GH LABS NAATOS PRODUCT FEASIBILITY ASSESSMENT

DELIVERABLE: VOICE OF THE CUSTOMER ANALYSIS PART II

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PRESENTED BY: MARKET ACCESS AFRICA

Market Access Africa is pleased to submit this second report (PART II) for an additional 4 countries, to GH Labs for market research and information gathering supporting the product development and commercialization of NAATOS. Some market insights represent a "lighter touch" vs the primary report as engagment was elicited with a limited set of stakeholders and institutions.

Botswana

1. **Diagnostic landscape**
2. Stakeholder feedback
3. Policy considerations
4. Deployment considerations

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Diagnostic Landscape | The majority of TB testing is done in the public sector free of charge and through a network of 53 National Health laboratories

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Key messages

Implications for NAATOS

1 The public sector is the main provider of TB testing, with testing only done in laboratory settings

- Public Sector processes largest proportion of TB diagnostics (>95%) and testing in private sector is limited. Most of the 35+ private sector laboratories conduct on microscopy and serological tests for TB, and very few private labs conduct molecular testing with GeneXpert and Truenat
- NAATOS might be difficult to integrate into the diagnostic algorithm because it does not provide the drug resistance profile required for TB initiation

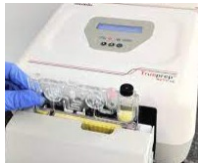
2 The current diagnostic algorithm is not optimized to screen and diagnose all possible TB cases

- The current focus on laboratory based testing using GeneXpert and TB LAM (predominantly for AHD clients and co-infected) potentially misses presumptive cases that fail to produce a spot sputum or those lost to follow up
- Lack of universal screening misses out asymptomatic cases within the communities and health facilities
- Introducing TB diagnostics at lower levels of care will strengthen active case finding

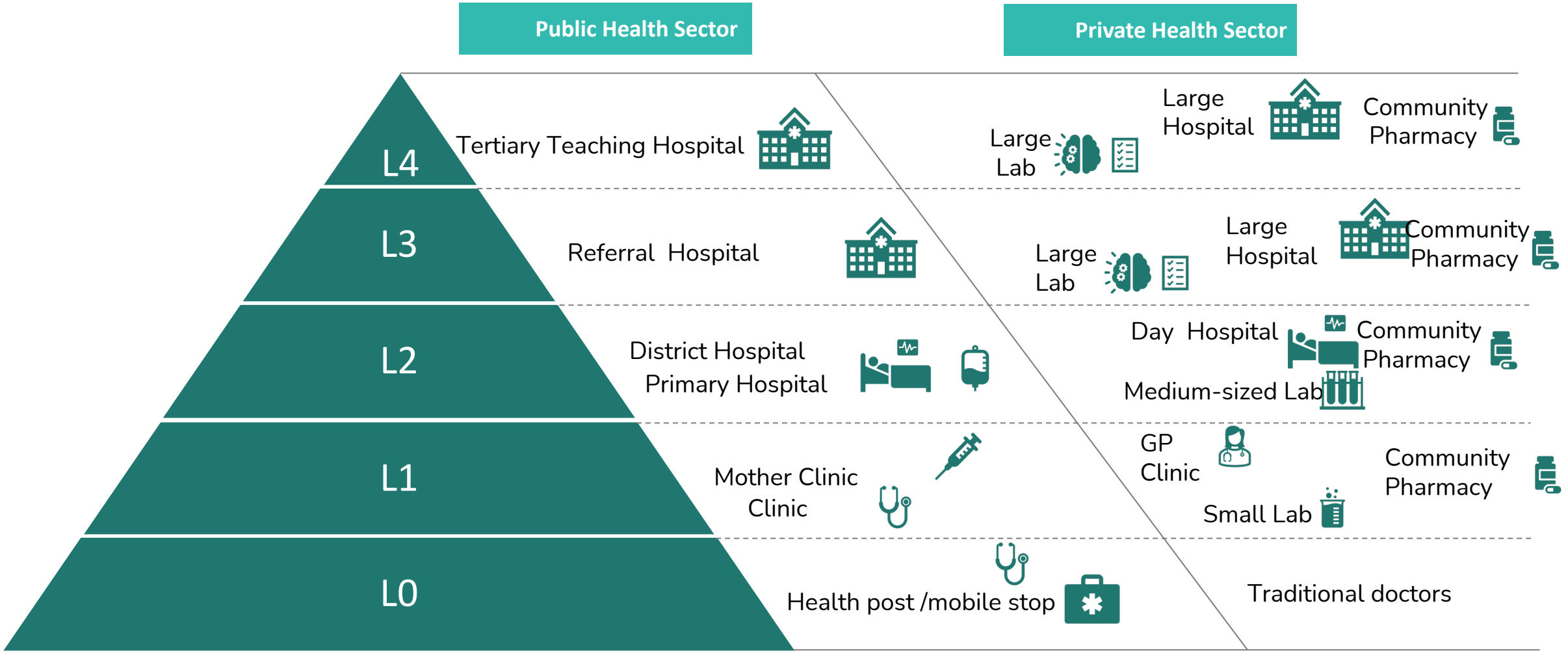
3 NAATOS might have a role to play in active case finding

- NAATOS presents an opportunity to serve as both a triage test and a screening tool within the active case finding strategy

Diagnostic Landscape | The current diagnostic tools are not optimized and the lab pushes back on adoption and scale up of POCTs

Trend and shifts	Description
1 Dominance of GeneXpert 	• GeneXpert Ultra is the recommended initial test for TB although some laboratories are still using ZN and fluorescent microscopy to diagnose TB • The stool processing method for GeneXpert was recently adopted for pediatric TB diagnosis • TB Culture ,DST and LPA are conducted only at the National TB Reference Laboratory with all positive cases referred from all TB testing laboratories country wide
2 New Technologies 	• The adoption of new technologies has not be optimal , to date the public sector is still to adopt the MolBio platform or other WHO recommended TB molecular testing platforms • The TB LAM test was adopted but still remain a laboratory based test due to reported challenges with “accountability and reporting of bedside tests” • CRP for TB triage is currently being trialed by the BNTP also as a laboratory based test
3 Stock outs 	• The stock out of Xpert cartridges was reported to be one of the biggest challenge/ barrier to timeous and effectiveTB diagnosis • There has been a change of distributorship for the Cepheid products in country, a new distributor was recently appointed • There have been challenges with the award of procurement contracts by the central procurement entity and purchases were being done using RFQs (request for quotations)
4 Service & maintenance	• There has been no service contract for the GeneXpert platforms for 5 years • Once off calibration was paid for by a CDC implementing partner during Year 1 of them implementing the laboratory systems strengthening grant • No calibration was done • No replacement of unfunctional modules was being done

Patients have a variety of treatment and diagnostic care options in the public and private sector in **Botswana**



Patient Pathway| TB screening is symptom-driven, but at L0 and in the majority of L1 health facilities, no diagnostic TB testing is done

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Patient arrival at clinic

- Goes through registration system
- Patient visit record
- Vital signs recorded
- If coughing patient is given a mask and fast tracked

Consultation Room

- Patient moves to consultation room
- TB screening done either as part of vital signs collection for ART clinics or consultation for general OPD services

Patient Assessment

- Assess whether patient has TB symptoms
- Symptomatic patients are captured in the TB suspects register

YES

Non symptomatic patients are usually missed Those who can not produce sputum can be treated empirically

TB symptom management

- Patients with TB symptoms given 2 specimen containers,
- One to collect a spot sputum at the facility and the other to collect early morning sputum and bring to health facility
- Non sputum samples can be collected

Sample handling & referral

- Facilities without onsite laboratories have scheduled access to transport to send samples to testing labs
- Most facilities do not have refrigerators to temporarily store samples appropriately

TB testing is only done in 13 clinics with laboratories the remainder refer to primary and district hospitals with lab facilities

Sample reception , processing

- Samples received from collection sites can be rejected based on laboratory criteria
- Most reported causes for rejection include receiving empty sample jars, samples without forms

Time to results is compromised as samples are rejected, and referring facilities have to trace the TB suspects to recollect new samples

Diagnosis and results

- TB testing is done on 4 module Genexpert or using microscopes where Genexpert are not available or not working
- Positive samples are referred to the reference lab for TB culture and Drug Sensitivity Testing

TB culture takes long to yield results

TB Management

- TB treatment and care is based on the outcome of laboratory testing
- Some patients are being initiated on treatment without a drug resistance profile because TB culture takes results TAT is long

xx Diagnostic gaps

Time

Patient presentation

Initial Screening and sample collection

Diagnosis

Patient treatment and management

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Diagnostic Landscape | Testing at lower levels of care and strengthening chain of custody process in the TB diagnostic pathway will aid in improving TB diagnosis

Challenges and proposed solutions for Clinical Workflow Improvement

	Missed TB Patients	Sample collection and transportation	Delays resulting in loss to follow-up	Long lead time between results and treatment
Challenge				
Proposed solutions	• Explore community-based approaches for point-of-care testing to identify TB cases outside of health facility settings • Implement TB triage and diagnostic testing at lower levels of care to improve case identification and reduce waiting times and loss to follow up	• Non sputum TB samples and test must be optimized • Sample transportation must be delinked from ambulances to ensure timeous referral of samples for testing thereby shortening time to results	• Strengthen chain of custody processes at every step in the clinical and diagnostic pathway to ensure only samples that meet the criteria for testing are moved to the next level • And any errors are corrected as close as possible to the point of collection	• The clinic workflow currently does not proactively and actively follow up patients with positive results or prioritize confirmatory testing or immediate initiation of TB treatment

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Product Value Proposition | Stakeholders expressed mixed views on the utility and value add of NAATOS in the Botswana TB program

Key takeaways

NAATOS presents an opportunity to serve as a triage test for TB and cost is going to a key determinant for its use

This is because additional testing for drug resistance profiles will be required for TB treatment initiation and hence its utility as a standalone test is reduced

There is a strong view from program managers and clinicians that the "laboratory does not like POCT, they prefer lab based testing"

This is based on their experience with the TB LAM which is being done in the lab and also the "push back" from the lab when CRP for TB triage was started "..all CRP tests are being sent to the lab"

Being a non sputum test the NAATOS is attractive due to convenience sampling. Sputum samples attract some stigma in health facilities with dedicated coughing spots clearly marked in clinics and hospitals

