Assessment and revision of TB Laboratory Network of Moldova

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FINAL REPORT

by

Dr. Uladzimir Antonenka,

TB Laboratory Expert

uladzimir.antonenka@gmail.com

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Contents

ABBREVIATIONS

Abbreviation	Meaning
BSC-IIa	bio-safety cabinet type IIa
BSL-3	biosafety level 3
DOTS	directly observed therapy short course
DST	drug susceptibility testing
EMB	Ethambutol
EQA	External Quality Assessment
FLD	first line drugs
INH	Isoniazid
LPA	line probe assay
MDR	multi-drug resistance (resistance against INH and RMP)
MIC	Microscopy
MoH	Ministry of Health
NRL	national reference laboratory of TB
NCF	national center for phthisiatry
NTP	national TB program
PHC	primary health care
QMS	quality management system
RMP	Rifampicin
SLD	second line drugs
SM	Streptomycin
SRL	Supranational Reference Laboratory
TAT	Turn-around time
TB	Tuberculosis

Executive summary

Tuberculosis (TB) remains a significant public health concern in Moldova, with an estimated incidence of 76 cases per 100,000 population in 2023, according to the WHO Global TB Report. Multidrug-resistant TB (MDR-TB) poses a major challenge, with 27.4% of new cases and 53.5% of retreatment cases resistant to first-line drugs. However, Moldova has made important strides in TB diagnostics and treatment, including a consistent treatment success rate exceeding 85% for new cases and the use of WHO-recommended rapid diagnostic tools (WRDs) in 94% of new or relapse cases.

The TB diagnostic network in Moldova operates on a tiered system. The National Reference Laboratory (NRL) serves as the central hub, accredited by ISO 15189 and supported by a partnership with the Supranational Reference Laboratory in Borstel, Germany. It performs advanced diagnostics, including MGIT culture, molecular assays such as Xpert MTB/RIF and line probe assays (LPA), and drug susceptibility testing (DST) for first- and second-line drugs. Three regional laboratories (Level 2) in Balti, Vorniceni, and Bender provide culture-based and molecular diagnostics. Level 1 laboratories, comprising 56 facilities, serve as the primary point of care for TB testing in communities across the country.

Key Achievements Moldova has achieved universal geographic coverage for TB diagnostics, ensuring access to testing even in remote areas. The NRL has implemented a cloud-based data collection system, enabling real-time monitoring and enhanced decision-making. Molecular diagnostics are widely available, with 90% of rifampicin-resistant TB cases undergoing second-line DST. The NRL's leadership in quality assurance and integration of digital tools has set a strong foundation for the network.

Key Challenges Despite these successes, challenges persist. Resource inefficiencies arise from duplicate testing across laboratory levels and over-reliance on smear microscopy, which has limited sensitivity. Many Level 1 laboratories show low positivity rates, reflecting weak links with TB clinicians and limited active case-finding. Infrastructure gaps, including inadequate ventilation systems and outdated equipment, and workforce shortages further constrain performance.

Recommendations

1. Revise Diagnostic Algorithm: Transition smear microscopy to a reflex test for Xpert MTB-positive specimens to assess infectiousness and for treatment monitoring. Prioritize Xpert MTB/RIF as the primary diagnostic tool for TB detection.
2. Optimize diagnostic workflows by eliminating duplicate testing and prioritizing molecular diagnostics like Xpert MTB/RIF as the primary tool for TB detection.
3. Strengthen collaboration between laboratories and TB clinicians through joint training and outreach to improve case-finding and referrals.
4. Address infrastructure gaps by upgrading ventilation systems, replacing outdated equipment, and improving laboratory layouts.
5. Expand workforce capacity by recruiting and training additional technicians, especially for high-risk and high-volume laboratories.

6. Introduce targeted next-generation sequencing (tNGS) at the NRL to enhance resistance profiling and support treatment for complex cases. Consider enhancing NRL capacity by hiring and training molecular biologists with expertise in advanced genomic technologies and bioinformatics. This will ensure the effective utilization of tNGS for drug-resistance detection and TB control.
7. Conduct a Diagnostic Network Optimization study to reorganize underperforming laboratories into logistics hubs while improving specimen transportation.

Conclusion Moldova's TB diagnostic network has made significant progress, particularly in the adoption of molecular diagnostics and real-time data collection. However, addressing inefficiencies, strengthening infrastructure, and expanding workforce capacity are critical to improving diagnostic efficiency and effectiveness. By implementing the proposed recommendations, Moldova can enhance its diagnostic network and move closer to its goal of TB elimination.

Introduction

Tuberculosis (TB) remains a critical public health concern in the Republic of Moldova, which is classified as a high-priority country for TB control within the WHO European Region. According to the World Health Organization's (WHO) Global Tuberculosis Report 2023, Moldova recorded an estimated TB incidence of 76 cases per 100,000 population, underscoring the significant burden of disease in the country. Multidrug-resistant TB (MDR-TB) presents a major challenge, with 27.4% of new pulmonary bacteriologically confirmed cases and 53.5% of previously treated cases demonstrating resistance to rifampicin and isoniazid.

Timely analysis of MDR-TB trends since 2016 reveals important dynamics. While the MDR-TB rate among new pulmonary bacteriologically confirmed cases has remained nearly unchanged at approximately 26.15%, there has been a slight decline in MDR-TB rates among previously treated cases, from 56.9% in 2016 to 53.5% in 2023. This downward trend may reflect the country's relatively good treatment success rates among new TB cases, which have consistently exceeded 85%, helping to prevent the development of drug resistance in patients receiving first-line therapy.

Moldova demonstrates notable achievements in TB diagnostics, meeting or nearing several global targets set by WHO. In 2023, 99% of new bacteriologically confirmed pulmonary TB cases and 92% of previously treated cases were tested for rifampicin resistance, reflecting a robust diagnostic framework for detecting drug-resistant TB. Furthermore, 90% of rifampicin-resistant TB cases were tested for susceptibility to fluoroquinolones, ensuring that most patients received appropriate second-line treatment regimens. Additionally, 94% of new or relapse TB cases were tested with WHO-recommended rapid diagnostics (WRDs) at the time of diagnosis, and 97% of these patients had their HIV status determined, indicating strong integration of TB and HIV services.

