the nationally standardised training material.

- During the Early Implementation Phase, additional training on the use of checklists is given to the GeneXpert Focal Points, testing site coordinators and RTLCs. This enables the trainees utilise the checklist during supervisory visits in their catchment areas.

Advocacy will be targeted at the inclusion of the standardised training for Xpert MTB/RIF into the curricula of Tanzanian educational and training institutions responsible for training testing site technicians.

QUALITY ASSURANCE

Policy and objectives:

- The NTLP, in collaboration of implementing partners, will ensure all Xpert MTB/RIF testing sites provide quality-assured testing services according to best practices;
- The NTLP will sensitise and provide training materials to all implementing partners on the approved national programme for quality assurance;
- The NTLP, via the Xpert focal person, will receive regular reports from all testing sites regarding the quality of testing (QA procedure logs, proficiency test results and quality indicator reports);
- The NTLP and CTRL (or delegated regional personnel) will conduct supervisory visits to testing sites to verify quality of testing and provide support;
- All sites shall be registered for and undertake regular EQA as part of GeneXpert Quality assurance.

Quality-assured results are accurate, reproducible and timely. To ensure quality-assured results, a comprehensive and standardised quality assurance system will be implemented in all clinical and testing sites providing Xpert MTB/RIF testing services in Tanzania:

- Support for sites in implementing all the requirements for quality assurance will be given by the GeneXpert Focal Person, GeneXpert Focal Points and implementing partners, and is a critical element to be covered during on-site supervisory visits.
- Quality assurance is just one part of a Laboratory Quality Management System, required to ensure quality of all a testing site's processes. Continuous quality improvement is a critical concept to be adopted by clinical and testing sites.
- Quality assurance activities for Xpert MTB/RIF test should not be seen in isolation; rather they should be integrated with quality assurance for TB smear microscopy and/or other testing, where possible.
- Quality assurance is part of the routine workload and is not a separate activity. All quality assurance activities must be documented using standardised forms. Feedback to testing sites and implementing corrective and preventive measures are the most critical aspects of any quality assurance programme. Quality assurance is needed whether Xpert MTB/RIF testing is performed at a testing site or a research site.

UTILISATION OF GENEXPERT STANDARD OPERATING PROCEDURES (SOP)

To ensure consistent implementation quality, the GeneXpert Focal Person will ensure harmonisation of all SOPs, documentation & forms. Compliance with national SOPs and algorithms will ensure

standardisation, in particular for biosafety, collection and transportation of sputum samples, test procedures, results implementation and database management, recording and reporting, National TB Diagnostic Algorithm, maintenance, troubleshooting, quality assurance, and supplies management. Refer to Annex I for a list of documents and tools and specific SOP considerations to be followed at all testing sites.

SUPERVISORY VISITS

The GeneXpert Focal Person, GeneXpert Focal Points, implementing partner technical advisor in co-ordination with the RTLC performs clinical site assessments using standardised checklists (Annex F)[11].

Clinical sites: The DTLC, RTLC and/or GeneXpert Focal Points will responsible for conducting regular supervisory visits to clinical sites in their region. Clinical supervisory visits will be documented using the Clinical Checklist (Annex F). All clinical sites will initially receive quarterly supervisory visits. Clinical sites that are performing well can visited less frequently. Supervisors will complete a standardised questionnaire during the visit, which will highlight problems and recommendations that will be returned to the site. Existing troubleshooting channels will then be utilised (*i.e.*, follow-up intervention visits). A brief narrative report of supervisions conducted must be compiled and submitted to the NTLP on a quarterly basis

Testing sites: The following checklists will be used during supervisory visits in the early implementation phase (Annex F): comprehensive, supervision, quarterly, pre-handover checklists. Supervisors undertaking testing site monitoring and supervision visits on behalf of the NTLP to assess Xpert MTB/RIF test implementation use these checklists. Comprehensive site visit assessment will be conducted as an initial assessment of site competency after installation, and annually thereafter.

All testing sites will initially receive quarterly supervisory visits by the GeneXpert Focal Person, DTLC & RTLC and/or designated GeneXpert Focal Point. Testing sites that are performing well can be visited less frequently. Supervisors will complete a standardised questionnaire during the visit, which will highlight problems and recommendations that will be provided to the site. Existing troubleshooting channels will then be utilised (*i.e.*, follow-up intervention visits). The data gathered by completion of the checklists will be used to update the Xpert MTB/RIF Tracking Tool (see Monitoring & Evaluation). A brief narrative report of supervisions conducted must be compiled and submitted to the NTLP on a quarterly basis.

Testing sites that are do not regularly submit quality indicator data and/or have high error/invalid/no results rates will be prioritised for additional support and re-training if necessary. Additional support and re-training is coordinated and performed by the GeneXpert Focal Person and/or designated GeneXpert Focal Point.

EXTERNAL QUALITY ASSURANCE

When a GeneXpert instrument is installed at a new testing site, it will be registered in the EQA program. Currently the NTLP is using a Xpert MTB/RIF proficiency test panel (EQA) provided by the CDC. To register, testing sites must supply contact details as well as postal address to the GeneXpert Focal Person (done at installation). Testing sites will receive sample from the start of the next EQA round after registration. Xpert MTB/RIF panels will be supplied quarterly and all sites must submit the

[11] Ideally, one GeneXpert Focal Point should be responsible for five testing sites; but no more than 10 testing sites

results form with the completed tests or with reasons why testing could not be completed to the address supplied, and to the GeneXpert Focal Person.

The CDC returns the outcomes of proficiency panels directly to the sites and to the GeneXpert Focal Person. The GeneXpert Focal Person will distribute results to the RTLC and the implementing partners. The testing site Quality Officer (QO) and GeneXpert staff must examine the returned results and any discrepancies must be investigated to determine the root cause. Corrective actions should be carried out, documented and reviewed for success. RTLC's should follow up with the site to ensure patient testing has not been affected. If a testing site continues to experience EQA discrepancies (*i.e.* in the next round of testing) then site will be contacted by the GeneXpert Focal Person and further actions taken.

All sites should participate in an EQA programme. Since the existing programme may not accommodate all sites in the future, alternative EQA programmes may be utilised provided they comply with quality standards. NTLP should be consulted on the choice of an EQA programme and should be provided with copies of EQA reports and corrective actions.

MONITORING AND EVALUATION (M&E)

Monitoring and evaluation of Xpert MTB/ RIF implementation is necessary to ensure the effective and efficient use of resources and also to measure the impact of Xpert MTB/RIF in order to guide and justify further scale-up. A robust monitoring and evaluation system includes appropriate indicators and support for data collection, reporting, and analysis.

In addition, it is especially important to monitor the effects that Xpert can have on treatment initiation rates and reduced time to treatment. Assessment of these effects requires a system that can link testing site and clinical site data. M&E of Xpert MTB/RIF test implementation activities are coordinated by the GeneXpert Focal Person centrally, at the CTRL/NTLP.

During the early implementation phase, many of the roles for the rollout will not have been defined, and the GeneXpert Focal Person in conjunction with the implementing partner will be responsible for collecting site data. However, in the routine testing phase, the responsibility for collecting monthly data becomes the responsibility of the RTLC. The RTLC and the GeneXpert Focal Points communicate directly with site supervisors, users, clinical and Health Care Workers who in turn collect the required data from registers, logs and the GeneXpert instrument. Site data will be analysed locally, for trends that may inform operational decisions and centrally to provide an overview of implementation at country level. The GeneXpert Focal Person must report the findings of on-going implementation to the NTLP and provide feedback to sites through the reporting structures.

PROGRAMMATIC AND CLINICAL QUALITY INDICATORS

In order to understand the impact of the Xpert MTB/RIF test on case detection, the management of cases, and other testing site processes, additional data need to be collected from clinical sites at the district or treatment-facility level. The quality indicator data that will be collected, analysed and reported monthly from testing sites is listed in Annex J. Other aspects of implementation, in particular data on cost-effectiveness and the impact on diagnostic delays and time to treatment initiation, are best evaluated by operational research studies rather than as part of the routine M&E.

TESTING SITE QUALITY INDICATORS

At the testing site, monitoring the use of Xpert MTB/ RIF ensures that established diagnostic algorithms are being followed, detects whether a particular instrument module is functioning sub-optimally or whether any users require additional training, and allows supplies to be effectively managed. Site-level information will be collected by the GeneXpert Focal Person and reported to the

CTRL and NTLP quarterly. This will allow guidance on any actions that need to be undertaken to improve effectiveness, efficiency or user performance, and to strengthen the supply-management process to prevent stock- outs or cartridges from expiring by exchanging cartridges among sites. The quality indicator data that will be collected, analysed & reported monthly from testing sites is listed in Annex K. Collection of the quality indicator data can be facilitated by using a GeneXpert Remote Monitoring solution.

XPERT MTB/RIF TRACKING TOOL

The Xpert MTB/RIF tracking tool is a Microsoft Excel based database that is used to monitor implementation at testing sites. The Xpert MTB/RIF tracking tool collates data on instrument placement, calibration dates, site contact information, training and training participant information, site assessment results, quality indicator data and EQA results. The Xpert MTB/RIF tracking tool is located on a centralised computer at the CTRL. The Xpert MTB/RIF tracking tool is regularly updated with monthly quality indicator data and is backed-up. The GeneXpert Focal Person manages the Xpert MTB/RIF tracking tool. The tool provides an easy option for analysing and reporting aggregated site data and allows a snapshot of Xpert MTB/RIF test implementation at country level.

Currently, the Xpert MTB/RIF Tracking tool is being used within the CTRL for collection of all testing site data related to Xpert MTB/RIF implementation, along with standard NTLP registers and other reporting tools. The NTLP is evaluating remote monitoring systems for collecting Xpert MTB/RIF instrument data, which may be implemented in the future, and may be used to replace or supplement existing data collection tools. Such implementation will be coordinated by NTLP and all implementing partners will be required to follow the recommended national approach with respect to remote connectivity.

XPERT MTB/RIF TEST ROLLOUT COSTING

To provide the cost of implementing and maintaining Xpert MTB/RIF test rollout in Tanzania, a five-year cost mapping exercise was conducted (Table 8). Details of the costing are provided in Annex K.

Table 8. Five-year cost mapping exercise Xpert MTB/RIF implementation Tanzania (USD)

Year*	2015	2016	2017	2018	2019
Number of GeneXpert instruments / sites[1]	New: 17 Existing: 67 Total: 84	New: 16 Existing: 84 Total: 100	New: 62 Existing:100 Total: 162	Existing:162 Total: 162	Existing:162 Total: 162
Capital[2]	US$338,300	US$320,320	US$1,249,114	-	-
Installation[3]	US$30,355	US$29,734	US$239,462	-	-
Training[4]	US$29,550	US$34,188	US$51,570	US$41,718	US$43,824
Supervision[5]	US$72,575	US$89,726	US$162,028	US$154,030	US$161,626
Consumables[6]	US$2,770,750	US$3,409,740	US$5,063,090	US$6,091,200	US$6,188,400
Warranty & maintenance[7]	US$6,300-12,600	US$7,200-14,400	US$9,000-18,000	US$14,400-28,800	US$14,400-28,800
GXAlert[8]	US$20,290	US$23,192	US$39,132	US$31,779	US$33,376
Programme evaluation[9]	US$3,000	US$3,150	US$3,308	US$3,473	US$3,647

* The inflationary cost is estimated at 5% per annum. Inflationary costs were excluded from concessionary items (GeneXpert instruments & cartridges)

RESOURCE MAPPING AND SUSTAINABILITY

The WHO estimated that in 2013, US$58 million was required to fund Tanzania's TB programme. However, 67% of the programme remains unfunded. This presents challenges when attempting to achieve the goal of placing one instrument per district, per the *National TB Laboratory Strategic Plan*, given the significant expenditure required versus resources available. Sustained efforts are required to mobilise resources to ensure uninterrupted operation of existing GeneXpert instruments, and to sustainably finance full district-level coverage. Coordinating and adequately mapping incoming resources associated with GeneXpert as per the previous sections (Coordination and Resource mapping) will allow sufficient time to incorporate on-going costs into the planning cycles of appropriate funding mechanisms. An electronic system will be established at the NTLP to assist with this function.