Stakeholder feedback on NAATOS value proposition

Simplifying the diagnosis of TB	• Stakeholders express a strong interest in simple, affordable, and easy-to-use diagnostic solutions that can be performed as close as possible to the patient • Convenient sample was a huge positive • Currently only clinicians are performing TB screening and given HRH issues some cases are missed • Service , calibration and stock outs challenges with the Genexpert have emboldened key opinion leaders of the need to find alternative ,comparable diagnostic tests
Negative Perception of NAATOS	• NAATOS not valuable as a independent screening test but can go hand in hand with other tests Being a tongue swab test the perception is low recovery since TB is concentrated in areas with immune system • Recovery of MTB in clients with disseminated TB or who are immunocompromised and in low HIV prevalence settings anticipated to be a huge barrier when using a tongue swab • Not being able to offer a drug resistance profile, or distinguish between MTB and MOTT
Challenging POCT TB test adoption landscape	• There is a strong perception of political interference in the technology adoption process, one KOL indicated "you have to win over a politician" and the other said " its kind of political ..." whilst the other identified tendering, procurement as key barriers for adoption stating that it depends on "who wants what .. and this can be politicial" on being asked about the context of introducing a new test
Decentralized TB testing	• Botswana has a well established community TB care program which can be leveraged on to provide decentralized testing • New tests with lower biosafety risk can be easily deployed for use outside of laboratory settings bring the testing closer to where people are • Current diagnostic tools are reported not to fully satisfy operational challenges in LMICs especially need for electricity , temperature controlled environments , cold chain logistical support and highly skilled technical staff • Genexperts which were once deployed in non lab settings were pulled back because clinicians argued testing was not their job and they were not being paid for it

Product Specification | Stakeholders provided feedback on the key considerations for NAATOS adoption (1/4)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Invalid rate	• NAATOS device-related failure for product feasibility must achieve a failure rate of <35%	• Sensitivity of test will be below that of Genexpert because of sample type	• Need to conduct sensitivity analysis on different sample types especially for extra pulmonary TB
Walk away operation	• NAATOS V1 requires only two to three user interactions before walking away and returning to record the result (excluding sample prep)	• Sample preparation step is critical and must be made easier with minimum complexity to allow staff to do other things whilst testing /processing is underway • Test must require no calibration and no maintenance	• Prototypes must require less infrastructure ,must be portable and can be used in a small facility with few rooms
Time to result	• NAATOS V1 must produce a result within <60 min (including sample prep time)	• Ideal: 25-30 minutes like other RDTs • If the test results take longer, it will take longer to serve patients and others might decide to leave the facility without being assisted	• Strong end user training must be emphasized • Invest in streamlining the workflow and detailing all required troubleshooting steps
Transportation	• NAATOS V1 must not require cold chain storage during shipment or storage	• Ambient temperature conditions for storage, handing and use • No cold chain requirements • Delivery vehicle to Central Medical Stores must meet stated specifications	• N/A
Shelf life	• NAATOS V1 must have a shelf life of >12 months • (Corporate presentation: shelf life of >18 months from the date of manufacturing)	• Requirement is that kit must be delivered with 80% remaining shelf life	• N/A

Product Specification | Stakeholders provided feedback on the key considerations for NAATOS adoption (2/4)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap/ Quotes from KOLs
Storage conditions	NAATOS V1 must be stored at 0 °C to 40 °C and 90% humidity	• Temperatures rarely exceed 40°C • Most areas usually hot and dry • Most health posts and some clinics do not have access to electricity and cold chain equipment • In the lab storage is "mostly (2-8)degrees or room temperature for reagents , cane be -20 degrees for reagents and -80 degrees for samples and DST drugs"	• N/A
Quality Control of Operation conditions	NAATOS V1 must operate at: • Temperature: +15 °C to +35 °C • Humidity: 25% to 80% relative humidity	• "Will require a swab based EQA program" • "QC must be done with every test " • Most areas usually hot and dry • Most health posts and some clinics do not have access to electricity and cold chain equipment	• Lyophilized /dried swab for EQA
Multiuse platform	NAATOS V1 must be designed as a multi target disease platform (TB, STI, etc.)	• "We have an obvious HIV/TB focus but if it can multiplex then cancers a priority" • " Cancer, STI, Hepatitis, NTDs and Leprosy" • "I am TB and impartial to TB l do not care about anyone else"	• Ability to multiplex will improve utility and acceptability to laboratory and to vertical programs
Manufacturing	NAATOS V1 must be manufactured at scale and with device fabrication and assembly process that is compatible with high-volume automation	• "Kit size of 10 test would be ideal for small sites" • "Battery must last longer than 8 hours and 6 spare rechargeable batteries must be provided"	
Product price	NAATOS V1 must have a price of no more than $5 USD per test • At full production (10MM units/year) • At initial release, 3x full production (1MM units/year) • At pilot production, 10x full production (50k units/year)	• "Must be affordable like the TB LAM" • "$3 per test " • "The issue of cost or affordability is above my pay grade"	• "Genexpert is expensive , government has not been able to buy new platforms or maintain current systems due to costs" – CDC TB Activity Manager • "Value for money" " Affordable , cost effective as social protection of TB patients is needed to prevent loss of productivity , cost less than 20% of household income" Fmr NTP Manager

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Policy Considerations | Critical policy enablers highlighted by stakeholders for a new TB NAAT test

1

Performance and Maintenance

- Sensitivity and specificity must meet WHO recommendations
- “WHO requirements are a bare minimum, there will be need to customize to Botswana’s needs”
- Throughput will be important for lab use consideration
- Should not require calibration and service and it if does , there should be no expectation to engage professionals to do calibration and QC
- End user trainings will be important and there is need to invest in improving the work flow

2

Evidence required and introduction process based on previous experience

- WHO recommendation is a pre requisite , research studies and in country verification is needed. A research proposal /protocol has to be developed and submitted to the BNTP
- ”With the Line Probe Assay (LPA) we had to convince the laboratory manager, win over the technical team and cascade to relevant stakeholders… it was a NTRL led process”
- “BNTP and lab conducts a clinical validation study that is then reviewed by the TWG”

3

Considerations for Implementation and Patient Flow Integration

- “Cost, model of delivery, temperature controls an who can be the best person to use the test “
- Registration with Botswana Medicines Regulatory Authority (BoMRA) is required from October 2023
- Piloting the test is required before implementation as was done for stool sample for pediatric patients and what is being done now for CRP for TB triage
- “For TB POCTs there is need to convince the laboratory like what the HIV program did, so many patients will be served on time, so many patients who have symptoms but can not produce sputum”

Policy Considerations | TB products generally have a well-defined but time-consuming policy pathway before it can be adopted and procured by NDOH

Policy process step	National TB Program	Private sector considerations
1 National policy endorsement 	• WHO GDG endorsement is a prerequisite for NTP adoption • Test now needs to registered with BOMRA • Local evidence required in the form of a pilot ,the laboratory and NTP are critical stakeholders	• Private sector expected to follow national guidelines • Current practice indicates some labs are using serology tests , some are using GeneXpert, some are referring to public sector laboratories
2 Clinical evaluation 	• In-country clinical evaluation will need to be conducted by National TB Reference Laboratory in collaboration with the NTP	• Private sector labs and facilities may conduct their own independent lab evaluation
3 Local studies and country planning 	• A protocol is developed by the NTP and Laboratory which details the sites and numbers to be tested and the reference methods to be used for assessment	• Private sector facilities and labs may conduct their own independent lab evaluation
4 Adoption, toolkit, phased implementation 	• Roll out new diagnostic tools is handled by NTRL and NTP usually with technical support from the PEPFAR TB program or their implementing partner • NTP will update the diagnostic algorithm and disseminate to all healthcare workers through trainings and mentorship	• Reimbursement potential by Medical Insurance Schemes is a huge consideration for the private sector

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Deployment Considerations | Interviewees highlighted specific challenges that may influence adoption of NAATOS by implementers and policy stakeholders

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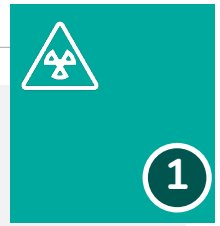
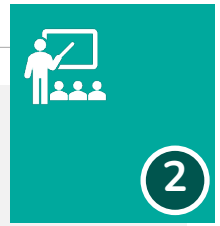


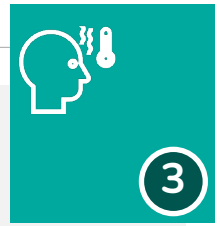
1 Workflow Integration

Symptom screening either done in central screening point or in specific departments
Currently clinicians are doing TB screening and those not using electronic medical records(EMR) usually miss TB screening because TB screening a mandatory step when consulting using EMR



2 Staff Training and Workload

There is need for adequate end user training
A community health worker must be able to use
Additionally incentives must be considered for decentralized testing due to Human Resources for Health (HRH) challenges
Small sites have few rooms and limited space so portability becomes critical



3 Patient Sample Collection

We are over relying on sputum and they are patient categories that have symptoms but fail to produce sputum
Use of a convenience sample is welcome
It also lowers the biosafety risk and allows the test to used in places with minimum infrastructure and by even community health workers

4 Resistance to Change

Resistance to change is a common barrier in adopting new technologies. Buy in from the MOH /NTP is critical .The laboratory has been pushing back on TB POCTs but ”people are liking the TB LAM to the extent of using it on HIV negative patients”

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Deployment Considerations | Recommendations and best practices for smooth product adoption

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1 **Needs Assessment and Stakeholder Engagement**

Promoter must proactively engage the NTP and NTRL to communicate what is new ,get their buy in and understand expectations

2 **Training Support & Ease of use**

Plan for end user training , streamline workflow , test must not require maintenance and calibration to enable decentralized use at community health worker level

3 **Ensure supply chain reliability and uptime of platform**

Establish mechanism to prevent stock outs of test kits, calibration and maintenance failure leading to interruption of services, which most KOLs cited as the biggest challenge with the current dominating platform GeneXpert

4 **POCT advocacy**

Consider supporting overall decentralization of testing or adoption of POCT policies and guidelines leveraging on the work done by the HIV Testing Services program. This is so because of the general push back from the laboratory is adopting POCT for other disease conditions

DRC

1. **Diagnostic landscape**
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Diagnostic Landscape | TB diagnosis is mostly (>95%) done through the public sector; Molecular tests are used in DR Congo as an initial test

