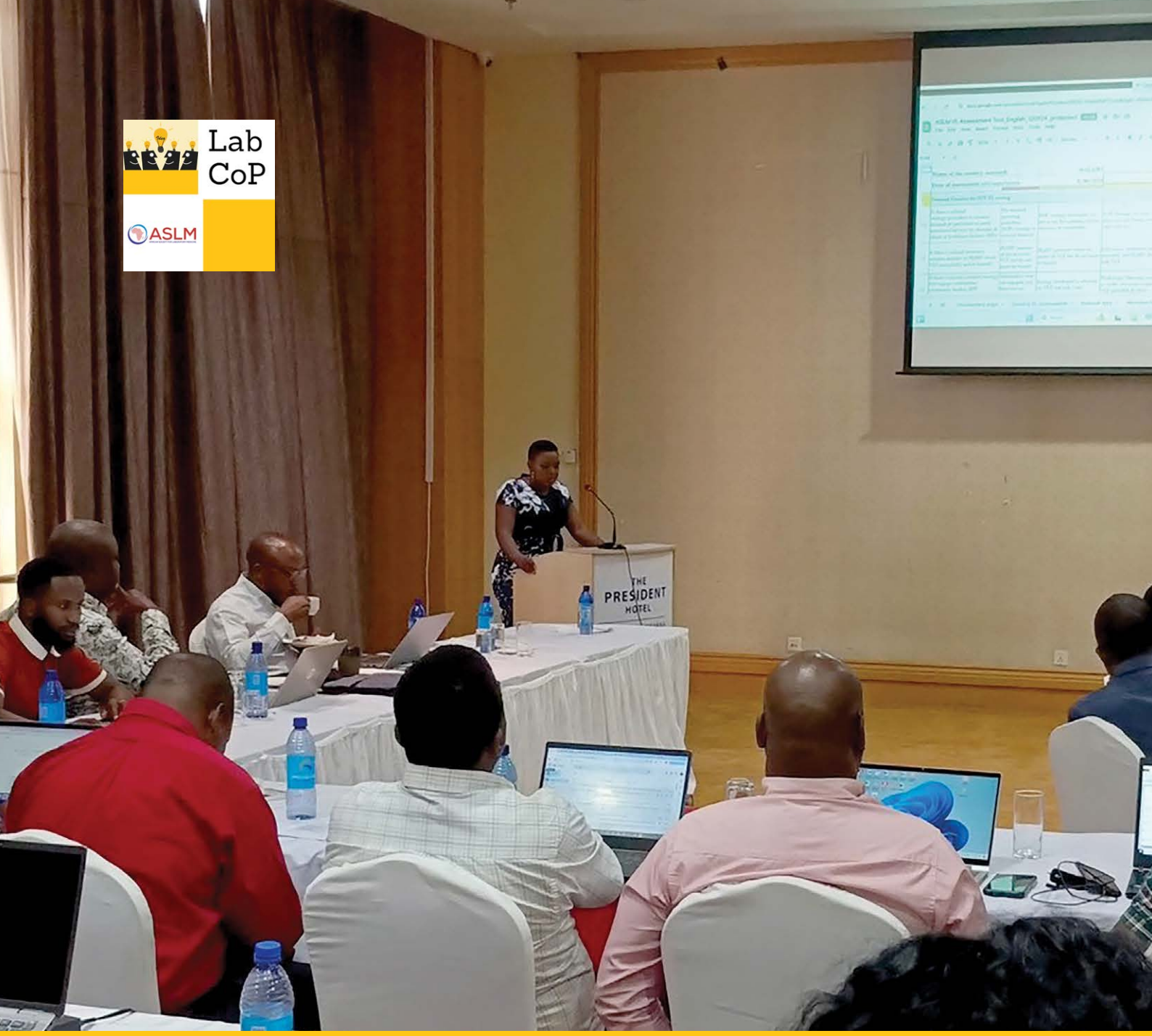

March 2026

Operational Guidance for Implementing Multiplatform TB Molecular Diagnostics

Country experiences and best practices

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

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List of Abbreviations

AMK	Amikacin
CDC	Center For Disease Control And Prevention
DNO	Diagnostic Network Optimisation
DR-TB	Drug Resistant TB
ERPD	Expert Review Panel For Diagnostics
EQA	External Quality Assurance
ETO	Ethambutol
FQ	Fluoroquinolone
GLI	Global Laboratory Initiative
GTC	Guanidium Thiocyanate
HMIS	Hospital Management Information System
INH	Isoniazid
ISRS	Integrated Specimen Referral System
LC-NAAT	Low Complexity Nucleic Acid Amplification Test
LIMS	Laboratory Information Management System
Lod	Limit Of Detection
MC-NAAT	Medium Complexity Nucleic Acid Amplification Test
MDR	Multi-Drug Resistant
MFL	Master Facility List
mWRD	Molecular Who-Recommended Rapid Diagnostic
MTB	Mycobacterium Tuberculosis
MTBC	Mycobacterium Tuberculosis Complex
NEDL	National Essential Diagnostic List
NPOC	Near Point Of Care

NSP	National Strategic Plan
NTP	National TB Program
NTRL	National TB Reference Laboratory
pDST	Phenotypic Drug Susceptibility Testing
PLHIV	People Living With HIV
PT	Proficiency Testing
RIF	Rifampicin
RR	Rifampicin Resistance
SLA	Service Level Agreement
SOP	Standard Operating Procedure
SRL	Supranational Reference Laboratory
TAT	Turnaround Time
TB	Tuberculosis
TB-NAAT	Tuberculosis Nucleic Acid Amplification Test
UNHLM	United Nations High Level Meeting
XDR	Extensively Drug Resistant

INTRODUCTION

To reach the Sustainable Development Goal of universal health coverage by 2030, countries must invest in a package of essential services, including diagnostics, at all levels of the health system[1]. Additionally, quality-assured laboratory networks equipped with rapid methods for diagnosis are essential to the success of the national tuberculosis (TB) program strategies and achievement of the End TB Strategy goal. However, TB diagnosis remains the weakest link in the cascade of care[2]. Each year, an estimated 3 million people with TB are either undiagnosed or untreated. A primary reason for this gap is the limited use of molecular WHO recommended rapid diagnostics (mWRDs). In 2023, only 30% of diagnostic sites had access to these tools, and 48% of people notified with TB were tested with an mWRD as the initial test[3].

To support a transition from sputum smear microscopy, WHO has recommended multiple classes of rapid molecular technologies for the detection of TB and drug resistance[4,5]. This provides national TB programs with options for centralised and decentralised testing including near point-of-care nucleic acid amplification tests (NPOC-NAAT), manual low complexity NAAT (LC-mNAAT: TB-LAMP), automated LC-NAAT (LC-aNAAT: Truenat MTB Plus /MTB-RIF Dx, Xpert MTB/RIF Ultra/XDR), and medium complexity NAAT (MC-NAAT: BD Max MDR-TB, Roche cobas MTB/MTB RIF/INH, Abbott RealTime MTB/MTB RIF/INH). The choice of platform will be based on the cost, diagnostic tier, the population served, throughput, the drug resistance profile and the infrastructure requirements (See Table 1).