Despite these successes, areas for improvement in diagnostic coverage remain. In 2023, 27% of pulmonary TB cases were not bacteriologically confirmed, which may reflect challenges in specimen collection, diagnostic capacity at peripheral laboratories, or reliance on clinical diagnosis in certain cases. While 94% of new or relapse cases were tested with WHO-recommended rapid diagnostic tools, further strengthening of diagnostic systems is required to ensure consistent laboratory confirmation and timely detection of drug-resistant strains.

A robust and efficient TB laboratory diagnostic network is vital for addressing these challenges. Accurate and timely diagnostic services are essential for guiding appropriate treatment, monitoring trends in drug resistance, and supporting Moldova's broader TB elimination goals. Recognizing this, the Ministry of Health, in collaboration with international partners, has prioritized strengthening the TB diagnostic network as a cornerstone of the NTP.

This report presents a comprehensive assessment of Moldova's TB laboratory network, identifying critical gaps and providing evidence-based recommendations to improve its capacity and efficiency. These recommendations align with WHO's global TB strategy and Moldova's national commitment to TB elimination.

Goals and objectives of the review

This review aims to provide a comprehensive understanding of the current state of Moldova's tuberculosis (TB) diagnostic network to support strategic decision-making and investment planning by the National Tuberculosis Program (NTP), the Ministry of Health (MoH), the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) Principal Recipient (PR), and other stakeholders involved in TB control. Specifically, the study is designed to:

1. Inform Planning and Investment: Enable stakeholders to effectively plan TB laboratory strengthening activities and prioritize investments for the upcoming years.
2. Describe Strengths and Gaps: Provide a detailed analysis of the current strengths and existing gaps in TB diagnostic services, including infrastructure, human resources, and technical capabilities.
3. Propose Reorganization Needs: Identify areas where reorganization or realignment of the diagnostic network could enhance service delivery and improve efficiency.
4. Develop Evidence-Based Recommendations: Deliver actionable, evidence-based recommendations for strengthening the TB laboratory network to meet national and global TB control objectives.

Objectives

1. Comprehensive Assessment of the Diagnostic Network
    - Evaluate the current structure, organization, and functionality of the TB laboratory network, including the National Reference Laboratory (NRL), regional reference laboratories, and peripheral laboratories.
    - Assess coverage and accessibility of TB diagnostic services across Moldova.
2. Gap and Needs Identification
    - Identify gaps in key areas, such as biosafety, diagnostic equipment, supplies, workforce capacity, and data management systems.
    - Highlight the needs for reorganization or enhancement to ensure alignment with the country's TB control goals.
3. Alignment with WHO Guidelines
    - Ensure diagnostic algorithms, technologies, and practices align with the latest WHO recommendations for TB and MDR-TB diagnosis.

4. Capacity Building and Training
    - Assess workforce capacity, identify training needs, and propose sustainable strategies to improve laboratory personnel competencies and retention.
5. Data-Driven Decision Support
    - Provide stakeholders with evidence-based insights to inform resource allocation, policy updates, and the integration of new technologies for TB diagnosis.
6. Recommendations for Strengthening the Laboratory Network
    - Propose interventions to optimize laboratory resource utilization, improve quality assurance systems, and strengthen specimen logistics.

Methodologies and approaches used for this review.

This review of the TB laboratory and diagnostic network in Moldova employed a combination of desk reviews, field assessments, and stakeholder engagements. The approaches were designed to provide a comprehensive understanding of the system's strengths and gaps while aligning with global TB control strategies and national objectives. Below are the methodologies utilized:

Desk Review

The desk review analyzed key documents, reports, and guidelines to understand the current state of the TB diagnostic network and its alignment with national and international standards. Documents reviewed included:

- National TB Program policies (2022–2025).
- Ministry of Health Orders no. 970/2023 and no. 121/2024.
- WHO and Global Laboratory Initiative (GLI) guidelines on TB diagnostics.
- Previous assessments, including the GLC mission reports from 2021 and 2023.
- Statistical data on TB incidence, treatment outcomes, and diagnostic performance metrics for Moldova.
- Sampling and specimen management protocols.

The desk review provided context on governance, operational frameworks, and historical challenges within the network.

Data Collection Tool

Modified Score-TB Package (eTool v2.1)

- Assessed the overall quality and capacity of laboratories, focusing on general laboratory quality management and the specific performance of diagnostic methods.
- Evaluated compliance with international standards, providing a quantitative measure of laboratory readiness.

The tool were critical in identifying areas for improvement and provided structured data for the analysis.

Field Visits and Direct Observations

A structured in-country mission was conducted between July 21 and July 31, 2024, to assess various tiers of the TB diagnostic network. Field visits included:

- **National Reference Laboratory (NRL)**.
- **All Regional Reference Laboratories (Level 2)**.
- **Representatively selected Peripheral Laboratories (Level 1)**.

The fieldwork focused on collecting insights into workflow efficiency, equipment use, staffing, and diagnostic capacity. The detailed agenda of the in-country mission is included in **Annex 1**.

Stakeholder Engagement

Meetings were held with key stakeholders to gather insights and validate findings. These stakeholders included:

- Director of Institute of Phthisiopneumology (IPP)– Doina Rusu;
- National TB Program (NTP) manager Valentina Vilc;
- Head of NRL Valeriu Crudu;
- Regional laboratory managers and staff.
- Principal recipients of GFATM funding (Victor Burinschi, Elena Romancenco) and international partners.

Engagements provided context on policy implementation, operational challenges, and opportunities for efficient coordination.

Implementation Timeline

The review was executed in four phases:

1. **Preparation Phase (June 27–July 19, 2024):** Desk review, tool selection, and logistical planning.
2. **In-Country Mission (July 21–July 31, 2024):** Field visits and stakeholder meetings. (See Annex 1 for the detailed agenda.)
3. **Data Analysis (August 1–August 31, 2024):** Compilation and synthesis of findings.
4. **Reporting Phase (September–November 2024):** Drafting and finalization of the comprehensive report.