FUNDING SOURCES

Since the Tanzanian MOHSW decided to adopt the WHO recommendations for the use of Xpert MTB/RIF in the diagnosis of HIV-associated TB and MDR-TB, the country has been the recipient of significant international support regarding its introduction. The following major global mechanisms have supported Xpert roll out in Tanzania:

Global Fund to Fight AIDS, Tuberculosis and Malaria: The Global Fund will be a critical source of support for GeneXpert rollout in Tanzania. Costs for one year of operations were included in the interim Global Fund proposal submitted in early 2014. It is imperative that Global Fund concept notes and proposal submissions developed between 2014 and 2018 include financing for GeneXpert rollout, taking into consideration the interim proposal grant awarded and other commitments. As future concept notes must be developed in collaboration with the national AIDS programme, joint budgeting and planning regarding GeneXpert is very much required between the two programmes.

Domestic funding: Increases in domestic funding allocations are required to ensure the sustained use of GeneXpert beyond the life of the various projects currently operating. A key step will be the inclusion of on-going running costs and commodities for the instruments into comprehensive council health plans at the district level. It is advised that a minimum of supervision and other system costs are included in the regional health management team and medium-term development budgetary submissions. Ownership of GeneXpert instruments by facilities and district authorities is important to ensure sustained use. This is why it is essential to involve the district and receiving facility authorities in the initial phases, and for close linkages to be formed between the NTLP and the Department of Diagnostic Services. Increasing domestic funding for the TB programme in general was highlighted as a key area for action by the MOHSW in early 2014. It is critical that funding for GeneXpert play a central role in those on-going discussions.

Unilateral and bilateral donors: This includes the US President's Emergency Plan for AIDS Relief (PEPFAR) through the US Centers for Disease Control and Prevention and the US Agency for International Development (USAID); World Bank: East Africa laboratory strengthening initiative; USAID TB2015 Task Order; and UNITAID/WHO TB Xpert Initiative. These donors are currently providing resources for GeneXpert instruments and activities in Tanzania. As these donors plan the next iterations of their support, it will be important for them to work with the NTLP early in the planning process to ensure that future projects are aligned to address coverage gaps, and strive to supplement the resources committed as captured by the on-going resource mapping. Evaluation of NTLP/CTRL data from on-going implementation will be critical to inform plans for roll out and financing.

SUSTAINABILITY CONSIDERATIONS

The reliance on donor funding and multitude of implementing partners in Tanzania presents many potential challenges for the sustainable rollout of the technology, common in many other sub-Saharan African countries. The differing timelines attached to donor-funded projects make coordination extremely important. In Tanzania, there is also a lack of affordability studies, making accurate costing and sustainability projections challenging.

Noting these challenges, a stakeholders meeting was held in May 2013 to assess the progress of introduction efforts, and to provide clarity regarding challenges. The meeting revealed that 100% of GeneXpert activities appear to be donor-funded with differing project end dates; however, all currently funded projects are expected to finish by 2016. It was also found that concurrent sputum smear microscopy was being done, there was duplication regarding placement of instruments, and a lack of common understanding and clarity at the national level regarding placement. Other observations regarding the status of GeneXpert in Tanzania from this meeting included:

- Inadequate infrastructure in facilities (air conditioning, clean area, refrigerators, adequate space, etc.).
- Agreed NTLP algorithm not implemented.
- NTLP guidelines not updated to reflect GeneXpert testing.
- Supply management weaknesses resulting in mass stock-outs and expiries of cartridges.
- Lack of standardisation (procedures, reporting, etc.).
- Inadequate training of staff.
- High rate of unsuccessful tests: errors, invalids, or no result.
- Lack of maintenance of GeneXpert.
- High rate of module failures.
- Inadequately communicated handover from implementing partners to NTLP.

PROPOSED RESOURCES ALLOCATION

Discussions between MOHSW and implementing partners, especially through the Development Partners Group of Health forum, have resulted in the following proposals for resource allocations:

Procurement of instruments (capital equipment)

- PEPFAR, USAID
- Global Fund to Fight AIDS, Tuberculosis and Malaria

Maintenance and running costs

- MOHSW—inclusion in national and district budgets
    - Comprehensive council health plans
    - Medium-term development framework
    - Regional health management team budget
- PEPFAR, USAID
- Global Fund to Fight AIDS, Tuberculosis and Malaria

Commodities

- PEPFAR, USAID
- Global Fund to Fight AIDS, Tuberculosis and Malaria
- MOHSW—inclusion in national and district budgets
    - Comprehensive council health plans

- Medium-term development framework
- Regional health management team budget

RESEARCH

Policy and objectives:

1. The NTLP in collaboration with other stakeholders and partners will develop a TB operational research strategy identifying priority research areas;
2. The NTLP and partners will review the priority research areas from time to time in order to address strategic shifts;
3. The NTLP encourages programmes to design and carry out operational research for generating science-based information to improve performance in their collaborations;
4. The NTLP will collaborate with researchers in the design, implementation, dissemination, and utilization of operational research findings.

The NTLP encourages organisations to perform operational research in Tanzania. Research should be directed to addressing the needs of the country and be in alignment with the strategic objectives contained in the *National TB Laboratory Strategic Plan*. Those parties introducing GeneXpert instruments into Tanzania for research purposes should follow the guidelines above. All research protocols must be submitted to NTLP for evaluation and will require ethical review by the National Institute of Medical Research (NIMR). Operational research topics include:

- Patient acceptability of patient vs. sample referrals,
- Compliance to algorithms;
- Costing of EMS and sustainability studies;
- Cost-effectiveness of testing all PLHIV (regardless of symptoms).

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ANNEX A: LABORATORY SERVICES SWOT ANALYSIS

Strengths
1. A strong NTLP.
2. Improved laboratory infrastructure at the national, zonal, and regional levels.
3. A well-coordinated, integrated laboratory network within the health care system.
4. Commitment and political will from government and support from partners.
5. Existence of national TB policies and standard guidelines.
Weaknesses
Access and infrastructure:
1. Inadequate infrastructure mainly at district and primary health facilities (health centres and dispensaries).
2. Inadequate capacity to carry out culture and drug susceptibility testing.
3. Inadequate sample transport and referral system for smear microscopy.
Equipment and supplies:
1. Inadequate laboratory supply chain management system.
2. Inadequate funding for TB laboratory equipment maintenance, certification, and service.
Human resources for health:
1. Inadequate qualified laboratory personnel and biomedical engineers.
2. Inadequate funding for short- and long-term training.
3. Inadequate mechanism to attract and retain technical staff.
4. Inadequate lab personnel at the CTRL (quality and safety officer and logistic and forecasting personnel).
TB laboratory monitoring and evaluation:
1. Inadequate coordination and supervision.
2. Inadequate laboratory management information system (LMIS).
Quality management:
1. Inadequate external quality assessment system implementation.
2. Inadequate training in preparedness' toward accreditation.
3. Slow progress toward laboratory accreditation.
4. Challenges in sustaining the quality of TB laboratory services during scale-up.
Governance, leadership, and coordination:
1. Weak laboratory services management and leadership capacity.
2. Poor coordination among stakeholders.
3. Inadequate advocacy for high-quality TB laboratory services.
Operational research to improve TB diagnosis:
1. Inadequate funds and technical capacity to conduct operational research and evaluation studies.
Opportunities
1. There is political will and commitment by the government to promote and support TB laboratory activities, which contribute to achieving NTLP 2016 targets and the Millennium Development Goals.
2. Increased international commitment to research on TB, new TB diagnostics, and vaccines.
3. The Primary Health Service Development Program (MMAM*) (2007–2017) is in place.
4. Proven credibility and reputation gained from collaboration with different local, regional, and international partners and stakeholders.
5. Readiness of communities to participate in TB control (*e.g.*, Sputum fixers).
6. Country flexibility to adapt to new approved TB diagnostic techniques.
Threats
1. The TB program is donor dependent, which poses a threat to sustainability.

* Mpango wa Maendeleo wa Afya ya Msingi (Primary Health Service Development Programme)

ANNEX B: NTLP SAMPLE REQUEST FORM

Ministry of Health and Social Welfare
National TB and Leprosy Programme

TB/LEP 01

REQUEST FOR EXAMINATION OF BIOLOGICAL SPECIMEN FOR TB AND LEPROSY

Name of health facility_____ Date of request ___/___/20___

Date of collection___/___/20__

Name of patient_____ Age_____ Sex (M/F)_____

Physical address (ward, street, village, house number)_____

Contact telephone/mobile no_____ TB District No_____

Area leader/ neighbour_____ Laboratory Serial No_____

Reason for examination

☐ Diagnosis. If diagnosis, presumptive RR-TB/MDR-TB? ☐ Yes ☐ No

Or

☐ Follow-up. If follow-up, month on treatment_____

HIV status	☐ Reactive	☐ Non reactive	☐ Unknown
Previosly treated for TB?	☐ Yes	☐ No	☐ Unknown
Specimen type	☐ Sputum	☐ CSF	☐ Peritoneal fluid
	☐ Skin smear	☐ Pleural fluid	☐ Lymph node
Test(s) requested	☐ Microscopy	☐ Xpert MTB/RIF	

Name and signature of person requesting examination_____

Contacts for results feedback (if available) DTLC / RTLC

RTLC Name_____ Email contact_____

DTLC Name_____ Email contact_____

Results (to be completed in the laboratory)

Labotratory serial no_____ Date of reception ___/___/20___ ☐ ZN ☐ FM

Date	Specimen	Appearance*	Result (Tick one)				
			neg	Scanty	1+	2+	3+
	A						
	B						
			N#	T#	TI#	RR#	I#
	Xpert MTB/RIF						

*Visual appearance of sputum (blood stained, purulent, mucous, mucopurulent, salivary)

N = MTB not detected; T = MTB detected rifampicin resistance not detected; RR = MTB detected rifampicin restance detected; TI = MTB detected rifampicin resistance indeterminate; I = Error / No result / Invalid

Date_____/_____/20_____ Examined by_____ Signature_____

Date_____/_____/20_____ Reviewed by_____ Signature_____

Skin smear result (to be completed in laboratory)

Ear lobe	Lesion

Date_____/_____/20_____

The completed form (with results) should be sent promptly to the treatment unit

ANNEX C: INSTRUMENT PLACEMENT

Site	Region	District	Supported	# Modules	# GeneXpert	Routine or Research
Mt Meru Regional Hospital	Arusha	Arusha urban	USAID	4	1	Routine
Amana	Dar es Salaam	Ilala 1	PATH	4	1	Routine
CTRL	Dar es Salaam	Ilala 2	World Bank/EDCPT	8	2	Routine
Ukonga Prison Health Facility	Dar es Salaam	Ilala	MMRC	4	1	Research
Temeke	Dar es Salaam	Temeke	FIND	8	2	Routine
Mwananyamala	Dar es Salaam	Kinondoni	ICAP/NTBP	8	2	Research
Mwananyamala Hospital IHA Research	Dar es Salaam	Kinondoni	IFIKARA	4	1	Research
Keko Prison Health Facility	Dar es Salaam	Temeke	MMRC	4	1	Research
Lugalo Military Hospital	Dar es Salaam	Kinondoni	Pharmaccess	4	1	
Segerea Prison Health Facility	Dar es Salaam	Ilala	MMRC	4	1	Research
Mnazi Mmoja Hospital	Dar es Salaam	Ilala 1	USAID	4	1	Routine
Sinza Hospital	Dar es Salaam	Kinondoni	USAID	4	1	Routine
Dodoma Regional Hospital	Dodoma	Dodoma urbah	WHO	4	1	Routine
Iringa	Iringa	Iringa urban	FIND	4	1	Routine
Bukoba Regional Hospital	Kagera	Bukoba	CDC	4	1	Routine
Kibong'oto National TB Hospital	Kilimanjaro	Siha	World bank	4	1	Routine
KCMC	Kilimanjaro	Moshi urban	KCRI	8	2	
Mirerani Hospital	Kilimanjaro	Hai	MGIT	4	1	Routine
Mawenzi Hospital - Moshi	Kilimanjaro	Moshi urban	USAID	4	1	Routine
Sokoine Regionala Hospital	Lindi	Lindi Urban	WHO	4	1	Routine
Mrara Hospital	Manyara	Babati	MGIT	4	1	Routine
Haydom Lutheran Hospital	Manyara	Haydom	NIMRI	4	1	Research
Musoma Regional Hospital	Mara	Musoma	WRP	6	1.5	Routine
Mbeya Referral Hospital	Mbeya	Mbeya urban	NTLP	4	1	Routine
Mbeya Regional Hospital	Mbeya	Mbeya urban	NTLP	4	1	Routine
Mbeya Medical Research Center	Mbeya	Mbeya urban	MMRC	8	2	Research
Mobile Clinic	Mbeya	Mbeya urban	MMRC	4	1	Research
Ruanda Prison	Mbeya	Mbeya urban	MMRC	4	1	Research
Kyela District Hospital	Mbeya	Kyela	NTLP	4	1	Routine
Mbeya Military Dispensary	Mbeya	Mbeya rural	Pharmaccess	4	1	
Apopo-sua	Mogorogoro	Morogoro urban	Apopo	4	1	Research
Morogoro Regional Hospital	Morogoro	Morogoro urban	USAID	4	1	Routine