While this mix of diagnostic platforms expands mWRD coverage and access, implementing such a diversified landscape of molecular technologies presents new challenges for programs and requires data-driven planning and system-level coordination to guide selection of sites and the appropriate tool/s to meet the need for the population served. Furthermore, programs must also carefully consider specimen referral, procurement, staffing, quality assurance, data management and monitoring and evaluation needs. Building on Recipe 5 which focused on the implementation of Truenat MTB Plus/MTB-RIF Dx, this guide summarises key insights from South Africa, Kenya, and Uganda, where a mix of molecular diagnostic approaches have been adopted to strengthen TB diagnosis.

[1] Pai M, Heitkamp P, Pillay Y. Integration of tuberculosis services within primary health care: converting challenges into opportunities (2025). The Lancet Primary Care. doi: 10.1016/j.lanprc.2025.100056

[2] Pai M, Dewan PK, Swaminathan S. Transforming tuberculosis diagnosis (2023). Nature Microbiology. doi: 10.1038/s41564-023-01365-3

[3] WHO. Global TB Report 2024. https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2024.

[4] WHO consolidated guidelines on tuberculosis: module 3: diagnosis 2025. https://www.who.int/publications/i/item/9789240107984.

[5] WHO. Near point-of-care nucleic acid amplification tests (NPOC- NAATs) as a new diagnostic class for diagnosis of TB using sputum and tongue swabs (2026). https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/diagnosis-treatment/npoc-tongue-swabs-and-sputum-pooling-for-tb/npoc-naats.

Table 1: WHO-recommended molecular tests for the detection of TB and drug resistance
adapted from the WHO operational handbook on tuberculosis and recommendations on NPOC-NAAT.

Class	Test (Manufacturer)	Instrument	Gene target	DST	LoD (CFU/ml)	WHO recommendation	Diagnostic Tier
NPOC-NAAT	MTBC Nucleic Acid Test Card (Pluslife)	MiniDock	IS6110, gyrB	No	50[6]	Initial detection of TB on sputum, and where sputum cannot be obtained, on tongue swabs.	Tier 1 basic peripheral laboratories, health clinics, mobile units, community sites without laboratories.
LC-mNAAT	TB-LAMP (Eiken Chemical)	HumaLoop T	IS6110, gyrB	No	N/A	Initial detection of TB on respiratory samples.	Tier 1 (peripheral) - community settings and health facilities without laboratories or with limited infrastructure or unreliable power.
LC-aNAAT	Truenat MTB Plus (Molbio)	Truelab Uno, Duo, Quattro	nrdZ, IS6110	No	30	Initial detection of TB and RIF resistance and concurrent testing with LF-LAM on urine samples in PLHIV.	
	Truenat MTB-RIF Dx (Molbio)		rpoB	RIF	N/A	Follow-on testing for RIF resistance after performing the MTB Plus test.	
	Xpert MTB/RIF Ultra (Cepheid)	GeneXpert I, II, IV, XVI, Infinity 6- or 10-color module	IS6110, IS1081, rpoB	RIF	16	Initial detection of TB and RIF resistance, concurrent testing on respiratory and stool samples of children, and concurrent testing with LF-LAM on urine samples in PLHIV.	Tier 2 (district/ intermediate) - healthcare facilities with clinical laboratories.
	Xpert MTB/XDR (Cepheid)	GeneXpert I, II, IV, XVI, 10-color module	*inhA promoter, katG, fabG1, oxyR-ahpC intergenic region, gyrA, gyrB rrs, eis promoter*	INH ETO FQ AMK	136 (unprocessed sputum) 86 (sputum sediment)	Follow-on detection of resistance to INH, ETO, FQ, and second-line injectable drugs.	Tier 2 (district/ intermediate) or Tier 3 (regional/ provincial)

[6] www.pluslifehkd.com/en/products

Class	Test (Manufacturer)	Instrument	Gene target	DST	LoD (CFU/ml)	WHO recommendation	Diagnostic Tier
MC-NAAT	RealTime MTB (Abbott)	m2000rt	IS6110, PAB	No	17	Initial detection of TB on respiratory samples.	Tier 3 (regional/ provincial) or Tier 4 (central/reference)
	RealTime MTB RIF/ INH (Abbott)		rpoB, katG, inhA	RIF INH	60	Follow-on testing for RIF and INH on respiratory samples after performing the RealTime MTB test.	
	BD MAX MDR-TB (BD)	BD MAX	IS6110, IS1081 rpoB, katG, inhA	RIF INH	20	Initial detection of TB on respiratory samples.	
	cobas MTB (Roche)	cobas 5800, 6800, 8800	*16S rRNA esx*	No	9	Initial detection of TB on respiratory samples.	
	Cobas MTB-RIF/INH		*rpoB katG inhA*	RIF INH	180	Follow-on testing for RIF and INH on respiratory samples after performing the cobas MTB test.	
	FluoroType MTB (Bruker-Hain)	FluoroCycler 12 FluoroCycler XT	*IS6110*	No	15	Initial detection of TB on respiratory samples.	
	FluoroType MTBDR (Bruker-Hain)		*rpoB, katG, inhA*	RIF INH	20	Follow-on testing for RIF and INH on respiratory samples after performing the FluoroType MTB test.	

**In some settings, district level can be part of the peripheral tier*

Implementing multiplatform TB molecular diagnostics

Given the current reductions in global health donor funding, National TB Programs (NTP) and National TB Reference Laboratories (NTRL) should closely collaborate in selecting the diagnostic tools that best serve the needs of their networks, balancing cost, coverage and access. A comprehensive and costed implementation plan is essential to guide each step of the process from assessing infrastructure requirements and staffing to training, data management and monitoring and evaluation (See Figure 1).