TB Laboratory diagnostic algorithm

The currently endorsed tuberculosis (TB) diagnostic algorithm in Moldova was approved in 2024 and integrated into the National Clinical Protocol "TUBERCULOSIS IN ADULTS," PCN-123. This updated algorithm reflects a structured approach to TB diagnosis, combining microscopy, molecular rapid testing and culture-based conventional methods.

The diagnostic process begins with identifying patients exhibiting clinical or radiological symptoms indicative of TB at primary healthcare institutions. These patients are referred to district or municipal phthisiopneumological services for comprehensive evaluation. At least two sputum samples, or alternative specimens such as bronchial lavage, gastric lavage, or nasopharyngeal aspirates, are collected for microbiological examination. Microscopic examination is performed on both samples, and one sample is analyzed using the molecular-genetic Xpert MTB/RIF Ultra test. This molecular method

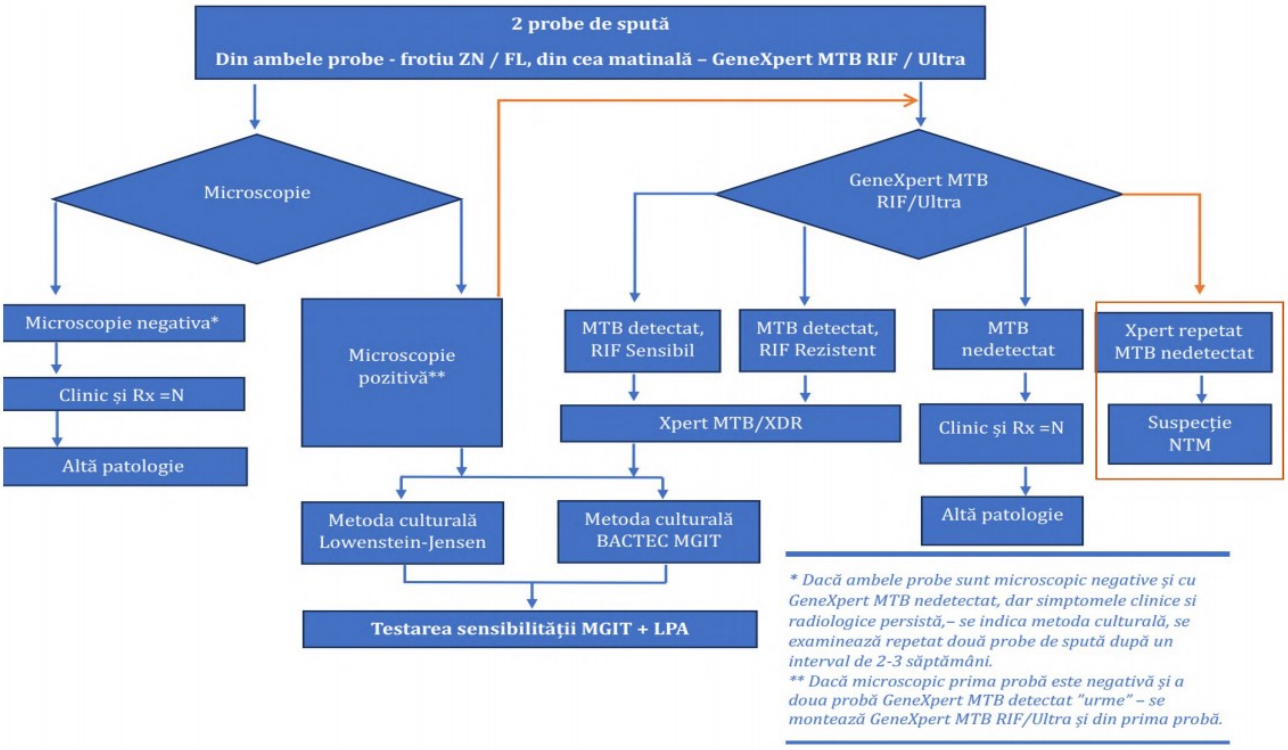


Figure 1: TB laboratory Diagnostic algorithm (2024)

detects the presence of Mycobacterium tuberculosis (MTBC) and rifampicin resistance, and it is also applied to non-sputum specimens for extrapulmonary TB diagnosis. For all MTB-positive cases further molecular testing is conducted using Xpert MTB/XDR to determine resistance to isoniazid and second-line drugs.

For confirmed cases (diagnosed microbiologically or clinically), samples are sent to reference laboratories for culture on Löwenstein-Jensen (LJ) or MGIT media. Phenotypic culture-based susceptibility testing is used for drug resistance confirmation and for testing new antituberculosis drugs.

Challenges and Recommendations

- **Reliance on Smear Microscopy**: Although still included, this method has limited sensitivity and should be replaced entirely with molecular diagnostics as a primary tool. The smear microscopy should stay only as a reflex test for Xpert MTB-positive specimens to determine the patient's infectious status and for treatment monitoring.
- To further align with international standards and enhance drug resistance profiling, Moldova should adopt **targeted next-generation sequencing (tNGS)**. This advanced molecular technique enables comprehensive resistance profiling within a turnaround time of just 3-5 days. Its application, particularly for multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), can significantly improve diagnostic accuracy and optimize treatment outcomes.

Laboratory network

Structure of the Laboratory Network

The TB laboratory network in the Republic of Moldova operates as a tiered system, providing diagnostic services across the national, regional, and district levels. The network is organized into three levels and designed to ensure comprehensive coverage and alignment with international TB control standards:

- **National Reference Laboratory (Level 3).**

The National Reference Laboratory (NRL), located at the Institute of Phthisiopneumology “Chiril Draganiuc” in Chișinău, serves as the central hub for tuberculosis (TB) diagnostics in Moldova. Accredited according to the ISO 15189 standard, the NRL ensures that its diagnostic processes meet the highest international quality and safety benchmarks, providing a cornerstone for reliable and accurate TB detection across the country.