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Key messages	Implications for NAATOS
1 TB Prevalence and case notification	• Tuberculosis (TB) constitutes a major public health problem in the DRC. According to the 2022 World Health Organization (WHO) global report, the country is ranked among the 30 countries with a high burden of TB, drug-resistant TB and co-infection TB/HIV. The country ranks second in Africa on the TB, TB/HIV and drug-resistant TB list • In 2021, the incidence rate of tuberculosis in the DRC was estimated at 318 cases per 100,000 inhabitants. The expected number of TB cases according to the WHO was estimated at 305,000 and the annual increase in cases was 6% compared to 13% in 2020.During the same year, the country notified 215,787 cases of all forms of tuberculosis, including 214,408 incident cases, 13% were children aged 0-14 years • In 2022, the country reported 248,761 cases of TB all forms, out of 287,969 expected cases, which represent 86% of the 2021-2023 TB National Strategic Plan target. As for drug resistant TB, the DRC notified 1,614 cases out of 6,000 estimated
2 Most of the TB diagnosis and management done through the public with a link to the private sectors	• Over 95% of TB diagnosis happen in the public sector The majority of patients with TB symptoms seek care in the Public sector. • In DR Congo, tuberculosis care is standardized and decentralized. To date, nearly 2,132 diagnosis and treatment centres (CDTs) treat patients with tuberculosis. The National Tuberculosis Program has a network of laboratories made up of nearly 2,132 microscopy laboratories in the periphery, 27 provincial laboratories for quality control (QC) including among them two (in Lubumbashi and Kisangani) which are intended to carry out culture on solid medium and a National Reference Laboratory (LNRM) carrying out culture (on solid and liquid medium) and drug sensitivity tests (DST) • The provision of care is sometimes provided by private structures in complementarity or in synergy with public structures. The private sector is subdivided into two categories: the private for-profit sector and non-profit faith-based organizations. Apart from the structures integrated into the NTP network, the mapping of private sector laboratories does not exist. As part of the current TB National Strategic Plan, it is planned to list private laboratories which offer TB diagnosis and which are not integrated into the NTP network. • For the provision of certain specific services, the NTP has signed contracts with private structures. Particularly for preventive and curative maintenance of certain equipment
3 DRC's TB products flow through multiple channels	• Available diagnostics tests include sputum smear microscopy (SSM), chest x-ray (CXR), GeneXpert, Truenat, fluorescent microscopy, microscopy MCNS, Culture & DST, immunodiagnostics, LPA, LAM and antibody tests • Microscopy was, in its time, the basis of tuberculosis screening. Currently, molecular tests are used in DR Congo as an initial test in sites that have a molecular tool (Truenat and Xpert). The country currently has approximately 363 GeneXpert machines distributed across all provinces and 38 Truenat machines in 4 provinces • LF-LAM is only implemented in a few facilities and a few provinces supported by some implementing partners but not coordinated by the TB Program in DRC

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Diagnostic Landscape

Patient arrival at clinic

- Goes through queueing system / security clearance
- Proceeds to records desk for file creation and recording

Triage

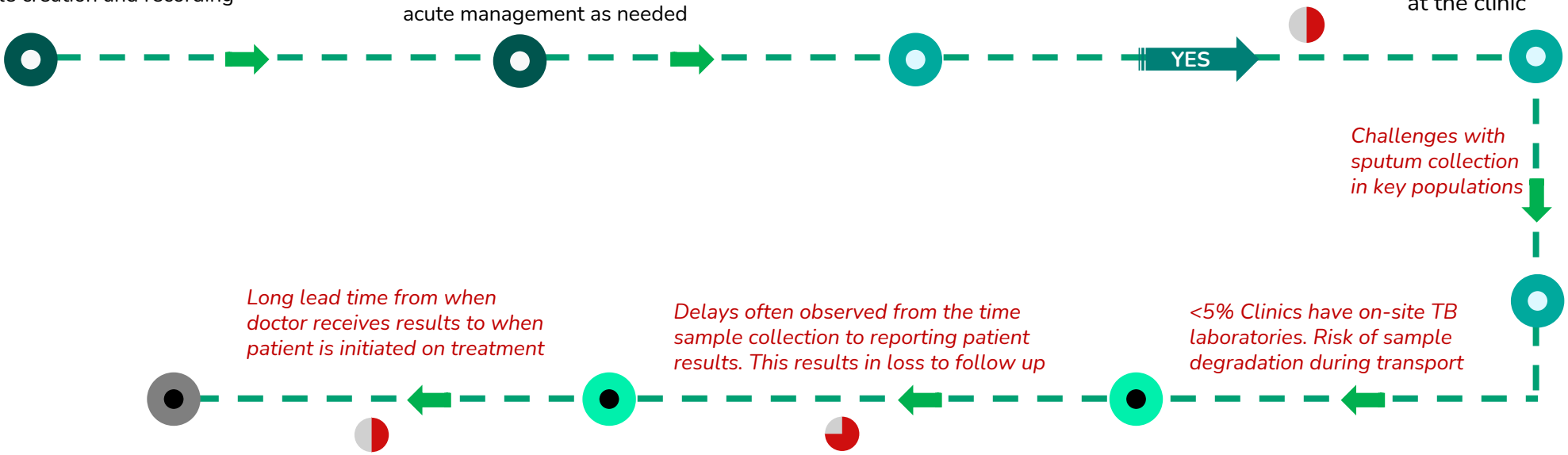
- Depending on the symptoms, patients are directed to either Chronic Management (HIV, NCD, etc.) for ongoing conditions or acute management as needed

Medical consultation

- Patient moves to Vital room for recording of vitals and creation of patient record

TB symptom management

- Patients with TB symptoms given a sputum cup, with options for sputum collection at home or at the clinic



Sample collection

- Sputum for microscopy, Truenat and GeneXpert.
- Gastric lavage for patients unable to spontaneously expectorate.

TB Management

- If positive, initiate Drug Sensitive TB Rx
- TB treatment is free throughout the DRC after the patient has been diagnosed with the disease.

Diagnosis and results

- Diagnostic process duration can take up to two hours for new patients
- Results available within 1 to 2 hours to the clinician
- TB result communicated through Community Health Care Workers - assist with the transfer of results

Sample submission and diagnosis

- Collected samples sent directly to the TB centre
- A focal point at the TB National Reference Laboratory and in each province closely monitor the transport of samples and regularly evaluate the system

xx Diagnostic gaps

- Time
- Patient presentation
- Initial Screening and sample collection
- Diagnosis
- Patient treatment and management

Diagnostic Landscape | Time to initiation onto TB treatment hinders proper follow-up, emphasizing the need for improved diagnostic strategies

Challenges and proposed solutions for Clinical Workflow Improvement

	Limited accessibility to testing and treatment	Staffing and personnel challenges at L1 & L2	Delays resulting in loss to follow-up	Challenges with sputum testing
Challenge				
Proposed solutions	• Build capacity for testing at L1 & L2 facilities • Ensure equitable distribution of essential diagnostic across Level 1 and Level 2 facilities to enhance TB diagnosis capabilities • Facilitate NTRL and the TB Provincial Laboratories to execute their mandates • Strengthen mechanisms for Equipment maintenance, Service and Repair	• Provide capacity building to staff, to enable them manage multiple tasks efficiently • Address staffing shortages through recruitment strategies.	• Optimized Sample Transport System: Strengthen the Hub Riders network with more frequent pickups and improved logistics. • Introduce better storage and handling protocols to preserve sample integrity during transit • Support the implementation of the current algorithm to make it responsive to the TB Epidemic in the country	• Standardize, structure and strengthen the specimen referral system and devise appropriate sample mechanisms applicable to each Province • Provide alternative diagnostic methods to sputum testing / focusing on non-sputum sample types • Establish access to point of care molecular testing at lower-level facilities like NAATOS

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Product Value Proposition | Stakeholders expressed several positive attributes of NAATOS that makes it an attractive option for adoption

Key takeaway

NAATOS presents an opportunity to serve as both a triage test and a screening tool within DRC's Test & Treat (TT) algorithm, enhancing the efficiency and accuracy of TB diagnosis.

Stakeholder feedback on NAATOS value proposition

Patient-Centric and Affordable Solutions	• Stakeholders express a strong interest in patient-centric, affordable, and easy-to-use diagnostic solutions. • The envisaged Nucleic Acid Lateral Flow Test for TB aligns with this vision, providing a closer-to-patient, cost-effective, and user-friendly option that could significantly benefit the community in terms of decentralized and democratised accessibility as well as time efficiency.
Positive Perception of NAATOS at L1 Facilities	• The feedback underscores a positive perception of Nucleic Acid Lateral Flow Tests (NAATOS) at L1 facilities. Stakeholders view them as well-understood, easy to introduce, and straightforward in implementation. • The familiarity and feasibility of lateral flow tests, coupled with their adaptability to clinic workflows, contribute to the optimistic outlook on NAATOS adoption.
Challenging Traditional Testing Approaches	• There is a recognized need to challenge traditional testing approaches and embrace more proactive strategies. The urgency of implementing NAATOS as a portable DNA-based diagnostic tool, linked to care, is emphasized. • This shift is positioned as a community-oriented approach to interrupting transmission, addressing the impractical timelines associated with conventional testing paradigms.
Integration into the TT Algorithm	• Similarly, as in neighbouring countries, beyond TB clinics, the test is seen as adaptable to routine generalist clinical care, offering scenarios like routine tongue swabs upon clinic entry, thereby capturing more TB clients lost through low sensitivity of the 5-symptom screening method. The flexibility of integration, especially with HIV care, is emphasized, aligning with the need for solutions beyond traditional TB algorithms.
Impact on TB Contact Testing Programs	• By simplifying sample collection, particularly among high-risk groups and household contacts, NAATOS is viewed as a potential game-changer in increasing TB diagnoses. This aligns with the broader goal of enhancing community-based testing and improving outcomes within high-risk communities.

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (1/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Invalid rate	• NAATOS device-related failure for product feasibility must achieve a failure rate of <35%	• Invalid rates of <15% more palatable early on in launch, but should ideally be <2%	• Cost of replacing failed cartridges will need to be factored into total cost benefit
Walk away operation	• NAATOS V1 requires only two to three user interactions before walking away and returning to record the result (excluding sample prep)	• User-friendly simplified testing process • Automated to ensure wide adoption in DRC. • Capability for multi-disease testing, and clear result interpretation without the need for complex procedures, to avoid invalid results reportedly seen with other tools like TrueNAT	• Prototypes testing into the hands of end users as early as possible • Usability & acceptability studies are key • Consider the clinic facilities the system will be in • Consider the users are nurses or paraprofessionals
Time to result	• NAATOS V1 must produce a result within <60 min (including sample prep time)	• Ideal: 30-minute test • Testing process that delivers results in under 30 minutes would mitigate the risk of patients leaving before receiving their diagnosis and treatment, a common issue in busy clinics with high patient turnover.	• N/A
Transportation	• NAATOS V1 must not require cold chain storage during shipment or storage	• Ambient temperature conditions • Transportation without refrigeration	• N/A
Shelf life	• NAATOS V1 must have a shelf life of >12 months • (Corporate presentation: shelf life of >18 months from the date of manufacturing)	• Ideal: Exceeding 18 months to reduce the need for frequent resupply and accommodate long-term storage capabilities. • Acceptable: 12 months	• N/A