Box 1 Country Example – South Africa: *The main drivers for diversification and introduction of additional platforms were to mitigate the risk of a single supplier for a large TB program and encourage competition in the market to drive down pricing. The risk of sole sourcing was evident in 2022 (post COVID) when the manufacturer could not meet the testing demand and incoming stock shipments had to be distributed/managed centrally to ensure fair supply across laboratories. Patient care was impacted due to long TATs and high specimen rejection rates of "old" specimens. A new tender process was introduced to allow all manufacturers of TB-NAATs to bid for low-, medium-, or high-throughput laboratories (a network of ~160 sites). This strategy promoted fair competition, allowing manufacturers to bid based on equipment suitability for each of these categories. Cepheid instruments were assigned the low throughput sites; BD the medium-volume sites, and Roche the high-volume academic/culture laboratories.*

Key steps in diversification - implementation overview

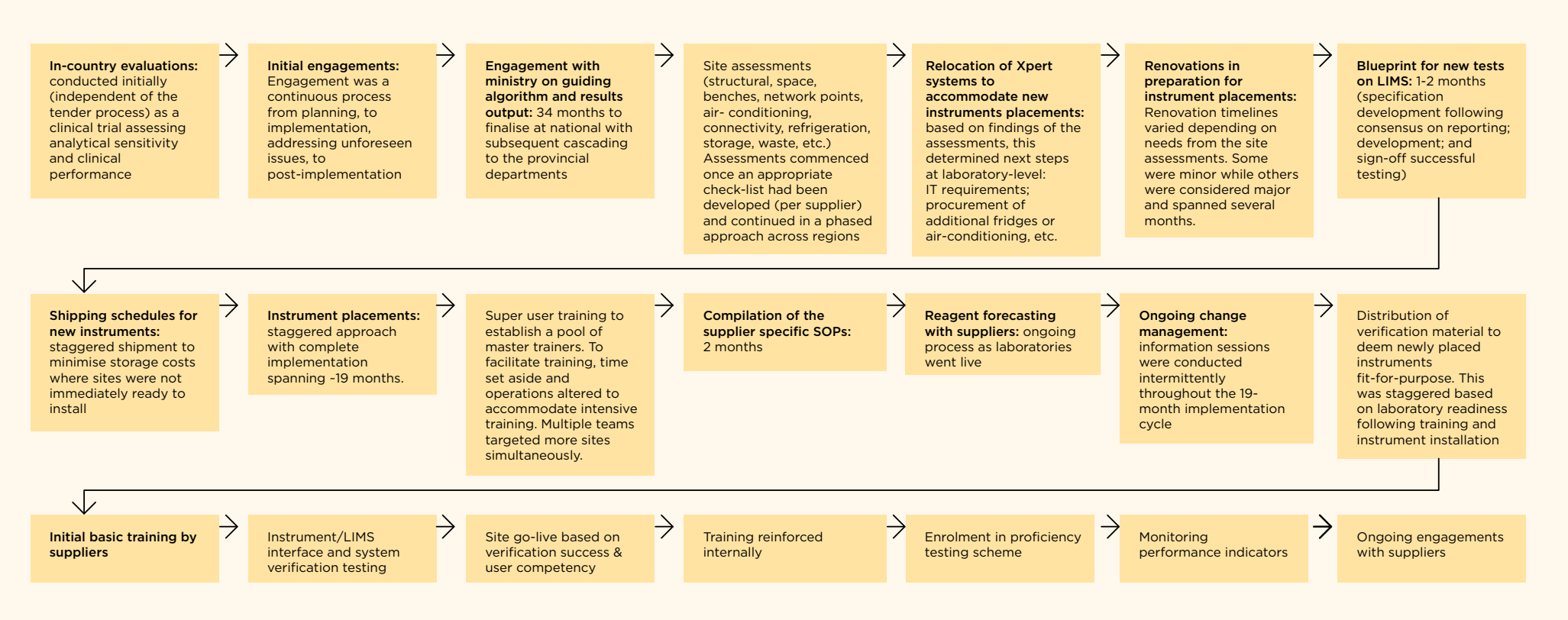

Figure 1: Implementation framework used to introduce MC-NAATs in South Africa.

Most steps and processes occurred in parallel i.e., while some sites were having assessments, the LIMS blueprint was being developed, other sites were undergoing renovations; and others were having instruments placed as their assessments did not identify any requirements or dependencies. The project coordination was managed centrally and arising issues discussed at weekly stakeholder meetings. As sites went live, any subsequent teething issues were addressed through on-site visits with ongoing centralised monitoring of performance indicators.

1. Assessing diagnostic network needs

A core team composed of the NTP, NTRL, lab directorate, quantification and procurement planning unit, implementing partners, clinicians, technical working groups or expert committees (academia/researchers) should be set up to lead the situational analysis and draft the implementation plan which will be further refined through stakeholder engagements. Some key questions to address during the situational analysis include the strength of the TB diagnostic network to meet the needs of the people with TB, the coverage of the diagnostic network to ensure access to molecular testing to all people with TB, and the efficiency of the diagnostic data management and specimen referral systems. Therefore, a deep understanding of the diagnostic network is a key first step. Diagnostic network optimisation (see GLI guide) presents an opportunity for programs to consolidate, integrate and optimise laboratory services across diseases and the health system[7, 8]. Such an analysis, combined with an understanding of the epidemiology, helps the TB program to identify where the needs or gaps are and which test can address these needs, recognising that the needs will vary across regions, districts or tiers of the health system.

1.1. Review the TB diagnostic network

Assessing the diagnostic network involves reviewing health facilities and TB diagnostic and treatment centres, including any planned expansions. Having an up-to-date master facility list is crucial for this assessment (e.g. Kenya's MFL). Evaluating the population distribution and facility locations helps pinpoint gaps in access to healthcare services. The next step is to map the TB diagnostic tests available at each health facility, noting the level of care (such as clinic, health post, district hospital, or tertiary hospital), sector (private or public), and whether public sector tests are provided for free or require payment. At this stage, having an equipment register detailing all available equipment, their locations, testing capacities, and current usage status is highly beneficial and recommended. Programs can leverage laboratory capacity mapping data if available. Additional data sources that can be consulted during this review are listed in Table 2.

Table 2: List of data that should be reviewed and sources

Analysis Need	Data type	Sources
Epidemiology	National, and subnational	NSP, WHO global reports, national reports, publications
Health Facilities	Number of health facilities & tier Population density Road network	MFL National Statistics Relevant ministry

[7] Albert H, Rupani S, Masini E, Ogoro J, Kamene M, Geocaniga-Gaviola D, et al. Optimizing diagnostic networks to increase patient access to TB diagnostic services: Development of the diagnostic network optimization (DNO) approach and learnings from its application in Kenya, India and the Philippines (2023). PLoS One. doi: 10.1371/journal.pone.0279677.

[8] GLI. A guide to stepwise implementation of diagnostic network optimisation 2025. https://www.stoptb.org/who-we-are/stop-tb-working-groups/global-laboratory-initiative-gli/gli-guidance-and-tools.