As the leading facility in the TB laboratory network, the NRL oversees quality assurance (QA) and external quality assurance (EQA) activities for all laboratories within the system. Equipped with advanced diagnostic technologies, it performs culture and drug susceptibility testing (DST) for both first- and second-line anti-TB drugs, utilizing liquid (MGIT) and solid media systems. The laboratory also employs Line Probe Assays (LPA) for rapid detection of resistance to critical drugs, including rifampicin, isoniazid, and fluoroquinolones. Additionally, the GeneXpert MTB/RIF system enables the rapid molecular detection of TB and rifampicin resistance, ensuring timely and accurate diagnosis.

In addition to its diagnostic functions, the NRL plays a vital role in capacity building and operational oversight. It provides training and supervision for regional and peripheral laboratories, strengthening the competencies of laboratory personnel throughout Moldova.

- **Regional Reference Laboratories (Level 2)**

Moldova has **three Level 2 Regional Reference Laboratories**, strategically located to provide advanced diagnostic services and support the peripheral network:

1. **Regional Laboratory in Balti (Northern Region).**
2. **Regional Laboratory in Vorniceni, Straseni (Central Region).**

3. **Regional Laboratory in Tiraspol (Transnistria Region).**

Their role and functionality:

- Perform culture-based diagnostics and drug susceptibility testing (DST) for first-line and second-line drugs.
- Provide molecular diagnostics using Xpert MTB/RIF to detect TB and rifampicin resistance.
- Perform Line Probe Assays (LPA) for rapid detection of resistance to critical drugs, including rifampicin, isoniazid, and fluoroquinolones.
- Serve as referral centers for peripheral laboratories in their respective regions.
- Participate in quality assurance programs managed by the NRL.

- **Peripheral Laboratories (Level 1).**

The Level 1 network comprises **56 Peripheral laboratories**, distributed across Moldova district hospitals and municipal health centers.

Their role and functionality:

- Serve as the primary point of contact for patients with suspected TB.
- Conduct sputum smear microscopy using Ziehl-Neelsen staining.
- Perform rapid molecular diagnostics using Xpert MTB/RIF on GeneXpert devices for TB detection and rifampicin resistance.
- Refer samples requiring advanced diagnostics (e.g., culture or DST) to Level 2 laboratories or the NRL.

Major Achievements

- The network is chaired by an NRL linked to the SRL Borstel, the partnership is confirmed by WHO.
- The network covers the complete geographic region of Republic of Moldova.
- Collaboration and communication between the laboratories of the network is well-developed and functional.
- Tasks and responsibilities of the different types and levels of laboratories are well defined. NRL plays the role of a strong network leader.

Challenges

- A strategic plan for national TB laboratory network development and strengthening is missing.

Recommendations:

- Plan and conduct a Diagnostic Network Optimization (DNO) study, considering expanding options for multidisease testing for HCV, HIV, etc. The aim of the study should be stepwise reduction of level 1 labs with low workload and performance, simultaneously improving sputum transportation to functional laboratories (for details see chapter 6.4).
- Develop a national strategic plan for further development and strengthening of the TB laboratory network.

National Reference Laboratory (NRL)

The National Reference Laboratory (NRL) is situated at the "Chiril Draganiuc" Institute of Phthisiopulmonology in Chișinău. It maintains a formal partnership with the Supranational Reference Laboratory (SRL) Borstel, Germany, recognized by the WHO. The NRL operates as the cornerstone of Moldova's TB diagnostic network, providing a comprehensive range of advanced diagnostic services. These include:

- Microscopy: Ziehl-Neelsen (ZN) and fluorescence microscopy.
- Culture and Drug Susceptibility Testing (DST):
    - Solid media (Löwenstein-Jensen, LJ) and liquid culture systems (MGIT).
    - DST for both first-line drugs (FLD) and second-line drugs (SLD), including new drugs such as bedaquiline (BDQ), clofazimine (CFZ), delamanid (DLM), and linezolid (LZD).
- Molecular Resistance Testing:
    - Genotype MTBDR*plus* and MTBDR*sl* (Bruker, Germany) for FLD and SLD.
    - Xpert MTB/RIF and Xpert MTB/XDR assays.

The NRL consistently participates in external quality assessments (EQA) using INSTAND panels and has achieved high standards with no significant deviations for many years.

Under the leadership of Dr. Valeriu Crudu, the NRL benefits from a knowledgeable and dedicated director who demonstrates strong management and technical expertise. The laboratory staff actively participate in international training programs and workshops, ensuring up-to-date competencies in cutting-edge TB diagnostic techniques.

In addition to its diagnostic services, the NRL is a hub for research and innovation. It regularly conducts evaluation studies of novel TB diagnostic methods and engages in research on the molecular epidemiology of TB. These efforts have resulted in publications in international peer-reviewed journals, showcasing the NRL's contributions to global TB research and control efforts.

The NRL receives diagnostic specimens from patients of the Institute of Phthisiopulmonology and 18 other healthcare facilities. The patients from the whole country may be directly referred to the Institute for the diagnosis confirmation.

A key feature of the NRL is its **integration of MGIT and GeneXpert systems with the Laboratory Information Management System (LIMS)**. This digital integration enables:

- **Paperless Data Flow**: Seamless transmission of results directly from diagnostic machines into the LIMS.
- **Efficiency**: Faster turnaround times for reporting results to clinicians and the National Tuberculosis Program (NTP).
- **Data Integrity**: Minimization of transcription errors and enhanced traceability of laboratory records.

The National Reference Laboratory (NRL) demonstrates robust diagnostic activity across various methodologies, maintaining its pivotal role in Moldova's TB diagnostic network. Below is a detailed discussion of its performance based on the provided data for 2023.