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (2/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Storage conditions	• NAATOS V1 must be stored at 0 °C to 40 °C and 90% humidity	• DRC's climate necessitates medical devices that can operate effectively in high-temperature environments without extensive cooling facilities, which are often lacking in rural healthcare settings.	• Data to determine how long kits can go beyond 40°C
Operating environment, temperature and humidity level	NAATOS V1 must operate at: – Temperature: +15 °C to +35 °C – Humidity: 25% to 80% relative humidity	• Temperatures rarely exceed 45°C, and winter mornings can be as low as 4°C within the clinics • Fridges for reagent storage can be a problem in the smaller L1 facilities, and scheduled power outages in larger facilities pose a risk	• Look at design to ensure that WHO TPP minimal standards can be met
Multiuse platform	• NAATOS V1 must be designed as a multi target disease platform (TB, STI, etc.)	• A diagnostic tool that can test for multiple diseases and assess resistance patterns is crucial for managing prevalent diseases like malaria, HIV/AIDS, and tuberculosis in DRC's healthcare landscape.	• Adoption decision more attractive by providing a comprehensive solution to diverse healthcare needs, matching the patient journey
Manufacturing	• NAATOS V1 must be manufactured at scale and with device fabrication and assembly process that is compatible with high-volume automation	• Align with initiatives by Africa CDC and Africa Collaborative Initiative • NAATOS should aim for local production to reduce import dependency and contribute to economic growth.	• Look at possible kit assembly solutions within Africa to support the initiative.
Product price	NAATOS V1 must have a price of no more than $5 USD per test – At full production (10MM units/year) – At initial release, 3x full production (1MM units/year) – At pilot production, 10x full production (50k units/year)	• Product affordability is critical for widespread deployment, especially in community settings. • Respondents express a desire for a low-cost test (with suggested price points ranging from $2 to $5)	• Definition of an "affordable" or "cost-effective" TB test goes beyond the test's individual price • Consider broader economic factors • Consider overall test cost, feasibility • Consider cost of community deployment • Overall cost-effectiveness involves considering the entire testing algorithm and implementation factors

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (3/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Sample preparation steps	• The sample prep module must achieve target sample lysis (percent recovered)	• There should be no manual sample purification	• Pathogen enrichment (concentration) step could improve sensitivity vs direct measurement/ testing a little volume of extracted swab solution
Sample volume	• The sample prep module must deliver the appropriate sample volume • (Corporate presentation: 150 - 200µL)	• Tests that require low sample volumes is critical, particularly for pathogen concentration methods that enhance detection sensitivity. • No measurement should be required	• Add all the sample or add 1-2 calibrated drops from buffer tube
Sample volume measurement	• The sample prep module must not require training to successfully and repeatably dispense target volume on the user interface within a reasonable tolerance	• No pipette measurement should be required	N/A
Instrument design / amplicon contamination	• NAATOS V1 must prevent the escape of amplification products and not contaminate the testing area	• Prevention of amplicon contamination should be possible by trained users of the test with all equipment provided in kit so that the strips are safe to discard in general	N/A
Data display	• NAATOS V1 must have a visual read out of the test result that can intuitively be interpreted	• Easy interpretation of results and seamless connectivity with national data systems are imperative for the integration of NAATOS into DRC's health reporting framework.	• Assess absolute necessity for 2 control lines? If required, then conduct usability studies to ensure requirements for instructions and training mitigate this risk
Safety	• NAATOS V1 must not pose a burn risk to the user during normal operation	• NAATOS should be a closed system to avoid biohazard exposure • Standard biohazardous waste disposal methods sufficing for waste management	N/A

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (4/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Power module	• The power module must support the required daily throughput	• A battery-operated device would be highly beneficial for uninterrupted operation, particularly in areas with frequent power outages. • Ensure continuous operation with rechargeable batteries	N/A
Field Testing and Real-world Performance	• *Not defined by GHL*	• Stakeholders are interested in how the test performs in diverse real-world settings beyond controlled laboratory environments	• Set up pre-clinical field testing with prototypes as early as possible
Consideration for Special Populations	• *Not defined by GHL*	• Effectiveness in special populations, like those unable to produce sputum, must be a consideration in NAATOS' development.	• Generate performance data with these population groups vs. current standard of care, i.e. Xpert Ultra all populations & TB-LAM for PLHIV
Quality control	• *Not defined by GHL*	• Internal control is essential to ensure the integrity of NAATOS test results, accounting for any processing errors • External controls that are compatible with local sample collection and testing processes	
Sample preparation module design	Confirm with GHL: – Random access not possible? – Can insert 1 to 4 samples at a time for extraction.	• The design should avoid the natural inclination of health workers to batch tests, which could undermine the rapid turnaround proposition of NAATOS.	• Prototype usability & behaviour studies to help shape training material, overcomes batching tendencies and maximise utilisation of random-access features

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (5/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Sensitivity	• NAATOS V1 must have a clinical sensitivity ≥ 80%	Varying responses from interviews – Sensitivity is a priority – Awareness of other evaluations, like MolBio, with lower sensitivity but considered "good enough." – Should meet or exceed the accuracy of existing methods – Willingness to accept slightly lower sensitivity (high 70s to mid-80s percent) if the specificity remains high – The importance of diagnostic yield and access is emphasized, even with potential decrements in sensitivity – Some stakeholders appreciate a balance between sensitivity and reaching people with no access to diagnostics today	• Data generation demonstrating impact and cost benefit of lower sensitivity assay • Focusing on diagnostic yield and access when an assay is feasible for community implementation
Specificity	• NAATOS V1 must have a clinical specificity ≥ 98%	• A high specificity (above 95%) is considered essential	• N/A
Data Management	• Confirm with GHL: • Is connectivity available?	• Result needs to be captured or read automatically as soon as test is complete • Tracking and tracing more effective when connectivity is added to a LF test	*Explore with GHL*
Sample Type	• NAATOS V1 will utilize a dorsal tongue swab sample	• Focusing on sputum alone might lead to an inferior test • Potential benefits non-sputum sample collection methods	• N/A
Treatment monitoring capability	• NAATOS V1 will not provide drug sensitivity	• The absence of resistance in a new test might be seen as a disadvantage	• Positioning of NAATOS into algorithm for settings where Xpert cannot go. Triage, community screening settings, and clinic level screening

1. Diagnostic landscape
2. Stakeholder feedback
3. **Policy considerations**
4. Deployment considerations

Policy Considerations | Critical policy enablers highlighted by stakeholders for a new TB NAAT test

1

Performance and Affordability

- Stakeholders consistently highlight the importance of the nucleic acid lateral flow assay providing results within an hour, being closer to the patient, affordable, and easy to use. Additionally, there's an emphasis on the test having good sensitivity and meeting the WHO Target Product Profiles (TPPs).

2

Alignment with Guidelines and Feasibility

- Adherence to Ministry of Health (MoH) guidelines is considered crucial for public sector market access. Moreover, feasibility factors, including how the new test fits into the current testing algorithm, addressing change management challenges with regards to sputum collection, drug sensitivity, and enhancing usability, are highlighted.

3

Considerations for Implementation and Patient Flow Integration

- Stakeholders express the need to evaluate the impact on workflow, particularly in high-volume settings.* Implementation considerations include determining who will run the test, ensuring ease of use by various personnel, and addressing timing issues within the patient flow. Factors such as preventing patients from leaving before receiving treatment and integrating the test seamlessly into the testing algorithm and patient flow are considered essential. Additionally, insights from stakeholders underscore the importance of considering the unique needs of specific populations, such as young children, in the implementation strategy.

Policy Considerations | TB products generally have a well-defined but time-consuming policy pathway before it can be adopted and procured by NDOH

Policy process step	TB	Private sector considerations
1 National policy endorsement	• WHO GDG endorsement is not a prerequisite for NTP adoption[1]. However, early engagement with national TB TWG critical • Registration with Agence Congolaise de Regulation Pharmaceutique(ACOREP)	• Private sector follow national guidelines
2 Clinical evaluation	• In-country clinical evaluation will need to be conducted by NTRL before it will be adopted by NTP	• Private sector labs and facilities may conduct their own independent lab evaluation
3 Local studies and country planning	• Additional field studies/implementation pilots may be requested to investigate operational, acceptability and feasibility questions. Decision made by MOH.	• Private sector facilities and labs often start with small scale pilot introduction before committing to larger volumes
4 Adoption, toolkit, phased implementation	• Roll out of TB new diagnostic tools is handled by NTP and implementing partners (e.g. USAID , Fonds Mondial), with support from NTRL • NTP together with its Technical Advisory Group, Guideline Review Committee and partners will develop, review and update the toolkit • Results from the field studies will support larger roll out	• Adoption driven by reimbursement requirements by Medical Schemes

1. Digital chest X-ray (CXR) and Alere LF-LAM were adopted before WHO GDG endorsement | 2. National Health Laboratory Services | 3. Health Technology Assessment | 4. South African Health Products Regulatory Authority | 5. National Priority Program (NPP)

1. Diagnostic landscape
2. Stakeholder feedback
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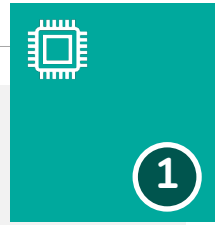
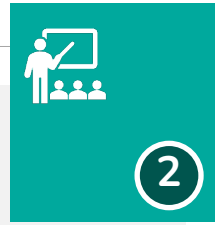
Deployment Considerations | Interviewees highlighted specific challenges that may influence embracing the adoption of NAATOS by implementers and clinic staff

MARKET ACCESS AFRICA



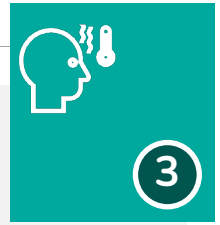
Infrastructure and Data management

Premises not compliant with standards.
Insufficient sources of electrical energy
Absence of LIMS and DHIS2 not appropriate for the laboratory. Delay in transmission of results



Staff Training and Workload

The need for comprehensive clinical & diagnostic training when rolling out a new algorithm is emphasized in the feedback. However, concerns about staff workload and associated resistance to new responsibilities may be barriers



Patient Sample Collection issues

The traditional method of sputum collection poses challenges, particularly in a fast-paced clinic setting. The process may be time-consuming and may not be feasible for patients who struggle to produce sputum

Resistance to Change

Resistance to change is a common barrier in adopting new technologies. Clinicians may be accustomed to existing diagnostics methods and introducing a new approach may face resistance

Deployment Considerations | Recommendations and best practices for streamlined product adoption (1/2)

1 Needs Assessment and Stakeholder Engagement

Identify the key stakeholders, including NTP, HIV Program etc, stakeholders, engage with them to understand the current situation, their need and explore opportunities to introduce the New diagnostic tool

2 Workshops, Advocacy and Training Planning

Partner with local health authorities and global entities to promote the new tool's adoption. Develop comprehensive training curricula, including data management and the diagnostic tool's operational aspects, tailored to the varying skill levels of healthcare workers in DRC.

3 Site-Specific Workflow Assessment

Proceed with the baseline assessment of TB diagnosis coverage, to determine where the instrument will be located. A TB diagnosis network assessment has been conducted in the country in the country with IDDS -USAID project that could be of value. Below are the criteria relating to the choice of provinces and intervention sites:

- Importance of TB notification (TBS and PR-TB)
- Accessibility and attendance,
- Existence of populations at risk;
- Low diagnosis coverage of GeneXpert and Truenat

Deployment Considerations | Recommendations and best practices for streamlined product adoption (2/2)

4 Overcoming workflow challenges

Implement on-site training sessions for laboratory and clinic staff that cover not only the operational aspects of the new tool but also troubleshooting, maintenance, and quality control measures. This should be informed by prior experiences with the integration of other diagnostic tools like GeneXpert, TB Urine LAM and TrueNAT

5 Integration into Primary Health Care Services & Community Services

Plan for the integration of the diagnostic tool into DRC's primary health care system by evaluating the tool's impact on clinical decision-making processes, patient flow, and overall clinic efficiency. Develop protocols for point-of-care testing that align with national TB control strategies. Address concerns of clinicians about workload by emphasizing the benefits of point-of-care diagnosis. Showcase successful precedents, such as the TB LAM test.