Site	Region	District	Supported	# Modules	# GeneXpert	Routine or Research
Ndanda Hospital	Mtwara	Masasi	World bank	4	1	Routine
Ligula Hospital	Mtwara	Mtwara Urban	WHO	4	1	Routine
Bugando Medical Center	Mwanza	Nyamagana	MMRC	4	1	Research
Butimba Prison Health Facility	Mwanza	Nyamagana	MMRC	4	1	Research
Geita Hospital	Mwanza	Geita urban	USAID	4	1	Routine
Sekou Toure Hospital	Mwanza	Nyamagana	PATH	4	1	Routine
Sengerema	Mwanza	Sengerema	USAID	4	1	Routine
Kibena (Njombe) Regional Hospital	Njombe	Njombe urban	USAID	4	1	Routine
Pemba	Pemba	Pemba	WHO	4	1	Routine
Bagamoyo	Pwani	Bagamoyo	Ifikara (IHI)	8	2	Research
Tumbi Hospital	Pwani	Kibaha	USAID	4	1	Routine
Mpanda Hospital	Rukwa	Mpanda	CDC	4	1	Routine
Ruhuwiko Military Dispensary	Ruvuma	Songea	Pharmaccess	4	1	
Songea Regional Hospital	Ruvuma	Songea	CDC	4	1	Routine
Kahama District hospital	Shinyanga	Kahama	CDC	4	1	Routine
Shinyanga Regional Hospital	Shinyanga	Shinyanga	WHO	4	1	Routine
Singida Regional Hospital	Singida	Singida urban	CDC	4	1	Routine
Tabora Regional Hospital	Tabora	Tabora urban	CDC	4	1	Routine
Bombo Hospital	Tanga	Tanga Urban	MGIT	4	1	Routine
Korogwe District Hospital	Tanga	Korogwe	CDC	4	1	Routine
Mnazi Mmoja Hospital	Zanzibar	Mjini	World bank	4	1	Routine

ANNEX D: PROPOSED DISTRICTS FOR PHASED INTRODUCTION OF GENEXPERT

REGION	FACILITY	ALL TB FORMS
Arusha	Monduli	454
Arusha	Karatu	421
Dodoma	Kondoa DC	308
Geita	Chato	492
Handeni	Handeni	309
Ilala I	Buguruni	559
Iringa	Mufindi	537
Iringa	Kilolo	282
Kagera	Karagwe	471
Kagera	Muleba	368
Kagera	Ngara	174
Kigoma	Kasulu	307
Kilimanjaro	Rombo	182
Kilimanjaro	Same	180
Lindi	Newala	356
Lindi	Nachingwea	257
Lindi	Kilwa	210
Manyara	Mbulu	816
Mara	Tarime -Rorya	1,342
Mara	Bunda	513
Mbeya	Mbozi	554
Mbeya	Chunya	543
Mbeya	Rungwe	538
Morogoro	Kilombero	728
Morogoro	Kilosa	721
Mwanza	Magu	485
Njombe	Makete	198
Njombe	Ludewa	194
Pemba	South & Central	59
Pwani	Mkuranga	388
Ruvuma	Mbinga	364
Ruvuma	Tunduru	345
Shinyanga/Simiyu?	Bariadi	804
Shinyanga/Simiyu?	Bukombe	486
Singida	Manyoni	300
Singida	Iramba	254
Tabora	Igunga	464
Tanga	Muheza	473
Tanga	Lushoto	392
Temeke	Mbagala Rangitatu	1,046
Temeke	Kigamboni	281
Zanzibar	Town & West	319

ANNEX E: PROVISIONAL METHODOLOGY TO ESTIMATE THE NEED FOR XPERT TESTS AMONG PEOPLE LIVING WITH HIV ATTENDING HIV SERVICES IN THE CONTEXT OF NATIONAL STRATEGIC PLANS FOR TB AND FOR HIV (HTM/GTB AND HTM/HIV)

SCOPE OF THE TOOL

The objective of this briefing note is to provide countries with a provisional methodology to develop a budget for their National Strategic Plans for TB and/or HIV, as well as a broad but conservative estimate of the projected annual costs of Xpert MTB/RIF cartridges. The tests are to be purchased and used for early detection of TB (screening + diagnosis) among people living with HIV (PLHIV) who already know their status and are in HIV care *(i.e.* pre-ART or on ART). This note is intended for use with HIV programme budgeting and forecasting tools as well as with the WHO TB Planning and Budgeting tool: http://www.who.int/tb/dots/planning_budgeting_tool/download/en/.

BACKGROUND

WHO recommends that all people living with HIV/AIDS be screened regularly for TB, based on a clinical algorithm. PLHIV with presumptive TB are defined as those with any one of the following symptoms: current cough, fever, weight loss or night sweats. PLHIV with presumptive TB should be evaluated for TB and other diseases. WHO recommends that Xpert MTB/RIF be used as the initial diagnostic test for TB in adults and children living with HIV; however, it is recognized that many clinical settings may still use microscopy as the initial diagnostic test for TB in PLHIV and that the coverage by Xpert MTB/RIF will gradually increase over time.

ESTIMATES AND ASSUMPTIONS USED IN THE TOOL

The calculation of the number of Xpert MTB/RIF cartridges needed is based on estimates and assumptions as detailed below. Some variables are given as default for every country, but most will need to be entered at country level, as they reflect the local situation with large variability from country to country and, over time, in a given country. Country-specific data should be derived from national epidemiological reports. Consideration also needs to be given for the shelf life of the Xpert MTB/RIF test, which is currently 12 months.

A. **Annual projected number of HIV positive (adults and children) in care at a clinic**, (pre-ART and ART) based on a baseline figure (2012). **This is a country entered variable.** The figure for 2012 is provided by the National HIV Programme and efforts should be made to avoid double counting. The projected figures for the years 2013 – 2017 are also calculated by the National HIV Programme.

B. **Percent of HIV positive (adults and children) in HIV care who are screened**. **This is a country entered variable.** The proportion of PLHIV who undergo screening for TB is 100%, ideally, but the real coverage must be measured by the National HIV Programme as part of its monitoring and evaluation plan, and the real figure for the 2012 baseline, with projected coverage to take into account envisaged scale-up, must be used.

C. **Average number of times screening is performed each year for a single person living with HIV**. **This is a country entered variable.** Ideally, PLHIV should be screened at every encounter with the HIV services. PLHIV being seen every three months at HIV services should be screened 4 times per year. Here, the estimated number of visits at HIV services per person living with HIV/ADIS should be entered (for example: 2, 3, etc.)

D. **15% of HIV positive (adults and children) in care at a clinic screened and found to have presumptive TB at each screening**. **This is a default estimate** based on an expert group decision

for the Spectrum model and should not be modified by countries. This assumption represents the best estimate of the average proportion of screened PLHIV who have one or more symptoms suggestive of TB, and are therefore classified as having presumptive TB.

E. **Percent coverage of Xpert testing for the 15% HIV positives presumed to have TB at each screening**. **This is a country entered variable.** Depending on the availability of Xpert, the actual coverage figure for 2013 should be known by the TB and HIV programmes, General Care Services and the country's public health laboratory network. The projections for expanding coverage (if any) for the years 2014-2017 should be jointly estimated by the TB and HIV programmes, in collaboration with General Health Services and the public health laboratory network.

F. The final **estimated number of HIV positive patients tested with Xpert** is the calculated product of the above estimates and assumptions (f = a x b x c x d x e) and represents the broad but conservative number of Xpert MTB/RIF cartridges to be purchased for any given year. **The default formula appears in the costing tool.**

ANNEX F: STANDARDIZED CHECKLISTS

Pre-installation Checklist

Installation Checklist

Comprehensive Checklist

Supervision Checklist

Quarterly Checklist

Pre-handover Checklist

	Document Title: GeneXpert Pre-Installation Assessment	
	Document No.	Effective Date:
	Version. 0	Revision No. 1
	Section:	Copy No.

PART I: LABORATORY PROFILE							
Date of Assessment/Audit							
Name(s) and Affiliation(s) of Assessor(s)							
Laboratory contact name (s)			Phone/email				
Laboratory Name			Region				
District			Town				
Postal Address							
Laboratory Telephone		Fax		Email			
Head of Laboratory			Telephone (Head of Lab)		Personal?		
					Work?		
Regional or District coordinator			Contact details				
Funding partners involved with Lab			Main aims				
Main access to site (road, air…)			Nearest MSD supply warehouse				
Is laboratory taking part in SLMTA or other accreditation?			No of stars/level				
Laboratory Level (check those that apply)			Laboratory Affiliation (check those that apply)				
	National	Regional / Provincial		Public		Academic	
	Zonal	District		Private		NGO/Religious Institution	

	Document Title: GeneXpert Pre-Installation Assessment	
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Laboratory Staffing Summary				
Profession	Number of Full Time Equivalents	Adequate for facility operations?		
Laboratory scientist		Yes	No	Insufficient Data
Laboratory Technicians		Yes	No	Insufficient Data
Laboratory Technologist		Yes	No	Insufficient Data
Cleaner/ lab attendant Data Clerk		Yes	No	Insufficient Data Has the cleaner(s) been trained in safe waste handling? Yes No
Driver for sample transportation		Yes	No	Insufficient Data Is the driver(s) dedicated for only laboratory? Yes No Has the driver(s) been trained in biosafety? Yes No
Does the lab have dedicated staff in the following areas		Yes	No	Insufficient Data
Quality manager		Yes	No	Insufficient Data
Safety officer		Yes	No	Insufficient Data
Stock manager / store person		Yes	No	Insufficient Data
Other:		Yes	No	Insufficient Data
		Yes	No	Insufficient Data
Briefly describe the laboratory network in the region/district, how many TB diagnostic centers and treatment centers? Are there other labs with GX in the region?				