- **Diagnostic Smears**: A total of **10,522 diagnostic smears** were analyzed, with a positivity rate of **14.1%** for the year. Positivity varied across quarters, with the highest rate in Q2 (18.3%) and the lowest in Q3 (13.7%). This reflects consistent performance, although Q2's spike may indicate seasonal or case-mix variations.
- **Follow-up Smears**: The NRL processed **3,179 follow-up smears**, supporting treatment monitoring. This workload underscores the NRL's contribution to patient management.
- **Culture Volume and Positivity**: The NRL processed **25,882 cultures**, with an overall positivity rate of **8.1%**. Quarterly positivity rates were stable, ranging from 7.8% to 8.4%. These figures align with expectations for solid media, which have lower sensitivity compared to liquid systems.
- The **contamination rate on solid media** averaged **3.2%**, well within acceptable limits, reflecting effective laboratory practices and sample handling.
- **Culture Volume and Positivity**: A total of **12,010 MGIT cultures** were processed, with a higher overall positivity rate of **12.5%**, indicative of its superior sensitivity compared to LJ media. Positivity rates fluctuated, peaking in Q2 (19.6%) and dipping in Q3 (10.1%).

- The average **contamination rate** for MGIT was **6.0%**, slightly higher than for LJ cultures but acceptable for liquid culture systems.
- **DST for First-Line Drugs (FLD)**: The NRL performed **920 DSTs** for FLD using MGIT, providing critical data for patient management. The volume varied significantly across quarters, with the highest activity in Q4.
- **DST for Second-Line Drugs (SLD)**: A total of **624 DSTs** for SLD were conducted, reflecting the laboratory's capacity to monitor drug-resistant TB.
- A total of **10,135 Xpert MTB/RIF tests** were conducted (30% of the annual testing volume of the whole county), with an MTB positivity rate of **14.1%**, consistent across most quarters. The RIF resistance detection rate among MTB-positive cases was **24.4%**.
- **Error and Invalid Results**: The proportion of tests yielding errors or invalid results was **3.2%**, within acceptable limits but with variability between quarters, peaking in Q4 at 5.0%. This highlights areas for potential improvement in sample preparation or equipment maintenance.
- **FL-LPA**: The NRL conducted **610 FL-LPA tests**, demonstrating strong capacity for rapid resistance detection against FLDs.
- **SL-LPA**: The laboratory also processed **342 SL-LPA tests**, reflecting its contribution to advanced diagnostics for complex MDR-TB and XDR-TB cases.

Table 1: Workload and performance parameters of NRL in 2023.

Methods	**Q1**	**Q2**	**Q3**	**Q4**	**Total**
Smear microscopy (Diagnostic)	2814	2619	2393	2696	10522
MIC+	303	479	327	379	1488
MIC+, %	10,8%	18,3%	13,7%	14,1%	14,1%
Smear microscopy (Follow-up)	862	723	804	790	3179
Culture on solid media (LJ)	6606	6443	6220	6613	25882
Positive cultures on solid media	516	544	525	520	2105
Cx+, LJ, %	7,8%	8,4%	8,4%	7,9%	8,1%
Contamination rate on solid media, %	2,9%	3,6%	3,5%	2,7%	3,2%
MGIT cultures	3691	1340	3323	3656	12010
Positive cultures, MGIT	434	263	335	465	1497
Cx+, MGIT, %	11,8%	19,6%	10,1%	12,7%	12,5%
Contamination rate, MGIT %	5,0%	6,0%	7,0%	6,2%	6,0%

DST for FLD in MGIT	249	123	216	332	920
DST for SLD in MGIT	170	141	138	175	624
Xpert MTB/RIF tests	2751	2417	2305	2662	10135
MTB detected (incl. Trace)	395	348	282	407	1432
MTB detected,%	14,4%	14,4%	12,2%	15,3%	14,1%
MTB detected RIF res. detected (RR)	93	81	68	107	349
MTB detected RIF res. detected (RR),%	23,5%	23,3%	24,1%	26,3%	24,4%
Error, invalid, no result, %	3,1%	1,4%	2,9%	5,0%	3,2%
FL-LPA	176	115	145	174	610
SL-LPA	116	86	68	72	342

The existing design of laboratory premises could not sustain adequate and safe workflow for a high-risk TB laboratory. For example, DST room situated closer to the laboratory entrance, is not ventilated and has no anteroom. In the case of biohazard infectious aerosols could be easily spread to clean areas. The lack of mechanical ventilation system with properly validated directional airflow additionally compromising laboratory biosafety.

Recommendations:

- To enhance efficiency and streamline operations, it is recommended to establish two specialized departments within the National Reference Laboratory (NRL): Clinical Diagnostics and Monitoring. This restructuring would align the NRL's activities more effectively with its dual roles in diagnostic service delivery and laboratory network management. research.
- To strengthen the National Reference Laboratory's capacity and align with the implementation of advanced molecular diagnostics, it is recommended to establish dedicated human resource capacity for two molecular biologists. These specialists should focus exclusively on the implementation, operation, and quality assurance of targeted next-generation sequencing (tNGS) and whole genome sequencing (WGS). Their expertise will be critical for:
    - Ensuring the smooth adoption of tNGS and WGS technologies.
    - Managing the associated workflows, data analysis, and result interpretation.
    - Establishing and managing collection of genomic and phenotypic data of all sequenced strains.
    - Supporting validation processes and maintaining compliance with international standards.
    - Driving research and capacity-building initiatives in the laboratory network.

- Give highest priority to the reconstruction of the NRL laboratory premises. Strongly and actively support the progress of the project wherever possible.
- In order to provide sufficient biosafety standard for culture and DST works, high risk laboratory areas should be reorganized in the way, presented in figures 2 and 3.
- In the frames of the hospital renovation a centralized hospital HVAC should be planned and aligned with laboratory floorplan presented in Fig. 3. It should be avoided that laboratory rooms of high-risk area will share the same ventilation system with other laboratory rooms.
- The HVAC system for the high-risk area should be able to maintain acceptable air exchange rate (6-12 ACH) and directional airflow from the entrance to the distant part of the room #112 and room #111.
- Constructing air-tight hatches (crossing counter) between room# 111 and room #112 (autoclave room); as well as room #112 and the corridor. This will allow safe transfer of contaminated materials for autoclaving and specimens.

Fig. 2 Recommended layout of high risk TB laboratory area.