Uganda

1. **Diagnostic landscape**
2. Stakeholder feedback
3. Policy considerations
4. Deployment considerations

GH+Labs

Diagnostic Landscape | TB testing is decentralized with the public sector accounting for 44% of the services

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Key messages

1 TB diagnosis and management is decentralized and incorporates the public and private sectors

- Uganda's national health system is decentralized and incorporates the public and private sectors, with the public sector accounting for 44% of the services
- The private sector is composed of the private not for-profit health care providers, private health practitioners, and traditional and complementary medical practitioners
- Health services are delivered through decentralized entities including facilities managed by 112 local government institutions, 22 municipalities, 181 counties, 1,382 sub-counties and 7,241 parishes

2 Uganda's lab system operates in a tiered structure, with TB diagnostics varying across the health system's tiers

- Uganda's lab system is tiered with 1 National TB Reference Lab (NTRL) in Kampala, 16 regional, 54 district hospital labs, 173 HCIV, and 969 HCIII labs, totalling over 1600 labs performing smear microscopy, 200 with fluorescent microscopy, and enhanced coverage with 320 GeneXpert, 40 TrueNAT, and 16 TB LAMP platforms across 328 sites. 27 of the GeneXpert are equipped with the 10-colour modules
- TB diagnostics vary across the health system's tiers. At lower levels, microscopy is predominantly used. Higher levels employ more advanced techniques, including radiology and rapid molecular diagnostics such as GeneXpert, Additionally, the lateral flow lipoarabinomannan (LF-LAM) assay is also in use, enhancing the country's diagnostic capabilities

3 Strategic Response and Funding have led to increased budgets for TB commodities and infrastructure

- The Multisectoral Accountability Framework for TB (MAF-TB) has been endorsed at the Prime Ministerial level, enabling cross-ministerial coordination for TB control within social protection programs
- Program-based budgeting has been implemented, and the NTLP, under the MoH, has seen increased government allocation and significant partner funding, accounting for 80% of financial needs. Efforts are made to enhance resource efficiency and coordination, with plans to further increase budgets for TB commodities and infrastructure

Diagnostic Landscape | Screening gaps lead to misdiagnosis, with nurses attributing symptoms to conditions like the common cold and cough

Patient arrival at clinic
- Security personnel manage the entry and direct patients to the reception.

Reception Desk
- Record the patient in the OPD register and handle patient file retrieval or creation for new patients.

Triage
- Assess whether patient has TB symptoms through 5 symptom questionnaire
- Depending on the symptoms, patients are directed to either Chronic Management (HIV, NCD, etc.) for ongoing conditions or acute management as needed.

TB symptom management
- Patients with TB symptoms given a sputum cup, with options for sputum collection at home or at the clinic

YES

Missed opportunity for patients to be screened TB, leading to no treatment initiation and onward community transmission

Challenges with sputum collection in key populations

Sample collection
- Collect sputum or relevant samples based on condition

Numerous Ugandan labs carry out sputum smear tests, but often forward samples to GeneXpert facilities for resistance testing, raising the risk of sample degradation en route

Delays often observed from the time sample collection to reporting patient results. Reported high initial loss to follow up to 30% in some facilities due to long turn-around time of laboratory results.

Long lead time from when doctor receives results to when patient returns to the clinic and is initiated on treatment

TB Management
- If positive, initiate Drug Sensitive TB Rx
- If RIF resistant initiated Drug Resistant TB Rx
- If neg, investigate further

Diagnosis and results
- On-site diagnostic testing may yield results within a period of 6 to 24 hours
- Clinic communicates TB result via direct call, an SMS alert, or a physical follow up by CHEWs (Community Health Extension Workers)

Sample submission and diagnosis
- Collected samples sent directly to the lab if on-site testing capacity is available
- If not, samples prepared and transported to a referral laboratory

xx Diagnostic gaps

Time

Patient presentation

Initial Screening and sample collection

Diagnosis

Patient treatment and management

Diagnostic Landscape | Time to initiation onto TB treatment hinders proper follow-up, emphasizing the need for improved diagnostic strategies

Challenges and proposed solutions for Clinical Workflow Improvement

	Infrastructure and Resource Constraints	Staffing and personnel challenges at L1 & L2	Delays resulting in loss to follow-up	Long lead time between results and treatment
Challenge				
Proposed solutions	• Build capacity for testing at L1 & L2 facilities • Emphasis on utilizing mobile and portable diagnostic tools like NAATOS to reach remote areas across Level 1 and Level 2 facilities to enhance TB diagnostic capabilities • Integration of TB diagnostics into existing healthcare services can help leverage resources.	• Put in place a system where healthcare workers share duties. This system should be based on methods that have worked well in Uganda and match the way local health services usually operate. • Utilize technology to provide remote training and support to healthcare workers to address staff shortages.	• Optimized Sample Transport System: Strengthen the Hub Riders network with more frequent pickups and improved logistics. • Digital tracking systems should be enhanced to include real-time alerts for sample pickups and results delivery. • Consider public-private partnerships to support the logistics of sample transport and results dissemination	• Expand the use of point-of-care tests like NAATOS that can deliver immediate results to minimize delays in treatment initiation. Integrate these tests into community outreach programs and strengthen referral networks to ensure patients receive timely treatment.

1. Diagnostic landscape
2. **Stakeholder feedback**
3. Policy considerations
4. Deployment considerations

GH+Labs

Product Value Proposition | Stakeholders expressed several positive attributes of NAATOS that makes it an attractive option for adoption

Key takeaway

NAATOS presents an opportunity to serve as both a triage test and a screening tool within Uganda's Integrated Test & Treat (ITT) algorithm, enhancing the efficiency and accuracy of TB diagnosis.

Stakeholder feedback on NAATOS value proposition

Patient-Centric and Affordable Solutions	• Stakeholders recognize the need for affordable, user-friendly diagnostic solutions. NAATOS aligns with this by offering a closer-to-patient, cost-effective, and easily-accessible testing option, which extends to decentralized use, enhancing accessibility and streamlining the process for improved efficiency.
Positive Perception of NAATOS at L1 Facilities	• NAATOS is viewed favourably due to its ease of understanding, simplicity, and straightforward implementation. The familiarity, feasibility, and compatibility with clinic workflows contribute to a positive outlook on its adoption in Uganda.
Challenging Traditional Testing Approaches	• NAATOS is seen as a step forward, offering a practical strategy to address the urgent need for proactive TB testing approaches. Its implementation as a portable DNA-based diagnostic tool linked to care is appreciated for its potential to disrupt traditional testing methods and contribute to community-oriented approaches for interrupting TB transmission.
Integration into ITT Algorithm and Generalist Clinical Care	• NAATOS is recognized as a versatile tool adaptable to Uganda's Integrated Test and Treat (ITT) algorithm, capable of supporting generalist clinical care by providing flexible testing routes beyond TB alone. The tool's integration, especially with HIV care, exemplifies the 5-symptom screening method's flexibility.
Impact on TB Contact Testing Programs	• By streamlining sample collection and reducing the need for batching tests, NAATOS is viewed as a catalyst for change among high-risk groups and household contacts. It's expected to enhance community-based testing and improve outcomes within high-risk communities, aligning with the broader goals of Uganda's TB control programs.

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (1/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Invalid rate	• NAATOS device-related failure for product feasibility must achieve a failure rate of <35%	• Invalid rates should ideally be <5%	• Cost of replacing failed cartridges will need to be factored into total cost benefit
Walk away operation	• NAATOS V1 requires only two to three user interactions before walking away and returning to record the result (excluding sample prep)	• User-friendly simplified testing process • Automated to ensure wide adoption in Uganda. • Capability for multi-disease testing, and clear result interpretation without the need for complex procedures, to avoid invalid results reportedly seen with other tools like TrueNAT	• Simplified operation and automated usability for diagnostic tests like NAATOS is important, especially considering the limited number of qualified health professionals and the prevalent practice of task-shifting in Uganda at L1/L2 facilities.
Time to result	• NAATOS V1 must produce a result within <60 min (including sample prep time)	• Ideal: 30-minute test • Testing process that delivers results in under 30 minutes would mitigate the risk of patients leaving before receiving their diagnosis and treatment, a common issue in busy clinics with high patient turnover.	• For samples sent to referral laboratories, the turnaround time can extend up to a week or more. These extended times highlight the need for rapid testing solutions like NAATOS to improve patient management and treatment initiation.
Transportation	• NAATOS V1 must not require cold chain storage during shipment or storage	• Ambient temperature conditions • Transportation without refrigeration	• N/A (the current specifications of NAATOS likely meet this requirement.)
Shelf life	• NAATOS V1 must have a shelf life of >12 months • (Corporate presentation: shelf life of >18 months from the date of manufacturing)	• Ideal: Exceeding 18 months to reduce the need for frequent resupply and accommodate long-term storage capabilities. • Acceptable: 12 months	• N/A (the current specifications of NAATOS likely meet this requirement.)

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (2/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Storage conditions	• NAATOS V1 must be stored at 0 °C to 40 °C and 90% humidity	• Uganda's climate varies from semi-arid in the northeast to more humid in the south. Medical devices used in Uganda must be robust enough to handle temperatures that can occasionally exceed 30°C in urban areas like Kampala, with appropriate humidity controls, especially in regions near Lake Victoria	• Investigate how long kits can withstand temperatures above 40°C, potentially adjusting storage conditions in design to meet WHO TPP minimal standards.
Operating environment, temperature and humidity level	NAATOS V1 must operate at: – Temperature: +15 °C to +35 °C – Humidity: 25% to 80% relative humidity	• Temperatures rarely exceed 45°C • Humidity levels can be high in places near Lake Victoria • Fridges for reagent storage can be a problem in the smaller L1 facilities, and scheduled power outages in larger facilities pose a risk	• Design modifications to ensure operation in high-temperature and high-humidity environments, such as those near Lake Victoria, accounting for frequent storage challenges and power outages.
Multiuse platform	• NAATOS V1 must be designed as a multi target disease platform (TB, STI, etc.)	• A diagnostic tool that can test for multiple diseases and assess resistance patterns is crucial for managing prevalent diseases like malaria, HIV/AIDS, and tuberculosis in Uganda's healthcare landscape.	• Adoption decision more attractive by providing a comprehensive solution to diverse healthcare needs, matching the patient journey
Manufacturing	• NAATOS V1 must be manufactured at scale and with device fabrication and assembly process that is compatible with high-volume automation	• Align with initiatives by Africa CDC and Africa Collaborative Initiative • NAATOS should aim for local production to reduce import dependency and contribute to economic growth.	• Look at possible kit assembly solutions within Africa to support the initiative.
Product price	NAATOS V1 must have a price of no more than $5 USD per test – At full production (10MM units/year) – At initial release, 3x full production (1MM units/year) – At pilot production, 10x full production (50k units/year)	• Product affordability is critical for widespread deployment, especially in community settings. • Respondents express a desire for a low-cost test (with suggested price points ranging from $2 to $5)	• Define "affordable" or "cost-effective" TB test goals based on the test's individual price. Consider broader economic factors, overall test cost, feasibility, and cost of community deployment. Evaluate cost-effectiveness involving considerations for the entire testing algorithm and implementation factors.