Analysis Need	Data type	Sources
mWRD Coverage	TB test menu by facility & tier Location of each TB testing site (with coordinates if possible) Equipment location (type and number available at each site) Number of catchment facilities for each testing site	NEDL/Equipment register/DNO report/ LabMap report
Test volume/ demand	Number of samples collected at each health facility Number of tests that can be performed per device/per testing site Number of tests conducted per year at each site	Test data/ LIS/ DNO report/site register

**MFL – master facility list; *DNO – diagnostic network optimisation (if report available)*

1.2. Define equipment placement criteria

Engagement with multiple stakeholders including manufacturers, researchers, clinicians, recipients of care, regulators, technical working groups, the private sector and civil society is essential to refine the needs, raise awareness and demand for testing and identify linkages with other programs. The technical working group leads the equipment selection and placement, identifying sites where integration is needed and where coverage needs to be improved. Discussions for site selection should also consider infrastructure and human resource requirements. For example, LC-NAATs are suitable for decentralised placement owing to their low infrastructure requirements. Battery operated Truenat assays can be placed at sites with frequent power cuts while TB-LAMP can be used in community-based screening. On the other hand, MC-NAATs

Box 2 Country Example: *In Uganda, stakeholder engagement helps in equipment and site selection and ensuring equitable deployment of diagnostic tools. Furthermore, the potential for multi-disease testing is a key criterion for equipment selection. Consideration is put on the nature of equipment, the tests it can do and the level where those tests are required. At the end of these meetings, a list of facilities is generated for final approval by top management of Ministry of Health. GeneXpert is being used at all tiers of the diagnostic network provided there is power supply, including in the TB mobile clinics. Truenat is used at lower-level laboratories (mainly HCIIIs) due to their limited infrastructure requirements. TB-LAMP has been deployed to increase testing capacity in high burden TB regions and for community testing using tuku-tuku (as they offer the capacity to test many samples at once). The country is planning to roll out NPOCs at lower levels including supporting the private sector.*

require sophisticated infrastructure and biosafety considerations, and so will be more suitable for more centralised placement. Additionally, considerations for drug susceptibility testing and concurrent testing protocols for children and PLHIV should be made.

1.3. Plan for the target number of tests

The country should calculate the annual number of mWRD tests needed to reach 100% access to mWRDs. This is guided by the national targets for notification and case finding. Assumptions made during this process should be clear and documented to enable the process to be replicated. Once the number of WRD tests that need to be conducted per year has been calculated, the country must then consider the existing mWRD instrument throughput, where these instruments are located, the number of cases per facility or per district, and the sample referral networks. The number of mWRD machines required to run the target number of samples should be calculated on a module basis to guide selection of the appropriate diagnostic tool.

Box 3 Country Example: *In Uganda, this process is done annually and the targeting is always aligned with the annual targets in the NTP strategic plan such as; TB notification target and proportion of patients to be tested by mWRD along with other routine data elements such as number needed to test (NNT) which is derived from the positivity rate or TB yield. The targets are assigned to regions, districts up to facility level and performance on these targets is reviewed during performance review meetings.*

1.4. Site assessments

Implementation of tests is associated with indirect costs related to equipment installation. Each of the proposed sites needs to be inspected for safety and operational functionality (e.g., testing and storage space, power supply and backup options, ventilation and/or temperature control, electrical and network connections) using a standardised checklist provided by the supplier, developed by the NTP, or from prior mWRD deployments. Renovations may also be needed when implementing MC-NAATs to accommodate the larger instruments and the need for optimised workflows. Therefore, it is important that these costs are accounted for during the planning phase.

2. Regulatory processes

Early in the planning process, programs should engage with regulatory authorities to discuss the proposed new tests and clarify the requirements for approval. A critical pathway analysis of regulatory and market entry processes for new TB diagnostics across Africa showed that regulatory approval processes can take anywhere from 3 to 12 months. However, as most regulatory systems rely on WHO recommendation/prequalification, some countries have mechanisms for expedited review. Therefore, it is essential that programs initiate these engagements well in advance of anticipated implementation dates. Timely engagement with the regulatory authorities for their buy-in is key in accelerating in-country approvals. Providing presentations on equipment performance and how it fits into the TB diagnostic network to relevant technical working committees or groups at the ministry of health helps raise awareness and facilitates the approval and adoption of the test.

2.1. In-country equipment evaluations

Multi-country studies that evaluate test performance or diagnostic yield are an essential component of the WHO review/recommendation process. Most national regulators will require in-country verification/evaluation as part of the registration process. In South Africa, evaluation of MC-NAATs, was conducted in collaboration with FIND as a comparative analytical evaluation of four centralised platforms, Abbott RealTime MTB and MTB RIF/INH, Hain Lifescience FluoroType MTBDR, BD Max MDR-TB and Roche cobas MTB and MTB-RIF INH[9] . Inactivated well-characterised M. tuberculosis (MTB) strains were used to assess analytical sensitivity and accuracy of the detection of resistance to INH and RIF. Each strain was tested in triplicate and Genotype MTBDRplus was used as the comparator test to assess reproducibility of detecting RIF and INH resistance. This study was the initial assessment of analytical sensitivities across all four assays and supported subsequent WHO recommendations regarding their use. As a result, the outlined scope may not be required before implementation. Programs and national tuberculosis reference laboratories (NTRLs) should decide which evaluation approach is appropriate and allocate adequate time and resources for its completion.

2.2. Update the diagnostic algorithm

Updating the diagnostic algorithm is needed to establish mWRDs as the primary diagnostic. Simultaneously, revisions to the national essential diagnostic lists need to be made as this supports procurement and financing decisions. As most algorithms reference specific suppliers or tests (e.g., Xpert), transitioning to a class-based system (such as LC-NAAT or MC-NAAT) or referring to the diagnostics as mWRD or TB-NAAT may be warranted. In South Africa, the designation “TB-NAAT” was adopted[10].

[9] de Vos M, Scott L, David A, Trollip A, Hoffmann H, Georghiou S, et al. Comparative Analytical Evaluation of Four Centralized Platforms for the Detection of Mycobacterium tuberculosis Complex and Resistance to Rifampicin and Isoniazid (2021). J Clin Microbiol.

[10] South Africa Revised TB Diagnostic Algorithms https://knowledgehub.health.gov.za/system/files/2023-09/TB%20ALGORITHMS.pdf

Following algorithm updates, it is critical to ensure that the refined protocol is disseminated to all healthcare facilities, with comprehensive training provided to healthcare personnel. Additionally, ongoing monitoring of the algorithm's implementation is necessary to ensure compliance. Programmes should incorporate monitoring strategies for the adoption of the revised algorithm, including retraining initiatives to reinforce procedural changes.

3. Procurement and supply chain

3.1. Supplier engagement

Having several suppliers servicing the same program can add new complexities. Therefore, programs should take a proactive approach by engaging with suppliers regularly and setting clear terms including:

- Agreement on shipping schedule for instruments and consumables, clarifying lead times, availability, order details and in-country approval processes to avoid procurement delays.
- Agreement on maintenance schedules (when, how), the number of in-country/regional engineers and expected travel times.
    - All-inclusive service level agreements are recommended (See ASLM Echo Sessions on SLA for molecular based testing[11]).
- Request for majority of spare parts to be in country or within the region to minimise downtimes.
- Establishing procedures for logging issues and the expected response times.
- Agreement on key performance indicators and how these will be monitored.
- Outlining conflict resolution procedures and escalation mechanisms.