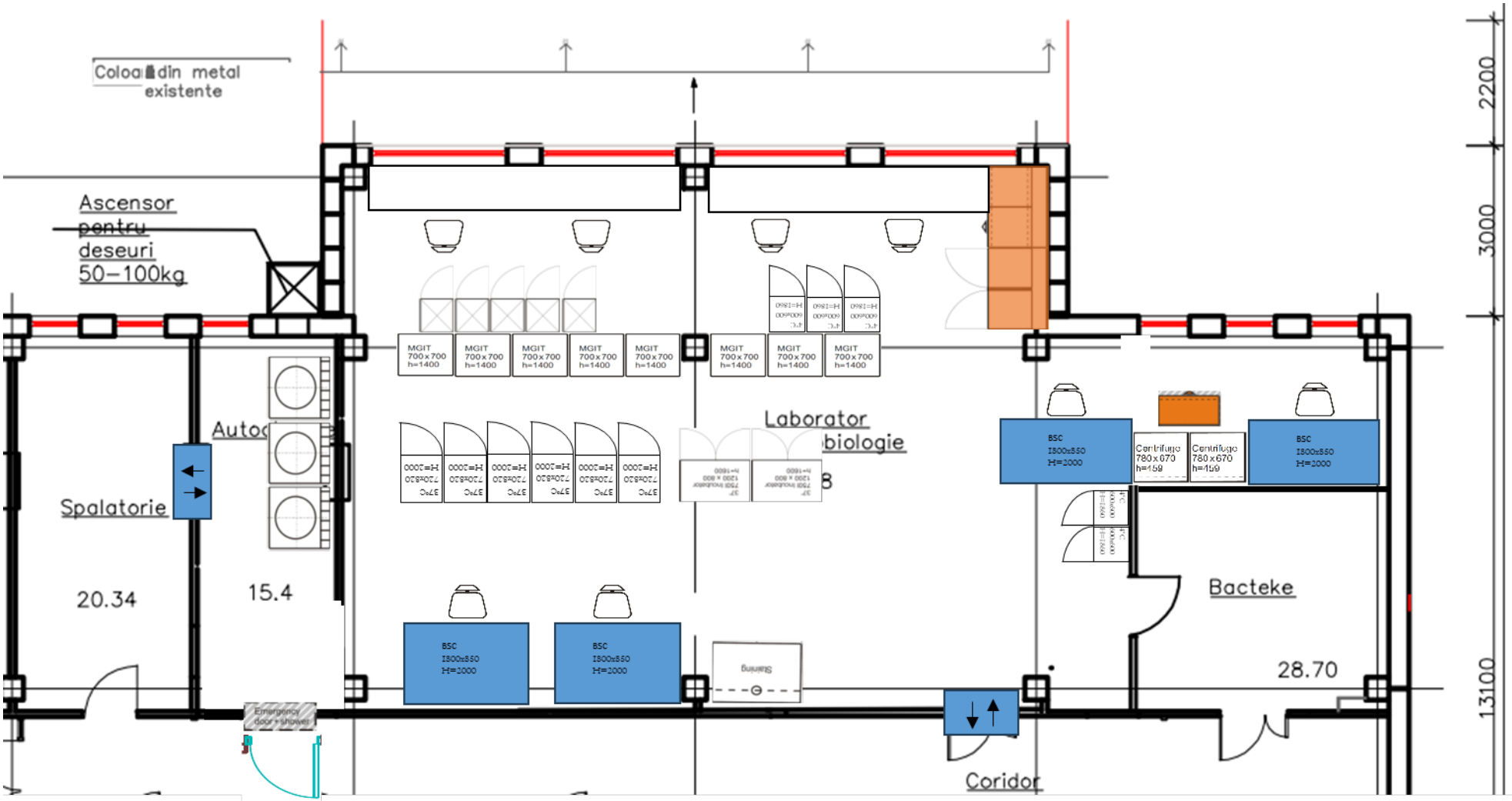
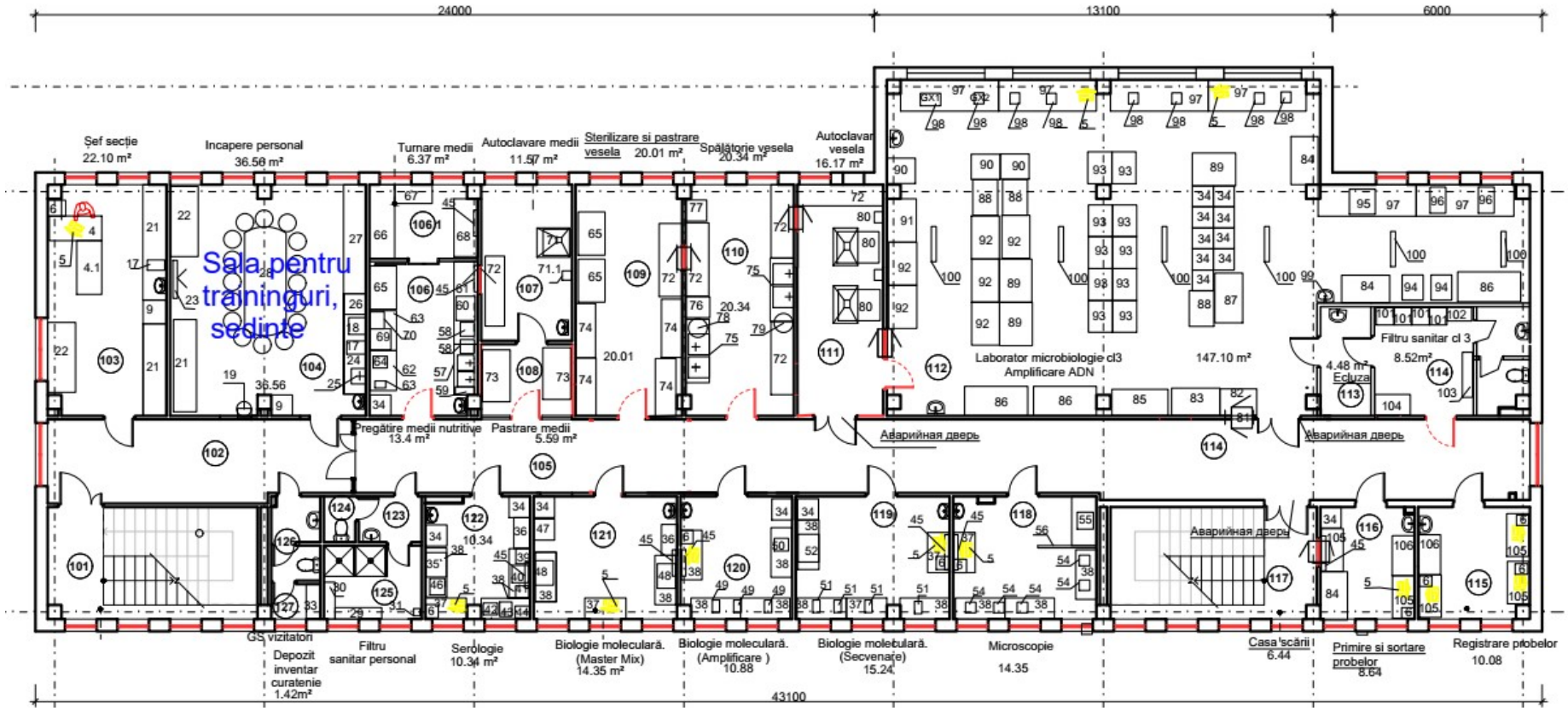