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (3/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Sample preparation steps	• The sample prep module must achieve target sample lysis (percent recovered)	• Minimal user interaction in the sample preparation process, addressing biosafety concerns and ensuring practicalities of sample handling are met.	• Pathogen enrichment (concentration) step could improve sensitivity vs direct measurement, testing a little volume of extracted swab solution
Sample volume	• The sample prep module must deliver the appropriate sample volume • (Corporate presentation: 150 - 200µL)	• Tests that require low sample volumes are critical • No measurement should be required	• Modify the protocol to allow for the addition of all the sample or or 1-2 calibrated drops from buffer tube to ensure sufficient volume for analysis.
Sample volume measurement	• The sample prep module must not require training to successfully and repeatably dispense target volume on the user interface within a reasonable tolerance	• Sample volume measurement should not require pipette training to ensure repeatability and accuracy.	N/A
Instrument design / amplicon contamination	• NAATOS V1 must prevent the escape of amplification products and not contaminate the testing area	• The design must prevent escape of amplification products and contamination of the testing area.	• Reinforce preventive measures of contamination by possibly reviewing and enhancing the device's physical barriers and ensuring proper user training.
Data display	• NAATOS V1 must have a visual read out of the test result that can intuitively be interpreted	• The result must have a visual read-out that is easily interpreted without requiring complex interpretation. • Seamless connectivity with national data systems are imperative for the integration of NAATOS into Uganda's health reporting framework.	• In additional to connectivity with existing data systems, incorporating a direct result printing feature in NAATOS would enhance accuracy and efficiency in reporting results.
Safety	• NAATOS V1 must not pose a burn risk to the user during normal operation	• NAATOS should be a closed system to avoid biohazard exposure • Standard biohazardous waste disposal methods sufficing for waste management	• Ensure that NAATOS adheres to high biohazard safety standards and provide comprehensive safety training to all end-users.

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (4/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Power module	• The power module must support the required daily throughput	• A battery-operated device that can work with frequent power outages and supports the required daily throughput.	N/A
Field Testing and Real-world Performance	• *Not defined by GHL*	• Stakeholders are interested in how the test performs in diverse real-world settings beyond controlled laboratory environments	• Set up pre-clinical field testing with prototypes as early as possible
Consideration for Special Populations	• *Not defined by GHL*	• Effectiveness in special populations, like those unable to produce sputum.	• Generate performance data with these population groups vs. current standard of care, i.e. Xpert Ultra all populations & TB-LAM for PLHIV
Quality control	• *Not defined by GHL*	• Internal control is essential to ensure the integrity of NAATOS test results, accounting for any processing errors • External controls that are compatible with local sample collection and testing processes	• Compelling need to integrate NAATOS into the national EQA mechanism to ensure the quality and reliability of TB diagnostics across all healthcare facilities. By including NAATOS in the EQA framework, we can enhance the proficiency testing of this innovative diagnostic tool, promote standardized practices, and strengthen the overall diagnostic landscape for TB.
Sample preparation module design	Confirm with GHL: – Random access not possible? – Can insert 1 to 4 samples at a time for extraction.	• The design should avoid the natural inclination of health workers to batch tests, which could undermine the rapid turnaround proposition of NAATOS.	• Prototype usability & behaviour studies to help shape training material, overcomes batching tendencies and maximise utilisation of random-access features

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (5/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Sensitivity	• NAATOS V1 must have a clinical sensitivity ≥ 80%	One respondent highlights the necessity for diagnostic tools to have over 95% specificity and 80% sensitivity. He notes that current tools sometimes yield false negatives or positives, impacting patient management. This emphasizes the importance of accuracy in tools like NAATOS for reliable patient care.	• Focus on generating data to demonstrate the impact and cost benefit of high sensitivity. Emphasize the importance of diagnostic yield and accessibility for reliable patient care, especially in community implementation.
Specificity	• NAATOS V1 must have a clinical specificity ≥ 98%	• A high specificity (above 95%) is considered essential to avoid false positives.	• N/A
Data Management	• Confirm with GHL: • Is connectivity available?	• Result needs to be captured or read automatically as soon as test is complete • Tracking and tracing more effective when connectivity is added to a LF test	• Explore with GHL on how to enhance data capture and connectivity, possibly integrating with existing health information systems like DHIS2.
Sample Type	• NAATOS V1 will utilize a dorsal tongue swab sample	• Concerns about non-sputum sample collection methods leading to an inferior test.	• There is a need for more data to support the use of dorsal tongue swab samples, which could potentially offer benefits over sputum samples in terms of ease and comfort for the patient, thus increasing testing compliance.
Treatment monitoring capability	• NAATOS V1 will not provide drug sensitivity	• The absence of resistance testing in a new test might be seen as a disadvantage.	• Positioning of NAATOS into algorithm, especially in settings where Xpert cannot go such as community screening settings, and clinic- level screening

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Considerations for Implementation and Patient Flow Integration

- Stakeholders express the need to evaluate the impact on workflow, particularly in high-volume settings.* Implementation considerations include determining who will run the test, ensuring ease of use by various personnel, and addressing timing issues within the patient flow. Factors such as preventing patients from leaving before receiving treatment and integrating the test seamlessly into the testing algorithm and patient flow are considered essential. Additionally, insights from stakeholders underscore the importance of considering the unique needs of specific populations, such as young children, in the implementation strategy.

Policy Considerations | TB products generally have a well-defined but time-consuming policy pathway before it can be adopted and procured by MoH

Policy process step	TB	Private sector considerations
1 National policy endorsement 	• WHO GDG endorsement is a prerequisite for NTLP adoption[1]. However, early engagement with national TB TWG critical • Once test is registered with NDA[3], the national TB TWG reviews the strength of the evidence and makes recommendations to the NTLP and partners on which, the NTLP and NTRL will draft guidelines.	• Private sector follow national guidelines.
2 Clinical evaluation 	• In-country clinical evaluation will need to be conducted by NTRL before it will be adopted by NTLP • MoH conducts cost effective study to assess cost of new intervention vs impact.	• Private sector labs and facilities do no conduct their own independent lab evaluation
3 Local studies and country planning 	• Additional field studies/implementation pilots are required to investigate operational, acceptability and feasibility questions. Decision made by MoH. • MoH TB Testing & Treatment Guidelines updated/developed and launched	• Private sector facilities and labs adopt results of MoH implementation pilot.
4 Adoption, toolkit, phased implementation 	• Roll out of new diagnostic tools is handled by NTLP[2] and implementing partners (e.g. IDI), with support from the National TB reference lab. • NTLP together with its Technical Advisory Group, Guideline Review Committee and partners will develop, review and update the toolkit • Results from the field studies will support larger roll out	• Adoption driven by reimbursement requirements by Medical Schemes

1. Digital chest X-ray (CXR) and Alere LF-LAM were adopted following WHO GDG endorsement | 2. National TB and Leprosy Programme | 3. National Drug Authority

1. Diagnostic landscape
2. Stakeholder feedback
3. Policy considerations
4. **Deployment considerations**

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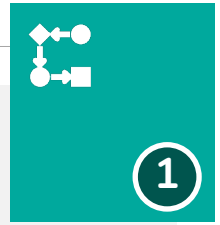
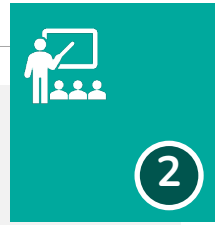
Deployment Considerations | Interviewees highlighted specific challenges that may influence embracing the adoption of NAATOS by implementers and clinic staff



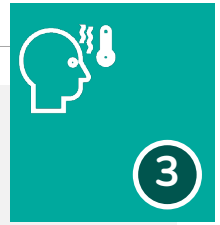
Workflow Integration

- A Senior Researcher at the Uganda Lung Institute suggests that the integration of NAATOS into existing workflows is a valid concern, especially considering the limited number of clinics with on-site TB laboratories.
- The tool needs to be strategically placed and fit seamlessly into current operational routines without overwhelming the existing infrastructure.



Staff Training and Workload

- The need for staff training is crucial, as indicated in the interviews and reports, particularly to adapt to the NAATOS diagnostic tool. However, considering the high patient volumes and existing responsibilities, adding new tasks without increasing staff or adjusting workloads could meet resistance



Patient Sample Collection

- The sensitivity of tongue swab versus sputum collection is a concern raised by a Snr MoH Clinician at Mulago, the National Referral Hospital. While she did not provide a direct comparison, she suggested that alternative sample collection methods like tongue swabs could enhance patient acceptance and expand testing, especially where sputum collection is not feasible.

Resistance to Change

- Resistance to adopting new technologies is a common theme across healthcare settings, as reported by NTRL TB Diagnostics Coordinator. Full advocacy is essential for the successful roll-out of NAATOS, requiring buy-in from all levels of the Ministry of Health and the healthcare system.

Deployment Considerations | Recommendations and best practices for streamlined product adoption (1/2)

1 Needs Assessment and Stakeholder Engagement

Engage key stakeholders relevant to Uganda's healthcare system, such as the Ministry of Health, National Tuberculosis and Leprosy Programme, and district health teams to demonstrate the added value of NAATOS over existing tools. Understand the TB diagnostic needs, infrastructural capabilities, and the human resources available within the current healthcare delivery model.

2 Advocacy and Training Planning

Develop partnerships with strategic partners who work alongside the TB program, such as KNCV and The Union, to advocate for NAATOS integration into national strategies. Explore varied funding strategies, including partnerships with the private sector and international funding opportunities.

Develop comprehensive training curricula, including data management and the diagnostic tool's operational aspects, tailored to the varying skill levels of healthcare workers in Uganda.

3 Site-Specific Workflow Assessment

Carry out a situational analysis of the existing laboratory network and capacities, including infrastructure, staff skills, and IT capabilities.

Address workflow integration by assessing each clinic's workflow to integrate NAATOS effectively, considering specific site requirements and staff roles.

Deployment Considerations | Recommendations and best practices for streamlined product adoption (2/2)

4 Overcoming Workflow Challenges

Plan for equipment and site preparation, considering Uganda's demand and intermittent power supply, and ensure biosafety and waste management protocols are in place.

Manage potential staff workload increases by demonstrating NAATOS's efficiency benefits and streamlining patient care.

5 Training Implementation and On-Site Support

Implement comprehensive on-site training sessions for laboratory and clinic staff that cover not only the operational aspects of the new tool but also troubleshooting, maintenance, and quality control measures, offering ongoing support for any challenges encountered.