Part 2: Laboratory Physical Infrastructure	
Checklist Question	YES/NO
1. Does the laboratory have a lockable door and secure windows?	
Comment	
2. Does the Laboratory have enough space including bench space to install GeneXpert and its related ancillary equipment	

Comment	
3. Does the laboratory have stable power supply? – count the plug sockets available	
Comment	
4. Does the laboratory have backup generators or solar power? Are they started manually? Is there sufficient fuel? How long does it take to start the alternate power supply	
Comment	
4. Does the laboratory have enough appropriate chairs and benches for testing and at reception (liquid impermeable and chemical resistant?	
Comment	
5. Does the laboratory have sufficient storage space for all consumables in temperature controlled environment (2-30°C)?	
Comment	
6. Does the laboratory have adequate waste disposal for infections materials? Describe below	
Comment	

Part 3: Laboratory Environment	
1. Does the laboratory have a means of controlling temperature between 2-30°C e.g. air circulation, thermometers, refrigerators? What is the normal temperature?	
Comment	
2. Review laboratory workflow and determined appropriate location for GeneXpert, computers, printers and scanners	
Comment	
3. Does the Laboratory have enough wash basins with soap dispensers	

Comment	
4. Does the laboratory have other large, electronic and or computer based equipment?	
Comment	
5. Does the laboratory have enough regular supply of PPE (gloves, masks, goggles)	
Comment	
6. Does the laboratory have refrigerator for storing sputum samples	
Comment	

Part 4: Laboratory Human Resources	
1. Does the Laboratory need additional personnel to implement GeneXpert? Specify type and number	
Comment	
2. Do laboratory staff have adequate computer skills for GX and reporting needs	
Comment	
3. Is someone responsible for computer maintenance, virus scanner updates etc	
Comment	
4. Do the Laboratory staff need additional training? Specify type of training	
Comment	

Part 5: Supply chain	
5. Describe the current supply chain	
Comment	
6. Is the supply chain adequate?	
Comment	
7. How long is the average lead time from ordering to receiving stock	
Comment	

Part 6: Clinic/hospital readiness	
1. Has the National TB algorithm for Xpert MTB/RIF testing been introduced to clinicians	
Comment	
2. Is there an established sample transportation system from other sites to the laboratory (Describe the current system, its adequacy, efficiency and coverage)	
Comment	
3. Is a sample referral system in place for additional testing for TB samples at referral laboratories (transportation of samples and results, schedules, triple packaging materials)	
Comment	
4. Is there any additional training needs for Clinical staff?	
Comment	

5. Are TB patients initiated at this site and how long does it take to initiate TB treatment?	
Comment	
6. Have any MDR cases previously been identified at this site and how are they handled?	
Comment	

Part 7: Current TB Diagnostics methods	
1. Does the laboratory current have another TB diagnostic method in use? If yes please specify methods	
Comment	
2. If the answer is YES above, indicate average monthly tests done including positivity rates	
Comment	
3. If the answer is YES to 19, are there staff dedicated to that method only? Are these the same staff who will use the GeneXpert?	
Comment	
4. How are results currently returned to clinician?	
Comment	
5. Which laboratory statistics are reported to the TB program and how?	
Comment	

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Part 8: Management Involvement (This maybe clinic, hospital, NTB, Ministry of Health etc.)	
1. Is Management aware of the implementation of GeneXpert at this laboratory?	
Comment	
2. During the assessment, did the assessors meet with management to discuss the implementation of the GeneXpert and the expectations from Laboratory and Management (This could take place before or after the assessments)?	
Comment	

Overall rating (Tick appropriate box and give reasons in the general comments section)							
Not ready		**Ready no work**		**Ready but minor changes**		**Ready Major changes**	
General comments							

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool
INSTALLATION CHECKLIST

TB LABORATORY GENEXPERT INSTALLATION CHECKLIST

This tool is intended to be used by staff/consultants undertaking laboratory monitoring and supervision visits on behalf of the National Tuberculosis Control Programme (NTP) to install GeneXpert equipment for Xpert MTB/RIF test implementation according to country specific instructions. The Site pre-assessment report should be reviewed prior to a site visit.

The Installation Checklist is used to ensure correct implementation of the Xpert MTB/RIF test. All sections must be filled with the assistance of appropriate supplementary documentation. Documents gathered must be copied to the GeneXpert focal person and the NTLP in a timely fashion.

Installation check list Tanzania			
Date of installation			
Facility name/ Laboratory name		Contact details facility: Name, phone, email	
GX lab responsible		Contact details Laboratory: Name, phone, email	
Partner organization (if required)		Contact details Partner Organization Name, phone, email	

GX serial number		Computer details (type, windows)	
GX Software details		Printer details	
Has pre-site check been completed and filed with CTRL?	YES NO		

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool
INSTALLATION CHECKLIST

Site plan			
Support by partners ending on date		Comments:	
Support to include:	Cartridges (number)	Calibration	Technical support:
	Statistical support	Computer support	Printer/Ink/Paper
	Extended warranty	Other:	
Training of lab staff using agreed standardized Tanzanian training	YES NO	Certificate provided	YES NO
Training of Clinical staff completed	YES NO	Certificate provided	YES NO
other training conducted	YES NO	Details:	
Do Laboratory staff have computing skills	YES NO	Level of proficiency (1 no skills, 5 programming skills)	1 2 3 4 5
Does laboratory have regular access to internet?	YES NO	Who pays for internet access	
If no internet how will monthly stats be communicated to program?			
Comments:			

Documentation					
SOP's and protocols in place				Where are documents?	Person responsible to complete
National GX testing algorithm	YES	NO	NA		
Sample transport	YES	NO	NA		
Sputum collection	YES	NO	NA		
GX request form	YES	NO	NA		
Waste disposal	YES	NO	NA		

Rejection criteria and recording	YES	NO	NA		
Laboratory processing protocols	YES	NO	NA		
Results reporting	YES	NO	NA		
Patient tracing	YES	NO	NA		
Initiation on to therapy	YES	NO	NA		
Reporting of RIF resistance to NTP	YES	NO	NA		
Collection and transport of samples for culture	YES	NO	NA		
Room and fridge temperature monitoring monthly sheets	YES	NO	NA		
Error record monthly sheet	YES	NO	NA		
Back up of computer	YES	NO	NA		
Update of virus software	YES	NO	NA		
GX register book for laboratory	YES	NO	NA		
Monthly statistics	YES	NO	NA		
Stock ordering protocol	YES	NO	NA		
Calibration ordering protocol	YES	NO	NA		
Spill protocol and spill kit in place	YES	NO	NA		
Incidence record	YES	NO	NA		
Comments:					

GeneXpert set up Tanzania specific				
Place the instrument on an appropriate surface	YES	NO	NA	See document "place the instrument on an appropriate surface"
Connect all the cables and UPS	YES	NO	NA	See document "connect all the cables and UPS"
Turn on the instrument	YES	NO	NA	Switch is at back of unit
Turn on the computer	YES	NO	NA	
Set up the local date and time on computer	YES	NO	NA	See document "change time and date"
Start the software, check that the modules are "available"	YES	NO	NA	see document start program and module availability
Configure the GeneXpert software according to English US: System Configuration, Language	YES	NO	NA	see document 5: GX DX regional setting
Assign instrument letter	YES	NO	NA	machine 1 =A, machine 2 = B etc; refer too document "Assign instrument letter"
Change Gx name to site name Tanzania A,B,C,D	YES	NO	NA	See document "change GX name"
Import the MTB-RIF ADF (Assay Definition File)	YES	NO	NA	AS per document "how to import assay definition file" (also available on all MTB-RIF CD)
Set up yearly archive files in export folder	YES	NO	NA	See document set up yearly archive files in export folder
Create a user admin account for NTBP access	YES	NO	NA	See document "create a user admin account"
Create a user admin account at least one onsite "super user"	YES	NO	NA	See document "create a user admin account"

All other users to have a detail account and password	YES	NO	NA	See document "create a user admin account"
Define system type configuration	YES	NO	NA	See document "Define user type configuration"
Set up system configuration	YES	NO	NA	See document "set up configuration"
Run verification samples (1 per module)	YES	NO	NA	As per GLI instructions included with GX
Did all samples run as expected	YES	NO	NA	*refer to GLI instructions
Save and print verification files (where possible)	YES	NO	NA	print results if possible and attach to verification sheet. Archive and delete files, call file GLI "site name" "date", see document "how to archive and delete GX files"
Print installation qualification (IQ)	YES	NO	NA	See document IQ report
Register GX with Cepheid	YES	NO	NA	See document IQ report
Register site with CDC EQA	YES	NO	NA	Site details, contact and email
Print error code chapter for lab reference	YES	NO	NA	Manual, Trouble shooting
Save PDF GX manual on desktop	YES	NO	NA	See document "Desktop Icons"
Save quick stats on desktop	YES	NO	NA	See document "Desktop Icons"
Save yearly stats files on desktop	YES	NO	NA	See document "Desktop Icons"
Where are tools kept	YES	NO	NA	
where are GX and Microsoft CD's kept	YES	NO	NA	
Does site have rewritable CD's for back up?	YES	NO	NA	
If yes where are they stored				

Comments:

To be filed with CTRL					
Verification runs	YES	NO	NA		
IQ report	YES	NO	NA		
Contact details	YES	NO	NA		
Agreement of partner support document	YES	NO	NA		
Comments:					
Is the machine fully operational and set to country specific standards	YES	NO	NA		
Comments:					

Conclusions:

Recommendations:

Sign Partner representative		Sign installer	
Sign CTRL responsible			

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Comprehensive site visit assessment)

This tool is intended to be used by staff/consultants undertaking laboratory monitoring and supervision visits on behalf of the National Tuberculosis Control Programme (NTP) to assess Xpert MTB/RIF test implementation. On-site supervisory visits form a critical part of the quality assurance programme associated with Xpert MTB/RIF implementation, and will be conducted at pre-determined time intervals as agreed by the NTP. Comprehensive site visit assessment will be conducted as an initial assessment of site competency after installation, and annually thereafter.

Review the instructions for assessors (page 2) before completing this assessment.

Name of Assessor(s)	
Title & organization of Assessor	
Name of laboratory being assessed	
Location of laboratory being assessed (City/Town, District and	
Name and Contact details for person at laboratory	
Name of partner organization providing GX support	
What support does the partner organization	
Date of last assessment / visit	
Reason for last assessment / visit	
Date of this assessment visit	

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Comprehensive site visit assessment)

Section A: Laboratory & GeneXpert instrument information

General	
What kind of facility is this? ☐ Reference laboratory ☐ Regional or district laboratory ☐ Peripheral laboratory	Additional comments:
What tests are performed at this laboratory? ☐ TB tests ☐ Microbiology and / or serology ☐ Clinical chemistry ☐ Clinical hematology ☐ Cytology and / or histology ☐ Parsitology ☐ Other_____	Additional comments:
What TB tests are performed at this laboratory? ☐ GeneXpert Xpert MTB/RIF test ☐ Smear microcopy ☐ TB culture ☐ TB Drug susceptibility testing ☐ Line Probe Assay ☐ Other_____	Additional comments:

Staff and training	
How many staff are employed at this laboratory (including clerical staff and drivers)?	
How many staff are certified to perform the Xpert MTB/RIF test?	
Who conducted the Xpert MTB/RIF test training?	
How many days was the Xpert MTB/RIF training course?	
Has a follow-up Xpert MTB/RIF training course been conducted?	
How many staff are currently doing Xpert MTB/RIF testing?	

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Comprehensive site visit assessment)

Referral & sample collection systems	
Are there satellite sites (clinics or hospitals) referring samples for Xpert MTB/RIF testing?	
If yes, how many satellite sites refer to this facility for Xpert MTB/RIF testing?	
Is there a sample transportation mechanism in place to send samples to this laboratory from satellite sites? If so, describe.	
How many kilometers to nearest satellite site?	
How frequently are TB samples collected from the satellite sites per week?	
Does the laboratory have refrigerator for storing sputum samples?	
Are any sputum samples for TB testing collected at this laboratory?	
If yes, is sputum collection done at a designated safe sputum collection booth/spot? Who supervisors sputum collection?	
Are suspects instructed how to produce good quality sputum?	
Are the patient details of samples found to be resistant to rifampicin communicated to a focal person (e.g. District TB Coordinator) within the TB programme?	
Are all samples with rifampicin resistant results sent for confirmation?	
Is there a sample transportation mechanism in place to send samples to a culture and DST laboratory?	

Infrastructure	
Does the laboratory have internet access?	
If yes, is internet access available in the TB laboratory?	
If yes, rate the consistency of the internet connection (0 – 7: where 0 is very inconsistent and 7 is highly consistent)?	
Is the laboratory connected to a generator?	
If yes, is fuel available for the generator?	
How long does the generator take to generate electricity?	
Rate the consistency of the power supply to the laboratory (0 – 7: where 0 is very inconsistent and 7 is highly consistent)?	