Fig. 3 Recommended layout of 1st laboratory floor, including high-risk area.



Level 2 laboratories

Findings: Moldova's TB diagnostic network includes three Level 2 Regional Reference Laboratories: Bălți, Vorniceni, and Bender. These laboratories play vital roles in TB diagnostics through culture-based testing, molecular testing, and drug susceptibility testing (DST). Analysis of test statistics for 2017–2023 highlights trends and challenges across the laboratories.

Table 2: Test Statistics for LJ, MGIT, and Xpert MTB/RIF (2017–2023)

Year	*Laboratory*	*LJ Cultures*	*LJ Positives*	*%*	*MGIT Cultures*	*MGIT Positives*	*%*	*Xpert Tests*	*Xpert MTB Detected*	*%*
2017	Bălți	11,454	1,054	9.2%	5,327	856	16.1%	2,295	329	14.3%
2017	Vorniceni	18,857	1,583	8.4%	5,734	1,219	21.3%	2,435	498	20.5%
2017	Bender	10,298	1,940	18.8%	1,402	386	27.5%	1,589	131	8.2%
2018	Bălți	10,938	1,043	9.5%	4,917	836	17.0%	2,308	293	12.7%
2018	Vorniceni	20,282	1,895	9.3%	6,774	1,337	19.7%	3,286	529	16.1%
2018	Bender	10,653	1,844	17.3%	1,639	434	26.5%	1,934	166	8.6%
2019	Bălți	10,651	936	8.8%	4,595	746	16.2%	2,116	265	12.5%
2019	Vorniceni	19,992	1,578	7.9%	8,672	1,072	12.4%	2,751	498	18.1%
2019	Bender	10,065	1,624	16.1%	1,934	407	21.0%	992	132	13.3%
2020	Bălți	8,102	571	7.0%	4,035	462	11.4%	909	185	20.4%
2020	Vorniceni	14,596	1,100	7.5%	9,236	845	9.1%	1,784	320	17.9%
2020	Bender	8,534	1,020	12.0%	1,872	354	18.9%	627	127	20.3%
2021	Bălți	7,914	676	8.5%	3,918	468	11.9%	1,358	246	18.1%
2021	Vorniceni	15,835	1,157	7.3%	7,402	688	9.3%	2,966	442	14.9%
2021	Bender	8,542	1,000	11.7%	3,116	566	18.2%	598	92	15.4%
2022	Bălți	8,015	717	8.9%	3,063	531	17.3%	1,886	241	12.8%
2022	Vorniceni	17,549	956	5.4%	3,635	379	10.4%	3,478	376	10.8%
2022	Bender	7,271	704	9.7%	5,682	708	12.5%	866	221	25.5%
2023	Bălți	9,195	696	7.6%	1,468	410	27.9%	2,398	292	12.2%
2023	Vorniceni	18,865	869	4.6%	4,329	485	11.2%	4,141	396	9.6%
2023	Bender	8,223	829	10.1%	3,324	372	11.2%	857	306	35.7%

Trends Observed

Declining Culture Volumes:

LJ and MGIT test volumes dropped across all laboratories over time, likely reflecting shift in logistics to NRL.

Xpert MTB/RIF Expansion:

Molecular testing increased, especially in Vorniceni, where Xpert volumes rose from **2,435 tests in 2017** to **4,141 in 2023**. Positivity rates dropped, reflecting improved case management or a shift in patient profiles.

High Positivity in Bender:

Bender consistently reports the highest positivity rates for LJ (18.8% in 2017, 10.1% in 2023) and MGIT (27.5% in 2017, 11.2% in 2023), reflecting its focus on high-risk cases in the Transnistria region.

Findings by Laboratory

Bălți Laboratory

- Performs **~200 FL-DST tests annually** and does not conduct SL-DST.
- Declining LJ positivity rates (from **9.2% in 2017** to **7.6% in 2023**) suggest either improved TB control or diagnostic inefficiencies.
- Challenges include aging infrastructure (non-functional autoclave, water still) and frequent duplication of Xpert MTB/RIF tests for the same patients.

Vorniceni Laboratory

- Focuses exclusively on molecular and culture diagnostics; **does not conduct pDST or SL-DST**.
- Culture positivity rates dropped significantly for both LJ (**8.4% to 4.6%**) and MGIT (**21.3% to 11.2%**) between 2017 and 2023.
- Challenges include inflated culture numbers due to unnecessary duplication (2 LJ and 2 MGIT per patient) and reliance on molecular diagnostics for drug resistance detection.

Bender Laboratory

- Performs **up to 160 SL-DST tests annually**, including for new drugs like bedaquiline and delamanid.
- Reports the **highest positivity rates for LJ, MGIT, and Xpert MTB/RIF**, underscoring its critical role in Transnistria.
- Challenges include biosafety issues (unsafe BSCs, inadequate ventilation) and aging workforce.