[11] LabCoP Echo Session Aug 2024: Demystifying Service-Level Agreements for Molecular-based testing https://www.youtube.com/watch?v=fnpEFajLoXA

3.2. Reagent forecasting

Uninterrupted testing requires careful planning for reagents, consumables, and accurate forecasting. When introducing a new mWRD, countries should plan transitions, factoring in higher test repeats and wastage during initial implementation. Forecasts must account for the initial implementation phase when users are still familiarising with new systems and workflows as this is typically associated with higher rates of test repeats, invalids and reagent wastage. Therefore, forecasting models should include a start-up buffer, informed by historical roll-out experiences, system complexity and supplier input, to prevent early-stock outs and interrupted testing services. Programs should coordinate with suppliers on order frequency, lead times, shelf-life, and storage requirements for kit components. Where feasible, programs should consider maintaining reserve stock to manage demand fluctuations.

Best Practice 1: Forecast Planning – South Africa

Preparing comprehensive annual forecasts helps accommodate seasonal testing fluctuations such as those resulting from active case finding campaigns or public holidays, as reflected in historical trends. Suppliers often require long-range demand projections to reserve manufacturing slots and prevent allocation constraints. In South Africa, the program used historical testing volumes from laboratory information systems and included considerations for lead time i.e., time from order placement to receipt at the site and buffer stock to mitigate supply disruptions. They collaborated with each supplier to develop reagent calculators to guide accurate ordering. These calculators determine the appropriate quantities of individual reagent components, based on the projected number of tests, and accounting for the varying pack sizes and quantities supplied for each item.

4. Staffing and training

An essential part of implementing mWRD tests is evaluating the necessary staff skills, expertise, and experience considering complexity of the test, sample type, and where the instruments will be placed. Comprehensive training is needed to address differences between current and new tools, including testing strategies, result reporting, turnaround time and invalid rates. Carefully scheduling the training to coincide with the arrival of commodities in the country helps ensure that implementation can begin promptly, minimizing any delay between training and test deployment. The timeline for this phase is variable and determined by overall implementation plan, number of sites, number of staff to be trained, and the chosen approach (on-site, centralised, or virtual). The program should select what is most effective to ensure full coverage. Training must include clinicians who influence test demand and all clinical personnel at both implementation and referral sites must be notified and provided with comprehensive training on the revised diagnostic algorithm, with training materials distributed to all relevant facilities.

Box 4 Country Example: *In Uganda, training materials are adapted from WHO/GLI or other technical partners and revised for use in line with IACET Standard. A centralised training for national and regional trainers takes 3 to 5 days depending on the complexity of the test. End users (laboratory personnel, clinicians and data staff) are trained on site for on average, 2 days. The national and regional trainers receive additional training material (technical and troubleshooting) to equip them to become superusers who provide routine remote or onsite support to testing facilities.*

5. Ensuring quality of TB testing

5.1. Considerations for workflows

Due to the different workflows across the WRD assays, the NTRL needs to ensure that supplier-specific SOPs are developed, and supplier-initiated training is provided. For example, during the pre-analytical process, sonication is required for the cobas MTB assay (See Figure 2). This is performed on a separate, dedicated instrument for one sample at a time. For the Abbott assays, two separate instruments are needed for DNA extraction and amplification and detection, with a manual transfer step in between. Additionally, MC-NAATs and Truenat are currently only recommended for respiratory samples while Xpert has recommendation for both sputum and extrapulmonary samples. These differences in the workflows need to be reinforced through supervision, mentorship and training during the rollout.

Box 5 Country Example – South Africa: *As moderate-complexity TB-NAAT platforms have WHO recommendation only for respiratory specimens, GeneXpert instruments had to be retained at the BD and Roche assigned sites, to allow for processing of extra-pulmonary specimens. Programmatically, clinical management is based on the rifampicin result and where resistance is detected by TB-NAAT, further testing follows via a reflex workflow which includes digestion/decontamination and concentration of the specimen with further molecular tests and TB-culture setup in parallel (for pDST should the culture flag positive).*

Step	Abbott	BD	Roche
Inactivation	3:1 IR Vortex 30-60 sec	2:1 BD Max STR Shake 10 times Pre-incubate 5min Shake 10 times	2:1 Cobas MIS Vortex 30-60 sec
Incubation	1 hr Vortex 20-30 sec at 20 min	25 min	1 hr
Sonication	-	-	1 min per sample Centrifuge 60 sec
Extraction + Amplification + Detection	Extraction: 4 hr 22 min (m2000sp) Transfer to m2000rt Amplification/Detection: 2 hr 30 min Total: 6 hr 52 min	Integrated system Total: 3 hr 41 min	Integrated system Total: 2 hr 30 min

Figure 2: Workflow comparison Abbott RealTime MTB and MTB RIF/INH, BD Max MDR-TB, Roche cobas MTB and MTB-RIF/INH

MIS- microbial inactivation solution; IR – inactivation reagent; STR – sample treatment reagent. Adapted from https://doi.org/10.1128/JCM.02168-20.

5.2. Considerations for results interpretation

Many MC-NAATs target multi-copy gene sequences which means they may outperform LC-aNAATs particularly in paucibacillary samples[9]. Certain platforms may only report rifampicin susceptibility while others provide susceptibility information for both isoniazid and rifampicin. Additionally, some platforms have a higher sensitivity for isoniazid resistance detection due to variations in target detection. Therefore, programs and the NTRL should provide clear guidance on result interpretation.

Best Practice 2: Standardising result reporting – South Africa[12]

In South Africa, the TB program worked with stakeholders to standardize reporting across the three diagnostic platforms. The BD MAX MDR-TB assay and Xpert Ultra use different terms for low-level positives, "MTBC Low Positive" and "MTB Trace Detected", respectively, therefore, the LIS was adjusted to match the format for Xpert Ultra "Trace" results for consistency. Since MC-NAATs detect isoniazid susceptibility while Xpert Ultra only detects rifampicin, the consensus was to suppress isoniazid results unless resistance is detected. Ongoing data review will monitor detection rates and susceptibility trends to assess differences between the platforms and their effects on patient care.

5.3. Internal and external quality control

Internal (IQC) and external (EQA) quality control are key elements for ensuring quality of TB testing. The LC-NAATs include an internal positive control in each cartridge to ensure validity of extraction, amplification and detection. For the Truenat assay, it is also recommended to periodically run the positive and negative controls supplied by Molbio to ensure the analyser is functioning correctly and for lot-to-lot verification of reagents. For the MC-NAAT assays, due to potential contamination of the molecular workflow, a positive and negative control must be included in each run. These controls are provided for the Abbott, FluoroType, and Roche assays. Documentation and monitoring of quality control results is necessary to identify any deviations and implement appropriate corrective action. An EQA program, including proficiency testing (PT) and on-site supervision, should deliver prompt feedback, corrective actions, and follow-up. The NTRL should determine the compatibility of existing external proficiency testing scheme for all mWRD platforms. There are various EQA programs for mWRD tests, and several NTRLs have created PT panels to monitor test quality. Programs must ensure existing proficiency testing aligns with new assays and regularly coordinate with suppliers for updates. The GLI has developed a dashboard showing external quality assurance panels and contact information for various providers.