GeneXpert instrument & Xpert MTB/RIF test	
Is the computer attached to GeneXpert instrument a desktop or laptop computer?	
Is the latest software installed on the computer?	
How many modules does the GeneXpert instrument at this laboratory have?	
What is serial number of the GeneXpert instrument?	
What is the installation date of the GeneXpert instrument?	
When was the last calibration performed?	
When is the next calibration due?	
Are any modules currently malfunctioning?	
Are any modules currently being replaced?	
Have any repairs and / or troubleshooting been done since the last visit?	
Is the GeneXpert instrument connected to an uninterrupted power supply (UPS / inverter)?	
Is the computer attached to the GeneXpert instrument connected to an UPS?	
Has the laboratory provided uninterrupted testing services, with no disruptions due to equipment failure or stock-outs in the last year (or since the last assessment)?	
If no, what was the duration of the interruption and how was the matter resolved?	
Does the laboratory repeat Xpert MTB/RIF tests where an invalid result or error was obtained? Explain.	

Section B: Laboratory assessment checklist

		Yes	Partial	No	NA	Comment
1.	**Documents and records**					
1	Does the laboratory have the GeneXpert operator's manual and Xpert MTB/RIF instructions for use (hard or soft-copy)?					
2	Does the laboratory have a copy of the current national diagnostic algorithm?					
3	Are the following GeneXpert standard operating procedures available and read by all operators? a. GeneXpert operation					
	b. GeneXpert maintenance					

		Yes	Partial	No	NA	Comment
	c. Waste management					
	d. External quality assurance procedures					
	e. GeneXpert troubleshooting					
4	Are Xpert results archived on a regular basis?					
5	Is database back-up conducted on a regular basis?					

2. Organization and personnel

		Yes	Partial	No	NA	Comment
1	Is appropriate documentation available in GeneXpert instrument operators' personnel files (training certificates, competency assessment, health monitoring etc.)?					
2	Are meeting minutes available that show that operators of the GeneXpert instrument attend general laboratory staff meetings regularly and that issues related to Xpert MTB/RIF testing is discussed?					

3. Client Management and customer service

		Yes	Partial	No	NA	Comment
1	Are records in place documenting training that the laboratory has provided to clients (clinicians or Health Care Workers) regarding the Xpert MTB/RIF testing algorithm, sample type and results interpretation?					
2	Are records in place documenting notification to clients regards delays or interruptions in Xpert MTB/RIF testing (due to equipment failure, stock outs, staff levels, etc.)?					

3	Is there a tool for regularly evaluating client satisfaction and is the feedback received effectively utilized to improve services?					
4	Are clients correctly requesting Xpert testing according to the agreed algorithm?					

4. Equipment						
		Yes	**Partial**	**No**	**NA**	**Comment**
1	Was the GeneXpert instrument verified on site prior to routine use as documented in the verification records?					
2	Was the GeneXpert instrument verified after servicing and repairs as documented in verification records?					
3	Is a root cause analysis conducted following equipment malfunction and are issues identified resolved by an adequate corrective action system?					
4	Is a system in place for ordering of calibration kits, servicing and instrument repairs?					
5	Are repair orders monitored to determine if the service has been completed?					
6	Are there back-up procedures for equipment failure (including SOPs for handling specimens during these times, identification of a back-up laboratory for testing, and referral procedures)?					
7	Are records in place documenting that maintenance/servicing needs are routinely communicated to upper management?					

5. Internal & external audits						
		Yes	**Partial**	**No**	**NA**	**Comment**
1	Are records in place documenting that internal audits/assessments are regularly conducted?					
2	Are records in place documenting that recommendations for corrective/preventive actions have been developed and that there are clear timelines and ownership for follow-up?					
3	Are records in place documenting that external laboratory audits have been conducted?					
4	Are records in place documenting that reports from external audits have been communicated to laboratory management/GeneXpert instrument operators?					
6. Purchasing & inventory						
1	Are all orders tracked until delivery and inspected, receipted, and labeled with date of receipt when the orders are checked in?					
2	Is an inventory control system in place that includes (acceptance and rejection of consumables, recording of lot number, date of receipt, received by and date placed into service; specifications for storage of consumables)?					
3	Are inventory records complete and accurate, with minimum and maximum stock levels denoted?					
4	Is the consumption rate monitored?					
5	Are stock counts routinely performed?					
6	Is First-Expiration-First-Out (FEFO) practiced?					

7	Are expired products labeled and disposed correctly?					
8	Does the laboratory have sufficient clean, dry and temperature-controlled storage space for Xpert MTB/RIF test cartridges (2-30°C)?					
9	Does the laboratory have enough regular supply of PPE (gloves, laboratory coats)?					
7. Process control						
		Yes	**Partial**	**No**	**NA**	**Comment**
1	If specimens are not tested immediately, are they stored appropriately prior to testing?					
2	Are specimens and request forms of specimens submitted for Xpert testing adequately labeled/completed?					
3	Do the laboratory staff understand the algorithm? (question laboratory staff on key features of the algorithm to ascertain if they understand it)					
4	Did laboratory staff receive training in the diagnostic algorithm?					
5	If the laboratory processes more than one batch of samples at a time, is the maximum incubation time before loading into the cartridge less than 8 hours?					
6	Are specimens received from satellite sites packaged appropriately according to local and or international regulations?					
7	Are specimens transported to referral laboratories within acceptable timeframes (e.g. referral to NTRL for culture/DST)?					
8	Are referred specimens tracked properly using a logbook or tracking form?					

9	Does the laboratory participate in External Quality Assessment scheme (EQA) testing?					
10	Are the results of the two most recent EQA panels available in the laboratory?					
11	Were EQA results reviewed and feedback given to laboratory staff, and corrective actions taken for failed EQA?					
12	Does the laboratory staff check sputum samples for quality when received at the laboratory?					
13	Does the laboratory have an SOP and follow it on rejection of samples?					

8. Information management						
		Yes	**Partial**	**No**	**NA**	**Comment**
1	Are testing personnel identified on the requisition and/or report?					
2	Are test results recorded in a logbook or electronic record in a timely manner?					
3	When more than one instrument is in use for the same test, are test results traceable to the equipment used for testing?					
4	Are archived results (paper or data-storage media) properly labeled and stored in a secure location accessible only to authorized personnel?					
5	Is the record log filled completely and accurately, including a record of results received from other laboratories (e.g. NTRL)?					
6	Does the laboratory have a record of samples referred to NTRL for testing?					
9. Corrective action						

1	Are Xpert errors recorded in a log?					
2	Are records in place documenting that appropriate action taken after any errors were reported, e.g. Record made, supervisor/mentor notified, repeat testing if possible?					
10. Document management						
1	Are quality indicators (TAT, rejected specimens, stock outs, number of tests performed etc.) recorded?					
2	Are records in place documenting that quality indicators are reviewed and used to improve laboratory performance?					

Section C: On-site procedural verification

1) Examine the GeneXpert instrument and Xpert MTB/RIF test workstation in the TB laboratory.

		Yes	Partial	No	NA	Comment
11. Facility and safety						
1	Is the size of the laboratory adequate and the layout of the laboratory, as a whole, organized so that the workstation is positioned for optimal workflow?					
2	Is each individual workstation maintained free of clutter and set up for efficient operation?					
3	Does the equipment placement/layout facilitate optimum workflow?					
4	Are all needed supplies present and easily accessible?					
5	Are the chairs/stools at the workstations appropriate for bench height and the testing operations being performed?					

		Yes	Partial	No	NA	Comment
6	Is 10% bleach solution made freshly on a daily basis?					
7	Is the GeneXpert instrument correctly placed and installed according to manufacturer's instructions?					
8	Is the GeneXpert instrument(s) uniquely labeled and marked?					
9	Is the GeneXpert instrument(s) asset number(s) recorded in an equipment logbook?					
10	Has the maintenance of the GeneXpert instrument being performed and documented at least on a daily/weekly/ monthly basis as appropriate?					
11	Is the laboratory climate-controlled for optimum GeneXpert instrument function?					
12	Is the maximum and minimum temperature in the laboratory recorded?					
13	Is the laboratory properly secured from unauthorized access with appropriate signage?					
14	Is the laboratory fridge(s) free of staff food items?					
15	Are patient samples stored in a separate fridge from reagents and blood products in the laboratory refrigerators and freezers?					
16	Is sufficient waste disposal available and is waste separated into infectious and non-infectious waste, with infectious waste autoclaved, incinerated, or buried?					
17	Is an appropriate fire extinguisher available, properly placed, in working condition, and routinely inspected?					
18	Is a spill kit available and complete?					

		Yes	Partial	No	NA	Comment
18	Is an operational fire warning system in place in laboratory with periodic fire drills?					
19	Is personal protective equipment (PPE) easily accessible at the workstation and utilized appropriately and consistently?					
20	Are laboratory coats or gowns worn in the laboratory, but are not worn outside the work area?					
21	Are gloves and laboratory coats worn at appropriate times?					
22	Are drivers/couriers and cleaners working with the laboratory trained in biosafety practices relevant to their job tasks?					

2) Observe operators performing the Xpert MTB/RIF test (Note- this in an end-to-end evaluation i.e. from specimen processing to result reporting).

		Yes	Partial	No	NA	Comment
23	Did the operator organize the work area for the day's work?					
24	Did the operator add the correct volume of SR (sample reagent) to the sputum?					
25	Did the operator shake the sample, and mix twice before the end of incubation time?					
26	Was the incubation time 15 minutes (was a timer used)?					
27	Was the input volume transferred to the cartridge correctly?					
28	Did the operator start each new test in the GeneXpert instrument without any problem?					
29	Did the operator complete testing and dispose of cartridges appropriately?					

30	Did the operator seal the Xpert MTB/Rif reagents in a plastic bag before discarding?					
31	Did the operator dispose of all infectious materials (sputum cups, pipettes) properly (as per local guidelines for hazardous materials)?					
32	Did the operator clean the workbench with fresh 10% bleach before and after performing the Xpert MTB/Rif assay?					
33	Are operators able to easily retrieve primary test data on the instrument (e.g. for checking individual patient results, error codes etc.)					
34	Do all staff have their own passwords and are they used?					
35	Was the correct procedure followed for reporting of results?					

3) Check selected Xpert MTB/RIF test reagents to determine if all reagents in use (and in-stock) are currently within the manufacturer-assigned expiration dates.

		Yes	Partial	No	NA	Comment
36	Are all reagents in use (and in stock) currently within the manufacturer-assigned expiration dates?					
37	Are components of the kits mixed (i.e. SR buffer stored separately from cartridges)?					

4) Check 20 randomly selected Xpert MTB/RIF test request forms from the previous (one) month. Track the accuracy and completeness of data entry into each of the forms of documentation, namely request form, laboratory register and laboratory report form.

		Yes	Partial	No	NA	Comment
38	Were the patient and sample details correctly transcribed from the sample request form to the laboratory register?					
39	Were the results correctly transcribed from the Xpert MTB/RIF test report form to the laboratory report?					
40	Were the patient and sample details on the laboratory report form the same as the patient and sample details on the sample request form?					
41	Is the WHO reporting terminology used on the laboratory report?					