Address concerns about operational responsibilities and updated testing algorithms through clear clinical protocols and guidance.

6 Integration into Primary Health Care Services & Community Services

Plan for the integration of the diagnostic tool into Uganda's primary health care system by evaluating the tool's impact on clinical decision-making processes, patient flow, and overall clinic efficiency.

Showcase successful precedents and utilize feedback loops for ongoing optimization based on user experiences and performance data.

Deployment Considerations | Recommendations and best practices for streamlined product adoption (2/2)

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7 **Iterative Technical Optimization**

Conduct operational research and pilot studies to customize NAATOS for local conditions and provide compelling data to inform decision-making. One specific technical challenge noted by respondents is resistance testing, ensuring that there is a tool that remains sensitive and specific to local TB strains and resistance patterns. - how the NAATOS can bridge that gap

8 **Culture and Language Considerations**

Ensure that NAATOS materials and training are culturally appropriate and available in local languages to enhance understanding and acceptance among healthcare workers and patients.

9 **Regulatory Approval and Compliance**

Work with the National Drug Authority (NDA) and other regulatory bodies in Uganda to ensure NAATOS meets all regulatory requirements for importation, use, and quality assurance.

10 **Supply Chain Management & Sustainability Planning**

Develop a robust supply chain strategy to ensure consistent availability of NAATOS kits and reagents, considering Uganda's logistics challenges, especially in remote areas.

Zimbabwe

1. **Diagnostic landscape**
2. Stakeholder feedback
3. Policy considerations
4. Deployment considerations

GH+Labs

Diagnostic Landscape | TB testing is administered through public sector health facilities and testing mostly through microscopy

Key messages

1 The public sector is the main provider of TB testing, with test by private sector reports to the Ministry of Health and Child Care

2 Overall TB prevalence has been decreasing despite substantial high out of pocket costs and indirect costs

3 Molecular assays are the gold-standard for testing, while microscopy and chest X-ray are used as part of the screening toolkit in Zimbabwe

Implications for NAATOS

- The TB program is solely administered through the public sector: In instances where private health facilities provide services for the public, the facility is trained by, and reports to the Ministry of Health and Child Care
- Health facilities for TB: There are a total of 1,122 primary care facilities in the country. 106 Mission and district hospitals also provide services. There are also a few referral hospitals for TB management across the country, but patients are generally only referred to these facilities after diagnosis at lower centres

- In Zimbabwe, 16,300 TB cases were notified in 2021, from an estimated 30,000 incident cases, translating to a treatment coverage of 54%. The country has now been removed from the list of top 30 high burden countries
- The country still grapples with close to 14,000 missed cases annually, and a disproportionate burden of TB-HIV and drug-resistant TB. In addition, over 80% of TB patients experience substantial high out of pocket costs and indirect costs such as income loss, when accessing services, an important barrier to life saving treatment. Furthermore, finding TB in children remains elusive, with notifications in 2021 accounting for 5% of total notifications, against an annual global achievement of 10-12%
- Despite the increase in case notifications, drug-resistant TB cases increased in 2021 - 450,000 cases of Rifampicin-resistant TB were diagnosed

- Available diagnostics include sputum smear microscopy (SSM), chest x-ray (CXR) – with or without computer-aided diagnosis, GeneXpert, TruNat, RIF Ultra,
- TB screening is being encouraged at all levels of the health care system. All patients reporting to health care facilities are screened for TB, regardless of presenting complaints. Further testing may then be conducted based on the findings of the preliminary screening

Diagnostic Landscape | Systematic screening for TB is recommended for all patients reporting to public health facilities for any condition

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Patient arrival at clinic

- Goes through queueing system / security clearance
- Proceeds to records desk for file creation and recording

Vital Room

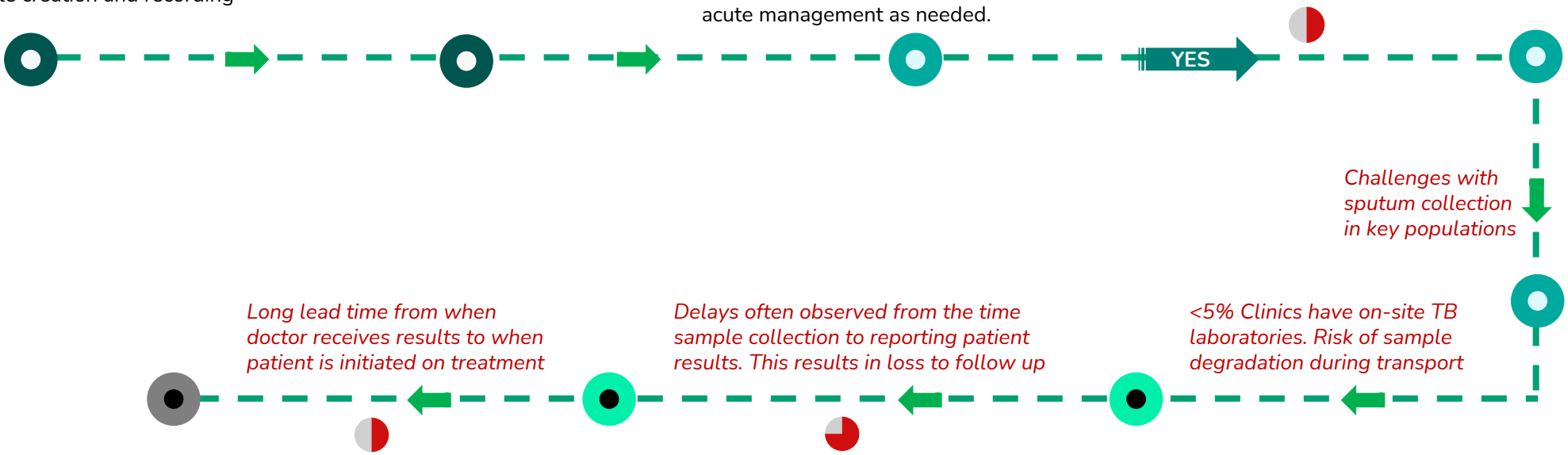
- Patient moves to Vital room for recording of vitals and creation of patient record

Triage

- Assess whether patient has TB symptoms. A presumptive TB case is anyone with a positive symptom screen and/ or BMI below 17, and/or abnormal chest x-ray
- Depending on the symptoms, patients are directed to either Chronic Management (HIV, NCD, etc.) for ongoing conditions or acute management as needed.

TB symptom management

- Patients with TB symptoms given a sputum cup



Sample collection

- Sputum samples generally utilised for pulmonary TB detection in adult patients
- Extrapulmonary TB samples dependent on symptoms. Samples include CSF, lymph node aspirate
- Diagnosis in children – Sputum, Naso-pharyngeal or naso-gastric aspirate, Stool, Tubercilun skin tests and chest X-rays

TB Management

- Treatment is provided under the DOTS – directly observed treatment system
- Infectious disease hospitals may hospitalise patients during the intense phase of treatment
- At primary care level, patients report to the clinic daily to receive their doses

Diagnosis and results

- Duration is variable as some facilities in remote locations only have samples collected once a week. The sample collection vehicle also does a round trip collecting samples from all facilities on the route before returning to the lab
- Results via SMS or phone call from Laboratory to health facility, and occasionally hard-copy results

Sample submission and diagnosis

- Samples are collected at the health facilities.
- Majority of primary level facilities do not have lab facilities onsite. Therefore, samples are transported to the nearest district or mission hospital for testing.

xx Diagnostic gaps

- Time
- Patient presentation
- Initial Screening and sample collection
- Diagnosis
- Patient treatment and management

GH+Labs

Diagnostic Landscape | Time to initiation onto TB treatment hinders proper follow-up, emphasizing the need for improved diagnostic strategies

Challenges and proposed solutions for Clinical Workflow Improvement

	Limited accessibility to testing and treatment	Challenges with Sputum Testing	Delays resulting in loss to follow-up	Paediatric testing challenges
Challenge				
Proposed solutions	• Build capacity for testing at L1 & L2 facilities • Ensure equitable distribution of essential diagnostic across Level 1 and Level 2 facilities to enhance TB diagnosis capabilities • Introduce battery-operated device testing devices	• Provide alternative diagnostic methods to sputum testing / focusing on non-sputum sample types • Establish access to point of care molecular testing at lower-level facilities like NAATOS	• Implementation of testing at point-of-care in a way that ensures treatment is possible at same visit • Implement connectivity solutions with NAATOS for efficient data management systems • Increase administrative oversight for these facilities to ensure efficiency	• Provide alternative diagnostic methods to sputum testing • Address staffing retention challenges. • Provide additional training to enable staff to manage multiple tasks efficiently

1. Diagnostic landscape
2. **Stakeholder feedback**
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Product Value Proposition | Stakeholders expressed several positive attributes of NAATOS that makes it an attractive option for adoption

Key takeaway

NAATOS presents an opportunity to serve as both a triage test and a screening tool within Zimbabwe's algorithm, enhancing the efficiency and accuracy of TB diagnosis.

Stakeholder feedback on NAATOS value proposition

Patient-Centric and Affordable Solutions	• Stakeholders express an interest in increasing the access to testing at L1 facilities, thereby reducing the turnaround times to treatment initiation
Positive Perception of NAATOS at L1 Facilities	• Stakeholders view NAATOS as well-understood, easy to introduce, and straightforward in implementation. The familiarity and feasibility of lateral flow tests, coupled with their adaptability to clinic workflows, contribute to the optimistic outlook on NAATOS adoption
Impact on TB Contact Testing Programs	• The potential impact of NAATOS on systematic screening of at-risk/ vulnerable populations
Potential adoption of other samples for testing	• The program is currently focused on sputum for pulmonary TB which presents some challenges, particularly for children. The tongue swab offered by NAATOS

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (1/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Invalid rate	• NAATOS device-related failure for product feasibility must achieve a failure rate of <35%	• Invalid rates of <15% more palatable early on in launch, but should ideally be <2%	• Cost of replacing failed cartridges will need to be factored into total cost benefit
Walk away operation	• NAATOS V1 requires only two to three user interactions before walking away and returning to record the result (excluding sample prep)	• User-friendly testing process, including the integration of pre-preparation and testing phases into a streamlined system • Ease of use in operation is especially important when considering the clinic facilities where the system is targeted for implementation, and users such as nurses or paraprofessionals	• Prototypes testing into the hands of end users as early as possible • Usability & acceptability studies are key • Consider the clinic facilities the system will be in • Consider the users are nurses or paraprofessionals
Time to result	• NAATOS V1 must produce a result within <60 min (including sample prep time)	• Ideal: 30-minute test • Testing process that delivers results in under 30 minutes would mitigate the risk of patients leaving before receiving their diagnosis and treatment, a common issue in busy clinics with high patient turnover.	• N/A
Transportation	• NAATOS V1 must not require cold chain storage during shipment or storage	• Ambient temperature conditions • Transportation without refrigeration • Consideration for swab transportation from small facilities with small volumes to consolidate testing	• Additional components to the kit (as optional components) such as swab transport tubes – with accompanying stability data
Shelf life	• NAATOS V1 must have a shelf life of >12 months • (Corporate presentation: shelf life of >18 months from the date of manufacturing)	• Ideal: Exceeding 20 months to reduce the need for frequent resupply and accommodate long-term storage capabilities. • Acceptable: 18 months	• N/A