[9] de Vos M, Scott L, David A, Trollip A, Hoffmann H, Georghiou S, et al. Comparative Analytical Evaluation of Four Centralized Platforms for the Detection of Mycobacterium tuberculosis Complex and Resistance to Rifampicin and Isoniazid (2021). J Clin Microbiol.

[12] https://aslm.org/resource/september-2025-labcop-extended-echo-session-from-policy-to-practice-the-operational-realities-of-the-south-african-tb-diagnostic-multiplatform-approach/

Best Practice 3: Role of the national TB reference laboratory in ensuring quality of testing in an expanded decentralised laboratory network in Uganda

Uganda operates an ISO:17043 accredited EQA program for mWRDs, developing and sending proficiency testing (PT) panels to laboratories twice a year via specimen referral. Facilities report PT results using the SRL Uganda Online PT Reporting System (See Figure 3), where NTRL also uploads feedback. NTRL Uganda is now preparing PT panels for NPOC-NAAT (based on the Pluslife MiniDock Detection System), to support NPOC-NAAT quality assurance.

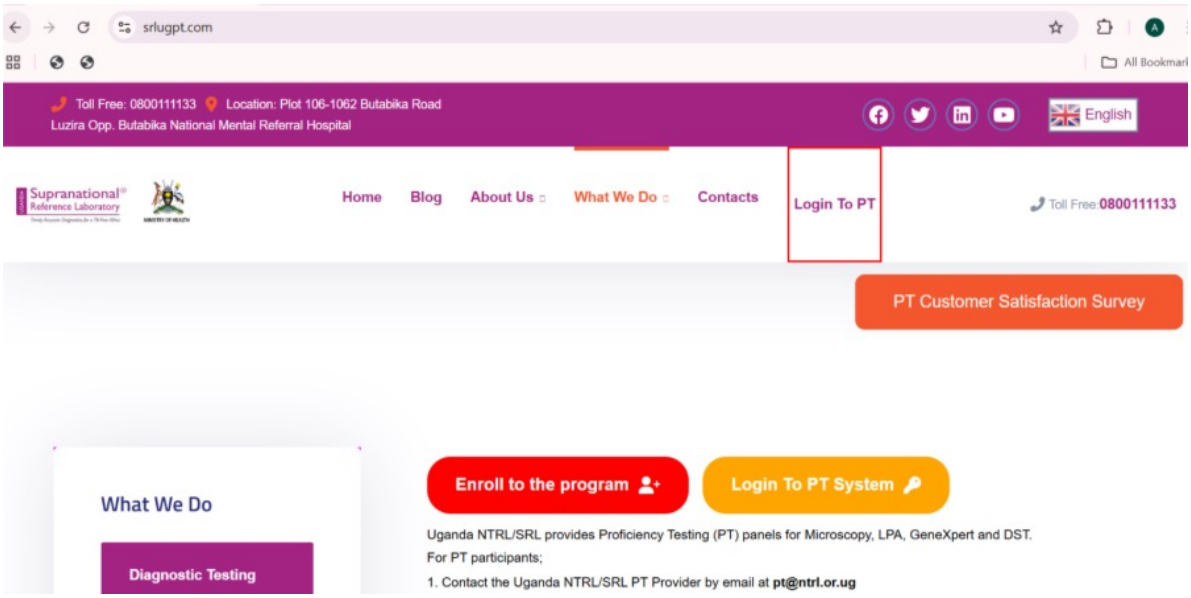

Figure 3: NTRL Uganda PT Reporting System

5.4. Environmental monitoring

This is becoming a key consideration as not all mWRD platforms are “closed” systems. For example, the Xpert Ultra/XDR is considered a closed platform because all extraction and amplification processes occur within the cartridge. In contrast, for the MC-NAAT assays, manual handling of the extracted nucleic acid is required prior to amplification. Therefore, it is essential to develop SOPs for environmental sampling and controls and reinforce good clinical laboratory practices to minimise the risk of contamination. This includes running a blank cartridge and swabbing surfaces using sterile swabs and molecular grade water. A positive result means there is contamination and the area/equipment must undergo a decontamination protocol, for example with 10% bleach followed by 70% ethanol, before re-testing. It is important that decontamination procedures are detailed and the required supplies provided.

Best Practice 4: Environmental sampling and controls – South Africa

Environmental sampling and controls are implemented to detect and monitor potential sources of contamination within the laboratory environment. This includes routine and ad hoc sampling of critical areas such as sample preparation benches, biosafety cabinets, instrument surfaces, reagent storage areas, and high-touch points along the testing workflows. Sampling locations and frequency are determined using a risk-based approach, prioritising areas with a higher contamination risk due to workflow design, testing volume, or historical non-conformances. Results from environmental monitoring are reviewed regularly and used to guide corrective action, workflow adjustment and staff retraining where needed.

5.5. Biosafety considerations

The general guidance for LC-NAATs is that the biosafety considerations are comparable to those for sputum smear microscopy[6]. Therefore, routine laboratory biosafety precautions, such as personal protective equipment, dedicated bench space, minimising aerosol generation and attention to room ventilation and directionality of airflow, should be applied. MC-NAATs are typically placed at the central/reference laboratory tier, where culture or line probe assays are offered. Therefore, biosafety considerations appropriate for that tier level laboratory, including enhanced containment and infrastructure, should be in place.

5.6. Waste management

All clinical specimens and used consumables should be treated as potentially infectious, and standard precautions, as well as national and local regulations for handling and disposal of medical waste should be followed. MC-NAATs tend to generate large volumes of solid and liquid waste requiring adaptions to existing waste logistics. Additionally, Roche systems generate guanidium thiocyanate (GTC), requiring additional considerations for its safe disposal to minimise risk to the environment. (See Recipe 7 on the management of GTC waste and Echo Session on Roche/CDC/ASLM's waste cost assessment framework).

[6] WHO Operational handbook on tuberculosis: Module 3: Diagnosis 2025 [cited 2025 10 August]. Available from: https://www.who.int/publications/i/item/9789240110991

6. Specimen transportation and data management

6.1. Map out specimen transport networks

Well-designed specimen referral networks are the backbone of strong diagnostics network. Where testing is centralised, a strong specimen referral network with defined result return ensures access to timely testing and linkage to care. When integrated with referral for tests other than TB, this can expand the coverage of diagnostic testing to underserved communities.