5) Check 20 randomly selected Xpert MTB/RIF test results from the previous (one) month. Record the average laboratory turnaround time (TAT) as determined by the difference between the sample receipt date & time and the date & time the Xpert MTB/RIF test was reported. Record the result below:

TAT
What is the average TAT for Xpert MTB/RIF test at this laboratory?
☐ < 4 hours
☐ 4 – 8 hours
☐ 8 – 12 hours
☐ >12 hours

Section D: Xpert MTB/RIF test data analysis summary

PERIOD (mmYYYY) to (mmYYYY)

GENEXPERT MTB/RIF TEST DATA **(Last three (3) months combined data for all instruments at the facility visited)**	Total
# Xpert tests MTB not detected	
# Xpert tests MTB detected RIF not detected	
# Xpert tests MTB detected RIF resistance detected (check that these cases are reported to RTLC)	
# Xpert tests MTB detected RIF indeterminate (check graphs for resistance patterns)	
# error results (more than 5% over 3 or more months report to focal point)	
# invalid results (more than 2% over 3 or more months report to focal point)	
# no result (more than 2% over 3 or more months report to focal point)	

Section E: Problem identification; Complete if machine is not fully functional

ON SITE OBSERVATIONS	OK	PROBLEMS IDENTIFIED
Save a copy of the IQ report	☐	
Save a copy of the system log report (all)	☐	
Save a copy of last 3 months .gxx files	☐	
	If YES	**Document problems identified**
Is the machine, computer, UPS, cable visually damaged?	☐	
Do you have to open GeneXpert software manually?	☐	
Is each individual GX workstation cluttered and dirty?	☐	
Were there any critical errors (e.g. 1004, 1005, 2014) since the last assessment / visit?	☐	
Has regular maintenance been performed & recorded?		
	Yes	
Are fan filters dirty?	☐	
Are cartridge bays dirty?	☐	
How many tests have been performed since the last plunger maintenance?		
How many cartridges are in stock?		
What are the expiry dates of the remaining stock?		(dd/mm/yyyy)
Will stock run out or expire before next consignment?	☐	

Section F: Non-conformances & corrective actions

Non-conformity	Recommended corrective action	Follow-up required

Conclusions:

Recommendations:

Signature of assessor: _____

Date: _____

Signature of recipient of report: _____

Designation (e.g. Site Manager, Clinician): _____

Date: _____

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool
SUPERVISION CHECKLIST

TB LABORATORY SUPERVISION CHECKLIST

This tool is intended to be used by staff/consultants undertaking laboratory monitoring and supervision visits on behalf of the National Tuberculosis Control Programme (NTP) to assess Xpert MTB/RIF test implementation. On-site supervisory visits form a critical part of the quality assurance programme associated with Xpert MTB/RIF implementation, and will be conducted at pre-determined time intervals as agreed by the NTP. Ad hoc supervisory visits may also be required, for example when following up poor performance in external quality assurance panel testing or poor laboratory indicators. The assessment report from the most recent visit should be reviewed prior to a site visit.

The Supervision Checklist is used to monitor on-going implementation of the Xpert MTB/RIF test. The checklist must be used for supervision site assessments, the follow-up of non-conformances from previous site assessments, and for troubleshooting when previous the quality indicators from the site indicate high failure rates or when the site reports technical problems that require an intervention.

Not all sections of this checklist is compulsory:

- Section A- Compulsory for all visits
- Section B- Compulsory for troubleshooting visits only
- Section C: Compulsory for current and follow-up of non-conformances only

SECTION A: COMPULSORY FOR ALL ASSESSMENTS AND SITE VISITS

Name of Assessor(s)	
Title & organization of Assessor	
Name of laboratory being assessed	
Location of laboratory being assessed (City/Town, District and Country)	
Name and Contact details for person at laboratory	
Name of partner organization providing GX support	
What support does the partner organization supply?	
Date of last assessment / visit	
Reason for last assessment / visit	
Date of this assessment visit	

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool
SUPERVISION CHECKLIST

GENEXPERT INSTRUMENT DETAILS	
What is serial number of the GeneXpert instrument:	
When was the last calibration performed?	(ddmmyyyy)
When is the next calibration due?	(ddmmyyyy)
If calibration is due in the next three months, have preparations made for the calibration?	
Is Cepheid currently replacing any faulty modules?	
Have any modules been replaced since the last visit?	
Is the GX in a temperature-controlled area? What are average max and min temps?	°C to °C

GENEXPERT ITEMS	**OK**	**PROBLEMS IDENTIFIED**
The laboratory provided uninterrupted testing services, with no disruptions due to equipment failure in the last three months (or since the last assessment). If no how many days was the lab non operational?	☐	
Inventory records are complete and accurate, with minimum and maximum stock levels denoted	☐	
The laboratory provided uninterrupted testing services, with no disruptions due to stock-outs in the three months (or since last assessment). If no how many days was the lab non operational?	☐	
Feedback from the most recent round of EQA has been received and corrective action performed (if needed)	☐	
Quality indicators (number of rejected specimens, number of tests performed, rifampicin resistance rate, error rate etc.) recorded	☐	
Xpert errors are recorded in a log (if trouble shooting visit attach a copy or use to complete error code section below)	☐	
	yes	
Lab register complete and up to date	☐	
All current GeneXpert operators trained certified users	☐	

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool
SUPERVISION CHECKLIST

ON SITE OBSERVATIONS	OK	PROBLEMS IDENTIFIED
Save a copy of the IQ report	☐	
Save a copy of the system log report (all)	☐	
Save a copy of last 3 months .gxx files	☐	
	If YES	**Document problems identified**
Is the machine, computer, UPS, cable visually damaged?	☐	
Do you have to open GeneXpert software manually?	☐	
Is each individual GX workstation cluttered and dirty?	☐	
Were there any critical errors (e.g. 1004, 1005, 2014) since the last assessment / visit?	☐	
Has regular maintenance been performed & recorded:		
	yes	
Are Fan filters dirty?	☐	
Are Cartridge bays dirty?	☐	
How many tests have been performed since the last plunger maintenance?		
How many cartridges are in stock?		
What are the expiry dates of the remaining stock?		(dd/mm/yyyy)
Will stock run out or expire before next consignment?	☐	

PERIOD_____(mmYYYY) to _____(mmYYYY)

GENEXPERT MTB/RIF TEST DATA **(Last three (3) months combined data for all instruments at the facility visited)**	Total
# Xpert tests MTB not detected	
# Xpert tests MTB detected RIF not detected	
# Xpert tests MTB detected RIF resistance detected (check that these	
# Xpert tests MTB detected RIF indeterminate (check graphs for resistance	
# error results (more than 5% over 3 or more months report to focal point)	
# invalid results (more than 2% over 3 or more months report to focal point)	
# no result (more than 2% over 3 or more months report to focal point)	

SECTION B: COMPULSORY FOR TROUBLESHOOTING ASSESSMENTS

TROUBLESHOOTING	
Who instigated troubleshooting visit?	
Detail any previous problems that may be relevant?	
Details of current problem	
Has Cepheid been contacted? If yes what is the Code and who is responsible?	
Briefly describe trouble shooting already attempted and outcomes (attach communications if applicable)	

TROUBLESHOOTING	
Additional comments and observations:	
Conclusion and corrective actions taken on day of visit:	
Recommendations to be followed up and by whom?	
Has problem been resolved?	YES NO NA Comment:

Xpert MTB/RIF test

Laboratory monitoring & evaluation tool
SUPERVISION CHECKLIST

TROUBLESHOOTING	
Is further follow up required? If so, by whom?	YES NO NA Comment:

Check the results files since the last assessment visit and record up to 20 of the most recent error codes and which module they have occurred on:

ERROR CODES	MODULE	STAFF NAME	DATE

NON-CONFORMANCE	RECOMMENDED CORRECTIVE ACTION	FOLLOW-UP REQUIRED / HAS THE NON-CONFORMANCE BEEN ADDRESSED?

SECTION C: COMPULSORY FOR FOLLOW-UP OF NON-CONFORMANCES

Conclusions:

_____

_____

_____

_____

Recommendations:

_____

_____

_____

_____

_____

Signature of assessor:
_____

Date: _____

Signature of recipient of report:
_____

Designation (e.g. Site Manager, Clinician): _____

Date: _____

AFB & Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Quarterly checklist)

QUARTERLY TB LABORATORY CHECKLIST

Laboratory:		Technician: 1	
Supervisor:		Training- how and when?	
Date:		Technician 2:	
		Training- how and when?	

GENERAL ITEMS	OK	PROBLEMS IDENTIFIED
Room & furniture arrangement	☐	
Power supply	☐	
Water supply and drainage	☐	
Safe waste disposal	☐	
Personnel versus workload	☐	
General order and tidiness	☐	
Identification on forms, pots and slides	☐	

AFB ITEMS	OK	PROBLEMS IDENTIFIED
Microscopes & 100× objective	☐	
Small tools available	☐	
Balance, glassware, pure water (if stains prepared)	☐	
Supplies: stock, labeling, age	☐	
Smear quality	☐	
Staining & counterstain quality	☐	
Quality control slides used for routine? / for new stains?	☐	
Slide collection for EQA okay	☐	
Feedback from EQA received	☐	
Lab register complete, up to date (variation of positive results?)	☐	

AFB & Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Quarterly checklist)

QUARTERLY TB LABORATORY CHECKLIST (CONTINUED)

PERIOD (mmYYYY) to (mmYYYY)

AFB: take from report of last quarter or count from lab register

Suspect examinations:

Diagnostic smears:

no. examined _____ no. positive or scanty_____ % positive_____

Diagnosis patients:

no. examined _____ no. only 1 result_____ % 1 result_____

Smear-positive cases detected:

1+ and scanty diagnostic smears number_____ %

Positive/scanty cases not on treatment number_____ %

Follow-up sputa:

Total number _____

Positive or scanty_____ number_____ %

Conclusions:

Recommendations:

AFB & Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Quarterly checklist)

QUARTERLY TB LABORATORY CHECKLIST (CONTINUED)

What was the date of the last supervision visit? _____

Was corrective actions based on the results of the previous visit? _____

GX Technician 1: _____

Training- how and when certified? _____

GX Technician 2: _____

Training- how and when certified? _____

GENEXPERT INSTRUMENT DETAILS	
What is serial number of the GeneXpert	
When was the last calibration performed?	(ddmmyyyy)
When is the next calibration due?	(ddmmyyyy)
If calibration is due in the next three months, have preparations made for the calibration?	
Is Cepheid currently replacing any faulty	
Have any modules been replaced since the last visit?	
Is the GX in a temperature-controlled area? What are average max and min temps?	˚C to ˚C

GENEXPERT ITEMS	**OK**	**PROBLEMS IDENTIFIED**
The laboratory provided uninterrupted testing services, with no disruptions due to equipment failure in the last three months (or since the last assessment). If no how many days was the lab non operational?	☐	
Inventory records are complete and accurate, with minimum and maximum stock levels denoted	☐	
The laboratory provided uninterrupted testing services, with no disruptions due to stock-outs in the three months (or since last assessment). If no how many days was the lab non operational?	☐	
Feedback from the most recent round of EQA has been received and corrective action performed (if needed)	☐	
Quality indicators (number of rejected specimens, number of tests performed, rifampicin resistance rate, error rate etc.) recorded	☐	

AFB & Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Quarterly checklist)

Xpert errors are recorded in a log (if trouble shooting visit attach a copy or use to complete error code section below)	☐	
Lab register complete and up to date	☐	
All current GeneXpert operators trained certified users	☐	

ON SITE OBSERVATIONS	OK	PROBLEMS IDENTIFIED
Save a copy of the IQ report	☐	
Save a copy of the system log report (all)	☐	
Save a copy of last 3 months .gxx files	☐	
	If YES	**Document problems identified**
Is the machine, computer, UPS, cable visually damaged?	☐	
Do you have to open GeneXpert software manually?	☐	
Is each individual GX workstation cluttered and dirty?	☐	
Were there any critical errors (e.g. 1004, 1005, 2014) since the last assessment / visit?	☐	
Has regular maintenance been performed & recorded?	**Yes**	
Are fan filters dirty?	☐	
Are cartridge bays dirty?	☐	
How many tests have been performed since the last plunger maintenance?		
How many cartridges are in stock?		
What are the expiry dates of the remaining stock?		(dd/mm/yyyy)
Will stock run out or expire before next consignment?	☐	

AFB & Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Quarterly checklist)

NON-CONFORMANCE	RECOMMENDED CORRECTIVE ACTION	FOLLOW-UP REQUIRED / HAS THE NON-CONFORMANCE BEEN ADDRESSED?