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (2/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Storage conditions	• NAATOS V1 must be stored at 0 °C to 40 °C and 90% humidity	• The temperature and humidity conditions vary across the country. In some regions, maximum temperatures can be close to 40 degrees Celsius	• Data to determine how long kits can go beyond 40°C
Operating environment, temperature and humidity level	NAATOS V1 must operate at: – Temperature: +15 °C to +35 °C – Humidity: 25% to 80% relative humidity	• Temperatures rarely exceed 45°C, and winter mornings can be as low as 4°C within the clinics • Humidity levels can be high in places • Fridges for reagent storage are generally not available in the smaller L1 facilities, and power outages across the country pose a risk	• Look at design to ensure that WHO TPP minimal standards can be met
Multiuse platform	• NAATOS V1 must be designed as a multi target disease platform (TB, STI, etc.)	• A diagnostic tool that can test for assess resistance patterns is crucial for tuberculosis in Zimbabwe's healthcare landscape.	• Adoption decision more attractive by providing a comprehensive solution to diverse healthcare needs, matching the patient journey
Manufacturing	• NAATOS V1 must be manufactured at scale and with device fabrication and assembly process that is compatible with high-volume automation	• Align with initiatives by Africa CDC and Africa Collaborative Initiative	• Look at possible kit assembly solutions within Africa to support the initiative.
Product price	NAATOS V1 must have a price of no more than $5 USD per test – At full production (10MM units/year) – At initial release, 3x full production (1MM units/year) – At pilot production, 10x full production (50k units/year)	• Cost calculations would include cost per test, whether additional testing will be required before treatment can commence, ancillary costs such as environmental control for optimal testing conditions	• Definition of an "affordable" or "cost-effective" TB test goes beyond the test's individual price • Consider broader economic factors • Consider overall test cost, feasibility • Consider cost of community deployment • Overall cost-effectiveness involves considering the entire testing algorithm and implementation factors

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (3/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Sample preparation steps	• The sample prep module must achieve target sample lysis (percent recovered)	• There should be no manual sample purification	• Pathogen enrichment (concentration) step could improve sensitivity vs direct measurement/ testing a little volume of extracted swab solution
Sample volume	• The sample prep module must deliver the appropriate sample volume • (Corporate presentation: 150 - 200µL)	• Tests that require low sample volumes is critical, particularly for pathogen concentration methods that enhance detection sensitivity. • No measurement should be required	• Add all the sample or add 1-2 calibrated drops from buffer tube
Sample volume measurement	• The sample prep module must not require training to successfully and repeatably dispense target volume on the user interface within a reasonable tolerance	• No pipette measurement should be required	N/A
Instrument design / amplicon contamination	• NAATOS V1 must prevent the escape of amplification products and not contaminate the testing area	• Prevention of amplicon contamination should be possible by trained users of the test with all equipment provided in kit so that the strips are safe to discard in general	N/A
Data display	• NAATOS V1 must have a visual read out of the test result that can intuitively be interpreted	• Concerns were raised about interpreting results in the current iteration of the test. • Easy interpretation of results and seamless connectivity with national data systems are imperative for the integration of NAATOS into Zimbabwe's health reporting framework.	• Assess absolute necessity for 2 control lines? If required, then conduct usability studies to ensure requirements for instructions and training mitigate this risk
Safety	• NAATOS V1 must not pose a burn risk to the user during normal operation	• NAATOS should be a closed system to avoid biohazard exposure • Standard biohazardous waste disposal methods sufficing for waste management	N/A

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (4/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Power module	• The power module must support the required daily throughput	• A battery-operated device would be highly beneficial for uninterrupted operation, particularly as the country has been facing challenges with power supply	N/A
Field Testing and Real-world Performance	• *Not defined by GHL*	• Stakeholders are interested in how the test performs in diverse real-world settings beyond controlled laboratory environments	• Set up pre-clinical field testing with prototypes as early as possible
Consideration for Special Populations	• *Not defined by GHL*	• Effectiveness in special populations, like those unable to produce sputum, must be a consideration in NAATOS' development.	• Generate performance data with these population groups vs. current standard of care, i.e. Xpert Ultra all populations & TB-LAM for PLHIV
Quality control	• *Not defined by GHL*	• Internal control is essential to ensure the integrity of NAATOS test results, accounting for any processing errors • External controls that are compatible with local sample collection and testing processes	• Early engagement with to help develop swab-based control materials
Sample preparation module design	Confirm with GHL: – Random access not possible? – Can insert 1 to 4 samples at a time for extraction.	• The design should avoid the natural inclination of health workers to batch tests, which could undermine the rapid turnaround proposition of NAATOS.	• Prototype usability & behaviour studies to help shape training material, overcomes batching tendencies and maximise utilisation of random-access features

Product Specification | Stakeholders provided feedback on key considerations for NAATOS adoption (5/5)

Market Requirements	Current NAATOS Specifications	Notes on Stakeholders' Desired Specifications	Steps to Close Gap
Sensitivity	• NAATOS V1 must have a clinical sensitivity ≥ 80%	Varying responses from interviews – A heavy reliance on WHO prequalification for the quality assurance of the test	• Data generation demonstrating impact and cost benefit of lower sensitivity assay
Specificity	• NAATOS V1 must have a clinical specificity ≥ 98%	• A high specificity (above 95%) is considered essential	• Specificity data as part of the evaluation package
Data Management	• Confirm with GHL: • Is connectivity available?	• Possibility for integration into the Laboratory Information Management System would be an added advantage	*Explore with GHL*
Sample Type	• NAATOS V1 will utilize a dorsal tongue swab sample	• Stakeholders requested that the test be compatible with other sample types specified in the testing algorithm such as sputum, CSF and stool	• Possibly increase the range of sample types
Treatment monitoring capability	• NAATOS V1 will not provide drug sensitivity	• The absence of resistance in a new test might be seen as a disadvantage	• Positioning of NAATOS into algorithm for settings where sample transport to settings with Xpert is a challenge.

1. Diagnostic landscape
2. Stakeholder feedback
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Policy Considerations | Critical policy enablers highlighted by stakeholders for a new TB NAAT test

1

Performance and Affordability

- Stakeholders consistently highlight the importance of the nucleic acid lateral flow assay providing results within an hour, being closer to the patient, affordable, and easy to use. Additionally, there's an emphasis on the test having good sensitivity and meeting the WHO Target Product Profiles (TPPs).

2

Alignment with Guidelines and Feasibility

- Alignment with the National TB guidelines is important
- As the program is predominantly funded by donors, alignment with Global Fund and WHO guidelines will be critical

3

Considerations for Implementation and Patient Flow Integration

- Stakeholders express the need to evaluate the impact on workflow, particularly in high-volume settings.* Implementation considerations include determining who will run the test, ensuring ease of use by various personnel, and addressing timing issues within the patient flow. Factors such as preventing patients from leaving before receiving treatment and integrating the test seamlessly into the testing algorithm and patient flow are considered essential.

Policy Considerations | TB products generally have a well-defined but time-consuming policy pathway before it can be adopted by the NTP

Policy process step	TB
1 National policy endorsement	• WHO GDG endorsement is a prerequisite for NTP adoption. Early engagement with NTP and supporting agencies is beneficial.
2 Clinical evaluation	• Once test is WHO prequalified, in-country evaluation will be conducted by the National Medical Reference Labs. If performance is satisfactory, stakeholder engagement will be conducted for inclusion in the testing algorithm. • Cost-effectiveness analysis will also be conducted for inclusion in the algorithm.
3 Local studies and country planning	• Pilot projects may not necessarily be requested by the NTP. However, the manufacturer may request to conduct a local pilot to generate data which may be utilized to support the inclusion of the test in the national testing algorithm. Partnering with one of the technical partners to the NTP may facilitate the conduct of the pilot study
4 Adoption, toolkit, phased implementation	• Roll out of new diagnostic tools is handled by the NTP in conjunction with the Directorate of Lab Services. • Procurement is guided by the policies of the funding donor partners.

1. Diagnostic landscape
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Deployment Considerations | Interviewees highlighted specific challenges that may influence embracing the adoption of NAATOS by implementers and clinic staff

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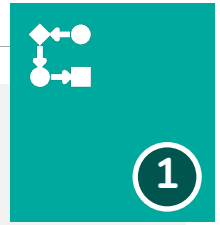
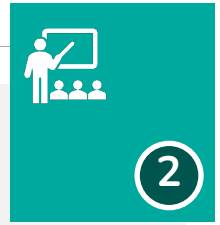


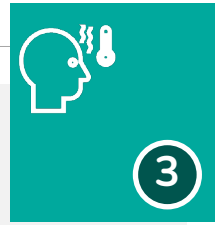
Workflow Integration

While there is a desire to increase testing capacity at L1 and L2 facilities, it is unclear how running the tests and recording results on-site would be integrated into the current workflow



Staff Training and Workload

Staff training will be a key requirement from the National TB Program for rollout. Nurses at L1 and L2 have a large workload. Additionally, staff attrition is a major challenge at L1 and L2 facilities resulting in a continuous need for training



Patient Sample Collection

Acceptability of tongue swab was raised as a concern. The program requested expansion of suitable samples for the NAATOS platform to include sputum, CSF and stool, which are the recognised samples.

Resistance to Change

The program is dependent on WHO-prequalification to convince stakeholders for deployment. Prequalified platforms face less resistance

Deployment Considerations | Recommendations and best practices for streamlined product adoption

1 Early Stakeholder Engagement

Early engagement of key stakeholders, including the Directorate of Lab Services, The National TB Program, Development partners and funders (e.g. UNDP/ Global Fund country team, Union Zimbabwe, USAID technical experts). Obtain their insights, address concerns, and build advocacy from influential groups

2 Provide support for in-country evaluation

Once the evaluation request is submitted to the Ministry of Health and Child Care, a budget will be shared for in-country evaluation processes. Due to budgetary constraints, the manufacturer will need to finance the evaluation by the National Medical Reference Laboratory

3 Roll-out stakeholder engagement

This would include programmatic and funding stakeholders. Stakeholders will be appraised on the results of the in-country evaluation and all quality assurance documentation (such as WHO Prequalification, clinical data from other settings, cost-benefit analysis, rational for inclusion in the algorithm)

4 Training for uptake

Training will be jointly conducted by the manufacturer and the Ministry of Health and Child Care. First phase is training of the trainers/ superusers. The trainers would then cascade training to all levels of care where the platform will be utilised. Provide ongoing support to address any challenges that arise during the adoption process

5 Continuous Feedback Loop

Establish a continuous monitoring and feedback loop. Encourage open communication with users to gather insights, address concerns promptly, and adapt the training and implementation process iteratively based on real-world experiences