Best Practice 5: Kenya's Integrated specimen referral system (ISRS)

In Kenya, a sustainable ISRS for all diseases is being implemented to reduce the inefficiencies due to fragmented, vertical specimen transport systems, and increase access to diagnostics. Building on insights gained from a peer-to-peer learning experience in Zimbabwe, a secretariat was formed to facilitate coordination at national and county levels and oversee the implementation nationally. A virtual academy was created to build capacity among end-users including hospital administrators, laboratory staff, health care workers, riders/drivers. The secretariat developed the ISRS policy, guideline, and implementation framework and supported counties in developing tailored operational plans (See example here). These plans detail the structure, operations, and management of the ISRS network within each county. All 47 counties now possess such operational plans and are in the process of launching them and advocating for resources from the county finances and the private sector (e.g., courier services, foundations, manufacturing sector, banks, wildlife conservatories) and other stakeholders. Contributions from the private sector include motorbikes, laboratory equipment/renovations, ISRS commodities and digital subscriptions. To facilitate efficient monitoring of the ISRS, a tracking system has been designed, integrated within the LIMS and accompanied by a dashboard displaying real-time status of specimens and results (See Figure 4).

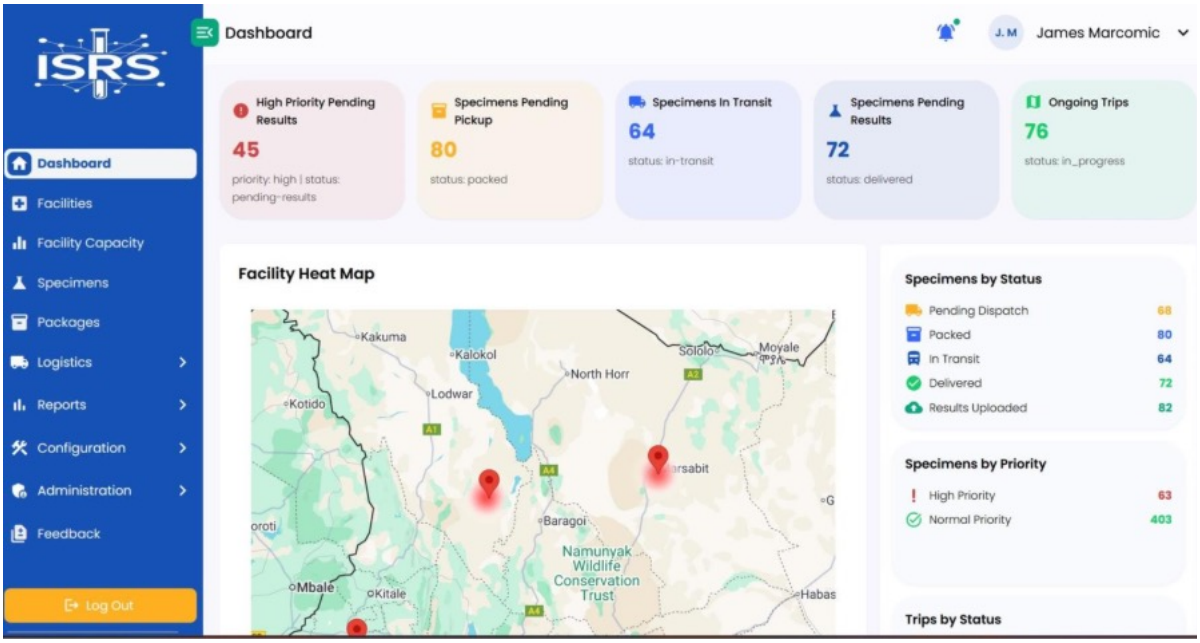

Figure 4: ISRS Tracking System Dashboard in Kenya

6.2. Develop blueprint for data management

The implementation plan should detail any requirements to change the recording or reporting forms to capture the expanding test menu and result formats. Additionally, the program should plan to integrate the digital data output from the instruments through existing diagnostic connectivity solutions and integrated into the laboratory information management system. Core functionalities should include remote performance monitoring, quality indicator tracking, and inventory management. Ideally, systems should be interoperable with patient management information systems to enable timely use of results for patient management and support surveillance. Where possible, automated clinical guidance notes aligned to the algorithm should accompany selected results to strengthen clinical management where a new algorithm has been adopted. Robust procedures must also be in place to ensure data confidentiality, security and reliable backup of patient information.

Best Practice 6: Uganda's connectivity solution, LabXpertDS

LabXpertDS is a locally developed data connectivity solution that enables electronic result reporting to clinicians and can be freely customized as needed. Since 2022, LabXpertDS has connected over 300 GeneXpert machines, 41 Truenat machines, and 70 digital chest X-ray machines, reporting over 3.5 million results and supporting the linkage of more than 2,800 persons with MDR/RR-TB to DR-TB treatment initiation centres. Successful deployment of this platform requires laboratory leadership support, skilled staff (system administrators, software engineers and field support teams), and resources for internet, training, and mentoring.

7. Monitoring performance indicators

As new tests are introduced, the program should assess whether existing recording and reporting forms require modification and identify the necessary tools for effective monitoring and evaluation. At a minimum, programs should align with the Framework of Indicators and Targets for Laboratory Strengthening under the End TB Strategy that assess the program's ability to detect TB using mWRDs provided universal DST and maintain quality of testing. Additionally, the WHO standard on universal access to rapid tuberculosis diagnostics provides a set of benchmarks that allow the program to monitor improvements in the TB diagnostic cascade. After establishing relevant indicators, the program must also determine the frequency of indicator monitoring and develop a comprehensive plan for implementing corrective actions as needed. Programs should also monitor the rate of ordering of new tests to identify sites with unexpectedly high or low testing rates that may need additional training or sensitisation. Furthermore, ongoing engagement with suppliers is essential to address potential challenges or recurring errors, thereby ensuring effective implementation.

Box 6 Country Example: *Uganda aligns its indicators to the Framework of Indicators and Targets for Laboratory Strengthening under the End TB Strategy. In the initial stages of implementation, recording and reporting is achieved by tweaking the available HMIS tools until the ministry of health makes a revision of tools to fully accommodate the new mWRD. For example, the following operational indicators will be prioritised during the early phase of implementing NPOCs: # of samples tested, # of samples rejected, # of positive NPOC results (positivity rate), # of positive NPOC tests with DST result, # Rif Resistant patients, # of error/invalid results (error rate), # devices working, # of reagent tests remaining. The outcome indicators will focus on how NPOCs are impacting on bacteriological confirmation and proportion of patients testing using mWRD in the respective testing facilities. (See Annex 1: Uganda M&E Framework).*