PERIOD (mmYYYY) to (mmYYYY)

GENEXPERT MTB/RIF TEST DATA **(Last three (3) months combined data for all instruments at the facility visited)**	Total
# Xpert tests MTB not detected	
# Xpert tests MTB detected RIF not detected	
# Xpert tests MTB detected RIF resistance detected (check that these cases are reported to RTLC)	
# Xpert tests MTB detected RIF indeterminate (check graphs for resistance patterns)	
# error results (more than 5% over 3 or more months report to focal point)	
# invalid results (more than 2% over 3 or more months report to focal point)	
# no result (more than 2% over 3 or more months report to focal point)	

AFB & Xpert MTB/RIF test

Laboratory monitoring & evaluation tool (Quarterly checklist)

Signature of the Supervisor _____

Signature of the lab staff _____

Conclusions:

_____

_____

_____

_____

Recommendations:

_____

_____

_____

_____

Partner handover of GeneXpert machines to NTLP check list Tanzania			
Part 1: Contact details			
Date of installation			
Facility name/ Laboratory name		Contact details facility: Name, phone, email	
GX lab responsible		Contact details Laboratory: Name, phone, email	
Partner organisation		Contact details partner Organisation Name, phone, email	
Part 2: Equipment details			
GX serial number(s)		Number of modules	
Laptop/Desktop		Brand of computer	
Windows version		Antivirus version	
GX Software version		Printer details	
UPS details		Battery/stabiliser details	
Comments:			

Part 3: Site plan			
Support by partners ending on date		Comments:	
Hospital or NTLP to take over (please mark as appropriate)	Cartridge supply (Average no. per month)	Calibration	Technical support:
	Statistical support	Computer support	Printer/Ink/Paper
	Other:		
At handover date estimate remaining cartridges and expiry		Any other outstanding issues?	
Have all GX passed calibration in the last month?	YES NO		
Attach report; If no explain, and detail what follow up action is being undertaken			
Has error rate over last 3 months been below 5%	YES NO	Attach report; If no explain	
Has total unsuccessful test rate been below 10%?	YES NO	Attach report; If no explain	
Has Cepheid examined last 3 month system log and .gxx files?	YES NO	Attach report; If no explain	
To the best of your knowledge and using all available tools is the GX machine in full working order as of hand over date?	YES NO		
Is this machine still under original warranty	YES NO	Date of warranty end	
Has any extended warranty been purchased	YES NO	Date of warranty end	

Was this site previously following NTLP testing algorithm?	YES	NO	If no which algorithm was used
Was this site previously supplying monthly indicators to the NTLP?	YES	NO	If no, what was agreement and can staff produce monthly statistics?
Are there any additional training needs to ensure a smooth handover?	YES	NO	Detail:
Have all staff performing testing completed and passed a certified training program for Xpert MTB/RIF testing	YES	NO	If no detail:
Have clinical staff completed sensitisation about MTB/RIF testing	YES	NO	If no detail:
Are standard NTLP procedures, SOPs, registers and other documents in pace	YES	NO	If no detail:
Additional comments:			

Part 4: Other documents to be Supplied at handover		
Certification document	YES NO NA	Supplied with machine
Verification documents	YES NO NA	*to be decided how many and what is required
System log and last 3 months .gxx files	YES NO NA	As per document, how to generate a system log report and How to archive and delete runs
New IQ reports	YES NO NA	As per document how to generate an IQ report
Copy of last 6 months maintenance records	YES NO NA	Copied from laboratory records, if any missing please explain below
Copy of staff training certificates for Xpert MTB/RIF	YES NO NA	Copied from laboratory records, if any missing please explain below
Evidence of clinical sensitisation	YES NO NA	Certificates, training schedule, meeting minutes
Provide a letter explaining handover to be sent to Cepheid as evidence of change of owner	YES NO NA	As per document….
Comments:		

Part 5: Completion of GeneXpert Handover	
Partner signs to declare handover of GX instrument in full working condition and has no further role apart from that documented above	
NTP CTRL signs to confirm receipt of GX machine in full working condition and takes responsibility for full site support, including reagent supply, calibration and technical support	
Comments	
Disputes:	
Further actions:	
Final handover date:	

ANNEX G: MINIMUM TESTING SITE INFRASTRUCTURE FOR GENEXPERT INSTRUMENT PLACEMENT

The minimum requirements for GeneXpert equipment installations are as follows:

- Lockable testing site with secure windows and limited access
- Functional air conditioning able to maintain a temperature below 30°C in the area GeneXpert is installed
- Able to maintain a relatively dust free environment
- Stable, secure bench space that allows a minimum of 2 inches space around the instrument
- Stable electricity supply, with secondary back-up systems in place and reliable (*i.e.* starts automatically and fuel is available)
- Meet minimum biosafety practices for TB
- Linked to regional MSD store with existing systems in place for stock delivery
- Linked to a TB department within the facility
- Sufficient staff to operate equipment
- Linked to EMS within the local area for shipment of samples to zonal or central culture laboratory

ANNEX H: GENEXPERT MAINTENANCE

Preventive maintenance procedures include (GeneXpert Product Insert):

Daily maintenance	• Remove cartridges • Disinfect bench around instrument • Monitoring and recording daily room temperatures
Weekly maintenance	• Restart GeneXpert instrument computer and software • Disinfect the cartridge bay interior
Monthly maintenance	• Disinfect instrument surface • Disinfect plunger • Clean the filter at the back of the instrument using cotton gauze, soap and water • Archive the results and burn on CD
Annual maintenance	• Perform calibration using remote calibration kit

ANNEX I: SOP CONSIDERATIONS

The following is a list of installation and training documents, tools and SOPs for use with Xpert testing which should be available at all testing sites:

Package 1 documents	Package 2 documents (in-country tools)
GeneXpert country- specific installation checklist	TB suspect screening tool
GeneXpert installation accompanying documents	Sputum testing national testing algorithm
GeneXpert Manual	Sputum sample testing request form for Xpert
Xpert MTB/RIF SOP	Laboratory Sample register
Xpert MSDS	Results reporting procedures
Xpert maintenance SOP	Sample TAT records
Xpert maintenance records	Patient tracing procedure
Xpert sputum sample collection SOP	Patient initiation onto treatment procedure
Xpert MTB/RIF WHO reporting codes	RIF detected reporting to NTLP procedures
Xpert patient ID recording codes	Stock ordering protocols
Xpert error records and corrective action log	Stock cards
Xpert monthly indicator reporting form	Incidence occurrence records
Xpert calibration log	Waste management procedure
Xpert error code list	Sample collection for culture
Xpert user training package	Sputum transport procedure
Xpert clinical training package	Spill management procedure
Sputum rejection criteria	Temperature monitoring records
PPE donning instructions	

The following information should be included in the relevant SOPs:

Case Definition, Documentation and Reporting

The following information is captured in the SOP for Case definition, Documentation and Reporting. Based on WHO recommendations [13], all cases diagnosed to have TB by Xpert MTB/RIF shall be case defined for TB cases:

- A bacteriological confirmed TB case: is one from whom a biological sample is positive by smear microscopy, culture, Xpert MTB/RIF or any other WRD. All such cases should be notified to the NTP;
- Rifampicin resistance TB (RR-TB) case: resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether mono-resistance, multidrug resistance, poly-drug resistance or extensive drug resistance.

The standardized reporting and reporting formats released by WHO capture Xpert MTB/RIF test information and include revised quarterly reports, testing site registers, patient registers, treatment cards, testing site request forms, presumptive TB registers, and MDR registers. All testing sites will be required to contribute data to quarterly reports for the NTP & CTRL.

The testing site supervisors should check and confirm statistical accuracy of the most recent quarterly reports directly from the GeneXpert equipment during supervisory visits and compile them for their district or region to assist with stock management and troubleshooting. Quarterly case finding should be reported by the Xpert testing site while the enrolment of cases in to care should be reported by the Treatment Initiation Centre. To facilitate this activity Referral Samples Logbook, Postal TB Sample Logbook and Sample Referral SOP will be utilized.

Laboratory Infrastructure requirements

- Uninterrupted power supply (UPS with minimum capacity of 2 hours and/or a generator with fuel supply);
- Closed room with temperatures no higher than 30^{o}C and air conditioning system in hot areas;
- Adequate storage room for cartridges with temperatures not higher than 28^{o}C;
- Secured location to protect Xpert instrument and computer from theft;
- Adequate space for sample receipt and preparation for testing;
- At least one 2-8^{o}C refrigerator for sample storage as needed;
- Reliable water supply with sink;
- Laboratory chairs and desks for paper work and documentation activities.

Biosafety requirements

- Waste disposal system for cartridges (*e.g.* incineration);
- Biosafety level equivalent to smear microscopy (*e.g.* cross-ventilated room);
- Gloves for sample handling;
- Containers for triple packaging of referral samples;
- Standard laboratory safety precautions and practices should be adhered to.

Sample referral system requirements

- The testing site networking for sample referral shall be based on geographic proximity from the GeneXpert MTB/RIF testing centre and samples will be transported using the current available courier system;
- The NTLP has a contract with EMS for shipment of samples in Tanzania;
- The goal of the NTP is for every TB centre to have access to GeneXpert testing. This will be achieved by referring samples via EMS from the peripheral/district site to the regional/district GeneXpert. Samples will be packaged using triple packaging as per NTLP manual and sent via EMS using a letter provided by the NTLP for shipment. The DTLC/RTLC will oversee this and ensure timely shipment and communication with the regional GX site to ensure all samples are accounted for.
- Samples will be tested by Xpert MTB/RIF test and the results returned by EMS to the DTLC/RTLC. All MTB detected regardless of rifampicin result will be communicated immediately by phone so as not to delay treatment initiation. In addition requests for repeat samples will be made by phone to reduce diagnostic delays.
- Samples requiring follow up culture can be sent to the nearest Zonal TB Referral Laboratories also by EMS with results returned the same way, by phone for critical results and hard copy by EMS.
- Not all Zonal TB Referral Laboratories are equipped for and will refer positive samples for further testing at the CTRL using EMS. Critical results will be returned to the RTLC by phone and hard copy by EMS.

The expected turn-around times:

- Delivery of Xpert MTB/RIF test results should be within 24 hours except on weekends.

- Test results for samples from outside of the testing site (referral samples) should be communicated by phone to the facility if MTB are detected and the physical result delivered within one week of result availability.
- Culture results should be communicated by phone and the hard copy returned within one week of result. In case of delays or the need for second line testing an interim report shall be generated and released.

ANNEX J: PROGRAMMATIC & TESTING SITE QUALITY INDICATORS

PROGRAMMATIC

1. Process indicators
    - The proportion of projected number of testing sites / number of active testing sites relevant to the projected need;
    - The number and proportion of notified cases (both new and relapsed) confirmed by bacteriologically (microscopy / culture / Xpert MTB/RIF);
    - The number and proportion of individuals found to have rifampicin-resistant TB by Xpert MTB/RIF or DST during the reporting period, disaggregated by patient group;
    - The number and proportion of individuals found to have rifampicin-susceptible TB by Xpert MTB/RIF or DST during the reporting period, disaggregated by patient group;
    - The number and proportion of clinical sites with onsite access to GeneXpert;
    - The number and proportion of clinical sites without onsite access to GeneXpert;
    - The number and proportion of clinical sites that have access to Xpert MTB/RIF testing through the referral network;
    - The number and proportion of new testing sites with onsite access to GeneXpert planned and budget secured;
    - The number and proportion of testing sites participating in Quality Assurance activities including PT/EQA.

2. Site indicators
    - The number and proportion of rifampicin- resistant cases detected by Xpert MTB/RIF that received further phenotypic DST during the reporting period;
    - The number and proportion of rifampicin- resistant cases detected by Xpert MTB/ RIF that were initiated on a WHO- recommended treatment regimen for MDR during the reporting period;
    - The number and proportion of rifampicin- susceptible cases detected by Xpert MTB/ RIF that were initiated on a WHO- recommended treatment regimen for MDR during the reporting period;
    - Average time from patient presentation (Visit 1) to initiation of treatment, disaggregated by rifampicin susceptible & rifampicin resistance;
    - Average time from sample collection to initiation of treatment, disaggregated by rifampicin susceptible & rifampicin resistance.