Annex 1: Example M&E Framework

Courtesy of the Uganda TB Reference Laboratory

Monitoring and Evaluation framework for the NSP 2025/26 – 2029/30

Goal	To reduce the incidence of TB by 6.5% from 198/100,000 population to 185/100,000 and the proportion of Leprosy cases that are children from 17% to less than 3%											
Results	**Indicators**	**Indicator definition/ calculation**	**Data sources**	**Periodicity**	**Who collects data?**	**Level of data**	**Baseline Value (Year)**	**Annualised Targets**				
SO 3: To increase treatment coverage for all forms of TB from 91% to 95% by 2029/30												
SO 3.3.1 Percentage of presumptive TB patients who accessed mWRD tesing increased from 81.5% to 90%	Proportion of individuals with presumptive TB that are tested with a mWRD	Number of individuals with presumptive TB that are tested with a mWRD /Total number of presumptive TB Cases Identified *100	DHIS2	Quarterly	District Biostat, NTLP	District National	81.50%	83%	85%	88%	89%	90%
SO3.4 Proportion of notified new and relapse TB cases that are bacteriologically confirmed increased from 66% to 90%	The percentage of all new and relapse TB cases notified whose diagnosis was confirmed bacteriologically	Proportion of notified new and relapse TB cases with bacteriological confirmation	DHIS2	Quarterly / Annually	District Biostat, NTLP	District National	66% (2024/25)	75%	78%	82%	86%	90%
SO 3.4.1 : The proportion of primary health-care facilities that have access to mWRDs either on site or through sample referral increased from 39% to 60%	Proportion of primary health-care facilities that have access to mWRDs either on site or through sample referral	Primary health-care facilities that have access to mWRDs either on site or through sample referral/ Total number of Primary health-care facilities *100	Labspatial Analysis Report	Annually	NTRL, NTLP	National	39% (2024)	40%	45%	50%	55%	60%
SO 3.5: The proportion of notified new and relapse TB patients tested using mWRDs increased from 84% to 90%	Proportion of notified new and relapse TB patients tested using WHO recommended rapid tests	TB patients diagnosed using WHO recommended rapid tests/Total number of TB patients (new & relapse) notified *100	DHIS2	Quarterly, Annually	District Biostat, NTLP	District, National	84% (2024/25)	85%	86%	88%	89%	90%

Goal	To reduce the incidence of TB by 6.5% from 198/100,000 population to 185/100,000 and the proportion of Leprosy cases that are children from 17% to less than 3%											
Results	**Indicators**	**Indicator definition/ calculation**	**Data sources**	**Periodicity**	**Who collects data?**	**Level of data**	**Baseline Value (Year)**	**Annualised Targets**				
SO 3: To increase treatment coverage for all forms of TB from 91% to 95% by 2029/30												
SO 3.7 MDRRR-TB Treatment coverage increased from 58% to 80%	Proportion of diagnosed MDR-TB patients who are enrolled on appropriate MDR-TB treatment	Proportion of diagnosed MDRRR-TB patients who are enrolled on appropriate MDR/RR-TB treatment	DHIS2	Quarterly / Annually	District Biostat, NTLP	District National	58% (2024/25)	60%	65%	70%	75%	80%
SO 3.9: The proportion of laboratories participating in EQA for molecular methods increased from 85% to 95 %.	Proportion of laboratories participating in EQA for molecular methods	Laboratories participating in EQA for molecular methods/Total number of TB Molecular laboratories *100	NTRL EQA Data Base	Biannually	NTRL	National	85% (2024/25)	87%	89%	91%	93%	95%
SO 3.9.1 : The proportion of TB testing laboratories that achieve a turnaround time of ≤ 48 h for ≥ 80% of samples received for mWRD testing increased from 36% to 80%	Proportion of TB testing laboratories that achieve a turnaround time of ≤ 48 h for ≥ 80% of samples received for mWRD testing	TB testing laboratories that achieve a turnaround time of ≤ 48 h for ≥ 80% of samples received for mWRD testing/ Total number of mWRD laboratories *100	DHIS2	Quarterly, Annually	NTRL,NTLP	National	36% (2024)	40%	50%	70%	75%	80%
SO 3.9.2: The proportion of laboratories passing EQA for molecular methods with satisfactory score increased from 73% to 90%	Proportion of laboratories passing EQA for molecular methods with satisfactory score	laboratories passing EQA for molecular methods with satisfactory score/Total number of laboratories passing EQA for molecular methods *100	NTRL EQA Data Base	Biannually	NTRL	National	73% (2024/25)	77%	80%	83%	86%	90%
SO 3.9.3: The proportion of laboratories participating in EQA for Microscopy from 66% to 80%	Proportion of laboratories participating in EQA for Microscopy	Laboratories participating in EQA for Microscopy/ Total number of AFB Microscopy laboratories *100	NTRL EQA Data Base	Quarterly	NTRL	National	66% (2024/25)	69%	72%	74%	77%	80%

Goal	To reduce the incidence of TB by 6.5% from 198/100,000 population to 185/100,000 and the proportion of Leprosy cases that are children from 17% to less than 3%											
Results	**Indicators**	**Indicator definition/ calculation**	**Data sources**	**Periodicity**	**Who collects data?**	**Level of data**	**Baseline Value (Year)**	**Annualised Targets**				
SO 3: To increase treatment coverage for all forms of TB from 91% to 95% by 2029/30												
SO 3.9.4: The proportion of laboratories passing Microscopy EQA with satisfactory score increased from 70% in 2024 to 85%	Proportion of laboratories passing Microscopy EQA with satisfactory score	Laboratories participating in Microscopy EQA with satisfactory score /Total number of laboratories participating in Microscopy EQA *100	NTRL EQA Data Base	Quarterly	NTRL	National	70%	75%	80%	85%	85%	85%
SO3.10: The proportion of patients notified with bacteriologically confirmed Rifampicin resistant (RR) pulmonary TB with DST results for Fluoroquinolones (FQ) increased from 51% to 90%	Proportion of patients notified with bacteriologically confirmed Rifampicin resistant (RR) pulmonary TB with DST results for Fluoroquinolones (FQ)	Patients notified with bacteriologically confirmed Rifampicin resistant (RR) pulmonary TB with DST results for Fluoroquinolones (FQ)/Total number of Patients notified with bacteriologically confirmed Rifampicin resistant (RR) pulmonary TB *100	DHIS2	Quarterly / Annually	District Biostat, NTLP	District National	51% (2024/25)	73%	80%	85%	87%	90%
SO 3.11: The proportion of notified patients with bacteriologically confirmed RR and FQ resistant pulmonary TB with DST results for Bedaquiline and Linezolid increased from 60% to 100%	Proportion of notified patients with bacteriologically confirmed RR and FQ resistant pulmonary TB with DST results for Bedaquiline and Linezolid	Patients with bacteriologically confirmed RR and FQ resistant pulmonary TB with DST results for Bedaquiline and Linezolid)/Total number of patients with bacteriologically confirmed RR and FQ resistant pulmonary TB *100	DHIS2	Quarterly / Annually	District Biostat, NTLP	District National	60% (2024/25)	70%	80%	90%	95%	100%
SO6.5 The percentage of diagnostic and treatment units reporting no stock outs of TB laboratory supplies (reagents, consumables) increased from 88% to 95%	Proportion of diagnostic and treatment units reporting no stock outs of TB laboratory supplies	Number of diagnostic and treatment units reporting no stock out of TB laboratory supplies and consumables/Total number of TB diagnostics and treatment units	LIS/DHIS2	Quarterly, Annually	D Biostat, NTLP	District, National	88%	89%	90%	92%	93%	95%

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