TESTING SITE

1. MONITORING THE GROUPS OF PATIENTS TESTED AND THE TEST RESULTS

The program currently requests that the testing indicators listed below be provided on a monthly bases to the GeneXpert Focal Person who reports to the NTLP programme manager along with a brief narrative:

- The number of Xpert MTB/RIF tests performed, disaggregated by reason for testing (*i.e.* by the group of either TB cases or individuals suspected of having TB);
- The number of tests with MTB DETECTED, RIF resistance NOT DETECTED;
- The number of tests with MTB DETECTED, RIF resistance DETECTED;
- The number of tests with MTB DETECTED, RIF resistance INDETERMINATE;

- The number of tests with MTB NOT DETECTED;
- The number of tests that had invalid results, no results or other errors.

In addition, these numbers are further disaggregated. The cases are categorised as follows:

Presumptive TB cases with no other factors	New
Presumptive TB cases who are HIV positive	HIV
Presumptive TB cases who are less than 15 years old	KID
Presumptive MDR cases	MDR
Retreatment cases	RT

(Cases can only be linked to a single category so for example an HIV positive 12-year-old is tested the code used is KID, or a presumptive MDR who is also HIV the code used is MDR)

2. MONITORING THE OPERATION OF THE GENEXPERT PLATFORM AND THE PERFORMANCE OF USERS

- The number and types of various errors. Identifying the most frequent types of errors can help troubleshoot the process, given that certain errors may be associated with the technique used to process samples; other errors may be related to mechanical problems with the instrument's modules or other issues, such as room temperature;
- The number of errors occurring by instrument module. If a particular module produces more errors over time compared with other modules, it may require repair;
- The number of errors occurring by user. If a particular user has an unusually high number of errors, further investigation of the specific error types is warranted, since some errors may be caused by the technique used to process samples;
- The number of tests lost due to power outages or surges;
- The number, duration, and causes of routine interruptions in the Xpert MTB/RIF testing service. Common causes of service interruptions include cartridge stock-outs, expired cartridges, no staff available, instrument breakdown, and computer breakdown;
- The number of instrument modules not functioning and the duration (in days) of module failure during the reporting period;
- The number of instrument modules overdue for calibration at the end of the reporting period.

3. Monitoring supply management:

- The number of cartridges in stock at the beginning of the reporting period;
- The number of cartridges received during the reporting period;
- The number of cartridges used during the reporting period;
- The number of cartridges that were lost or damaged;
- The number of cartridges in stock at the end of the reporting period;
- Whether there were any stock-outs during the reporting period, the duration of stock- out (in days);
- Number of cartridges that were lost or damaged before being used.

ANNEX K: COSTING

To provide the cost of implementing and maintaining Xpert MTB/RIF test rollout in Tanzania, a five-year cost mapping exercise was conducted using the following assumptions:

1. Currently, there are 67 GeneXpert instruments in Tanzania. To achieve the goal of 162 GeneXpert instruments by 2018, an additional 95 instruments would need to be placed between 2015 and 2018 *i.e.* 17 in 2015, 16 in 2016 and 62 in 2017.
2. The capital costs associated with instrument procurement are calculated as follows:

	2015	2016	2017
GeneXpert instrument (4 module + laptop)	US$17,500	US$17,500	US$17,500
Shipping	US$1,000	US$1,050	US$1,103
Uninterrupted power supply & batteries	US$1,200	US$1,260	US$1,323
Printer	US$200	US$210	US$221
Sub-total	US$19,900	US$20,020	US$20,147
Number of sites / instruments	17	16	62
TOTAL	**US$338,300**	**US$320,320**	**US$1,249,114**

3. Installation costs associated with instrument placement are shown below. These costs are estimated based on conducting a pre-installation site assessment (equivalent to one supervisory visit) and a site upgrade of US$1,000 per site (*e.g.* installation of air conditioner, upgrade to benches, upgrade to testing site security). Follow-up site visits (equivalent to one supervisory visit) were budgeted to take place at 15% of testing sites. In addition, all new testing sites receive a comprehensive assessment within three months of installation (*i.e.* two-day supervisory visit).

	2015	2016	2017
Upgrade costs per site	US$1,000	US$1,050	US$1,103
Pre-Installation assessment	US$315	US$331	US$348
Comprehensive assessment	US$415	US$436	US$458
Sub-total	US$1730	US$1,817	US$1,909
Number of instruments	17	16	62
Sub-total	US$29,410	US$29,072	US$118,358
Follow-up assessment	US$315	US$331	US$348
Number of follow-up sites	3	2	9
Sub-total	US$945	US$662	US$121,104
TOTAL	**US$30,355**	**US$29,734**	**US$239,462**

4. The training costs are estimated based on conducting one five-day classroom training for five new users and an on-site training (one day):

    - To accommodate the trainings of new users associated with instrument placement, two classroom trainings are proposed for 2015 and 2016 respectively. Four user trainings are proposed for 2017.
    - One training for GeneXpert Focal Points will be conducted annually.
    - In addition to these trainings, refresher on-site training will be conducted for existing sites every other year.

	Classroom	On-site
Travel	US$3500	US$200
Accommodation	US$500	US$75
Conference costs	US$550	US$0
Stationary	US$750	US$50
Contingency	$300	$50
Total	**US$5,600**	**US$375**

	2015	2016	2017	2018	2019
Classroom	2 × US$5,600	2 × US$5,880	4 × US$6,174	-	-
Sub-total	US$11,200	US$11,760	US$24,696	-	-
Focal Point training	US$5,600	US$5,880	US$6,174	US$6,483	US$6,807
Refresher training	34 × US$375	42 × US$394	50 × US$414	81 × US$435	81 × US$457
TOTAL	**US$29,550**	**US$34,188**	**US$51,570**	**US$41,718**	**US$43,824**

5. Supervisory visits. The costs of one-day and two-day supervisory visits are shown below. Site supervision visits are scheduled as outlined in this implementation plan:

    - New sites will receive one two-day visit (for comprehensive assessment) and two one-day supervisory visits per annum;
    - Existing sites that are performing optimally will receive two one-day supervisory visits per annum;
    - 30% of existing sites, which are estimated to be performing sub-optimally, will receive four one-day supervisory visits per annum.

	One day	Two day
Travel	US$200	US$200
Accommodation	US$75	US$150
Stationary	US$15	US$15
Contingency	$25	$50
TOTAL	US$315	US$415

	2015	2016	2017	2018	2019
New sites supervision	17 × (2 × US$315 + US$415)	16 × (2 × US$331 + US$436)	62 × (2× US$348 + US$458)	-	-
Sub-total	US$17,765	US$17,568	US$71,548		
Existing site supervision (Optimal)	47 × (2 × US$315)	59 × (2 × US$331)	70 × (2 × US$348)	113 × (2 × US$365)	113 × (2 × US$383)
Sub-total	US$29,610	US$39,058	US$48,720	US$82,490	US$86,558
Existing site supervision (Sub-optimal)	20 × (4 × US$315)	25 × (4 × US$331)	30 × (4 × US$348)	49 × (4 × US$365)	49 × (4 × US$383)
Sun-total	US$25,200	US$33,100	US$41,760	US$71,540	US$75,068
TOTAL	**US$72,575**	**US$89,726**	**US$162,028**	**US$154,030**	**US$161,626**

6. Consumables

The estimated costs of consumables are shown below:

- One calibration kit is used per instrument per year;
- It is estimated that 1500 Xpert MTB/RIF tests will be performed per instrument in the first year;
- It is estimated that 2500 Xpert MTB/RIF tests will be performed per instrument from year two.

Variable costs	
Shipment cost per cartridge	US$1.20
Alcohol 70%	US$0.05
Concentrated bleach	US$0.006
Tissue	US$0.79
Sputum containers	US$0.12
Gloves	US$0.05
Other costs (*e.g.* sample referral)	US$2
Sub-total	**US$4.22**
Cost per cartridge	US$9.98
TOTAL	**US$14,20**

	2015	2016	2017	2018	2019
Number of tests	17 × 1500 + 67 × 2500	16 × 1500 + 84 × 2500	62 × 1500 + 100 × 2500	162 × 2500	162 × 2500
Sub-total	193,000	234,000	343,000	405,000	405,000
Costs total	US$14.20	US$14.41	US$14.63	US$14.86	US$15.10
GeneXpert Calibration kits	US$450 × 67	US$450 × 84	US$450 × 100	US$450 × 162	US$450 × 162
Sub-total	US$30,150	US$37,800	US$45,000	US$72,900	US$72,900
TOTAL	**US$2,770,750**	**US$3,409,740**	**US$5,063,090**	**US$6,091,200**	**US$6,188,400**

7. Warranty & maintenance

Two options are available:

Option 1: Purchase of extended warranty	
Three-year extended warranty per instrument	US$6,900
Option 2: Module replacement (Preferred option*)	
Replacement cost of one module	US$900

* In 2014 (six modules of 62 instruments) were replaced. Extrapolating, it can deduced that it is more cost-effective to replace modules than purchase the extended warranty:

	2015	2016	2017	2018	2019
10% - 20% of existing instruments	7 - 14	8 - 16	10 - 20	16 - 32	16 - 32
Module replacement cost	US$900	US$900	US$900	US$900	US$900
Total	US$6,300-12,600	US$7,200-14,400	US$9,000-18,000	US$14,400-28,800	US$14,400-28,800

8. Remote connectivity

The following costs are associated with maintenance and support of the GXAlert remote monitoring system, which is being implemented in Tanzania:

Modems (for new installations)	US$250
Data per site per annum	US$120
Remote monitoring assistance per annum	US$1500
Local hosting per annum	$2000
Licensing & technical support	US$4500
Sub-total annual costs	US$8,000

	2015	2016	2017	2018	2019
New sites	17 × US$250	16 × US$263	62 × US$276	-	-
Sub-total	US$4,250	US$4,208	US$17,112	-	-
Existing sites	67 × US$120	84 × US$126	100 × US$132	162 × US$139	162 × US$146
Sub-total	8,040US$	US$ 10,584	US$13,200	US$22,518	US$ 23,652
Annual costs	US$8,000	US$8,400	US$8,820	US$9,261	US$9,724
TOTAL	**US$20,290**	**US$23,192**	**US$39,132**	**US$31,779**	**US$33,376**

9. Programme evaluation

The estimated cost associated with an annual partners meeting to evaluate Xpert MTB/RIF rollout and programme implementation is shown below:

	20 participants
Travel	US$150
Conference facilities	US$1,300
Stationary	US$50
Per diem	US$1,100
Contingency	$400
TOTAL	US$3,000

Other budgetary considerations

- Additional annual human resource costs are to be estimated by the country.
- The NTLP aims to increase the proportion of optimal performing sites to more than 90% by the end of 2016. Trouble shooting and re-training will play an important part of meeting this goal. Reducing the percentage of suboptimal sites will reduce the yearly costs related to future support.
- It is more cost effective to increase testing at fewer sites than to install additional instruments; therefore, the programme aims to utilize maximum capacity of instruments, or approximately 300 tests per month. To achieve this, the relocation of current instruments may be reassessed to ensure optimal placement. Patient referral from sites within the district will be encouraged and systems strengthened.
- To determine resource gaps, implementing partners will submit detailed budgets to the NTLP, and commit to at least two years of support following GeneXpert placement. In-country implementing partners will also provide annual estimates of costs, and describe what is covered by the budget, as well as the funding gaps. It is most important to provide a date for handover and to work with the NTLP in the months before handover to allow a smooth transition, including budgeting for sites.
- Cost effective implementation requires testing and clinical sites harmonization. For budgeting purposes, activities will be combined to reduce costs (*e.g.* clinical pre-installation assessments will be conducted at the same time as the testing site readiness assessment - either by the same person or with an additional clinically trained and authorised person).
- The number of cases diagnosed with MDR-TB has increased due to implementation of the Xpert MTB/RIF test. Additional costs to be considered as part of the broader programme include:
    - Transport of cases to Treatment Initiation Centres
    - Food and housing at a TB hospital
    - Cost of culture to confirm and monitor treatment program
    - Treatment costs

The current plan for decentralisation of MDR-TB services will reduce these costs further.