Recommendations

1. **Retain Bender as a Level 2 Laboratory**:
    - Support its role in SL-DST and advanced diagnostics, particularly for the high-burden Transnistria region.

- Address biosafety issues, including upgrading BSCs and ventilation systems.

2. **Centralize pDST at NRL**:
    - Transition Bălți and Vorniceni to Level 1 logistics hubs, focusing on specimen referral to NRL for centralized DST.
3. **Expand Molecular Diagnostics**:
    - Introduce **Xpert MTB/XDR** in all Level 2 laboratories to improve second-line resistance detection.
4. **Streamline Workflow**:
    - Enforce diagnostic algorithms in Bălți to prevent repeated Xpert MTB/RIF testing.
    - Eliminate duplicate cultures in Vorniceni to improve efficiency and resource utilization.
5. **Invest in Workforce and Infrastructure**:
    - Recruit and train new staff to address workforce shortages, particularly in Bender.
    - Replace outdated equipment in Bălți and improve infrastructure across all laboratories.

Conclusion

The Level 2 laboratories in Moldova demonstrate varied contributions to TB diagnostics. Bender's role in SL-DST highlight its critical importance to the Transnistria region in case of possible logistical challenges. By optimizing workflows in Bălți and Vorniceni and centralizing DST at NRL, the network can achieve greater efficiency and effectiveness in TB control.

Level 1 laboratories

Findings

The Level 1 laboratories serve as the backbone of Moldova's TB diagnostic network, providing essential diagnostic services to communities across the country. These laboratories are critical for ensuring early detection and treatment monitoring for tuberculosis (TB). However, field visits and data analysis reveal several inefficiencies and systemic issues that impact their overall performance.

Diagnostic Overview

- **Smear Microscopy**:
    - Smear microscopy using Ziehl-Neelsen (ZN) staining is the primary diagnostic method for many laboratories, especially for treatment monitoring.
    - In 2023, **43,581 diagnostic smears** were conducted, with only **997 positive results (2.3%)**, reflecting low diagnostic yield and limited sensitivity of the method.

- **Molecular Testing:**
    - Xpert MTB/RIF systems, including Ultra cartridges, are widely used, with **14,802 tests conducted** in 2023, resulting in **1,030 positive results (7.0%)**.
    - Positivity rates vary widely, with some laboratories achieving as low as **1.0%**, reflecting inefficiencies in patient selection (Table 3).
    - The total number of positive Xpert MTB/RIF tests is 3524 in 2023, in the same time the number of bacteriologically confirmed pulmonary cases in 2023 was ~1556 (Global TB Report 2024). This indicates that many patients diagnosed at Level 1 laboratories are unnecessarily re-tested at higher-level laboratories, wasting resources and delaying treatment initiation.

The following **Level 1 laboratories** were visited during the review:

- **AMT Ciocana**
- **AMT Botanica**
- **SR Ialoveni**
- **SR Orhei**
- **SR Florești**
- **SR Cahul**

Table 3: Xpert MTB/Rif statistics for the TB Laboratory network in Moldova

Laboratory	2017			2018			2019			2020			2021			2022			2023		
	Total	Positive	%	Total	Positive	%	Total	Positive	%	Total	Positive	%	Total	Positive	%	Total	Positive	%	Total	Positive	%
AMT Ciocana	342	10	2,9	278	10	0,0	604	35	5,8	54	1	1,9	67	4	6,0	148	7	4,7	201	2	1,0
AMT Riscani	159	15	9,4	400	22	5,5	391	21	5,4	150	12	8,0	76	12	15,8	205	7	3,4	189	4	2,1
AMT Centru	239	12	5,0	458	25	5,5	548	11	2,0	220	4	1,8	358	20	5,6	423	12	2,8	592	8	1,4
AMT Botanica	1381	39	2,8	1323	32	2,4	982	28	2,9	355	16	4,5	807	31	3,8	795	19	2,4	815	17	2,1
AMT Buiucani	645	28	4,3	458	16	3,5	280	7	2,5	272	8	2,9	148	10	6,8	284	7	2,5	412	13	3,2
Mun.Chisinau total	**2766**	**104**	**3,8**	**2917**	**105**	**3,6**	**2805**	**102**	**3,6**	**1051**	**41**	**3,9**	**1456**	**77**	**5,3**	**1855**	**52**	**2,8**	**2209**	**44**	**2,0**
SR Anenii Noi	657	55	8,4	661	28	4,2	443	31	7,0	210	21	10,0	339	22	6,5	372	26	7,0	311	16	5,1
SR Basarabeasca	141	10	7,1	263	12	4,6	61	3	4,9	62	3	4,8	36	1	2,8	102	7	6,9	42	1	2,4
SR Briceni	325	12	3,7	436	15	3,4	262	18	6,9	55	9	16,4	40	1	2,5	135	11	8,1	133	10	7,5
SR Cahul	897	37	4,1	1083	41	3,8	890	31	3,5	195	23	11,8	349	29	8,3	296	26	8,8	259	26	10,0
SR Cantemir	139	19	13,7	572	30	5,2	441	26	5,9	216	12	5,6	284	27	9,5	346	19	5,5	61	6	9,8
SR Calarasi	463	28	6,0	774	36	4,7	392	43	11,0	203	16	7,9	224	27	12,1	265	24	9,1	238	29	12,2
SR Causeni	407	35	8,6	581	55	9,5	433	42	9,7	286	26	9,1	390	27	6,9	531	34	6,4	520	41	7,9
SR Cimislia	575	21	3,7	694	30	4,3	409	9	2,2	142	5	3,5	204	3	1,5	174	0	0,0	104	2	1,9
SR Criuleni	189	53	28,0	978	66	6,7	598	50	8,4	289	24	8,3	453	30	6,6	584	44	7,5	344	28	8,1
SR Donduseni	455	15	3,3	449	14	3,1	377	8	2,1	126	8	6,3	111	4	3,6	393	7	1,8	400	13	3,3
SR Drochia	662	37	5,6	705	20	2,8	350	20	5,7	203	19	9,4	155	7	4,5	350	16	4,6	164	20	12,2
SR Edinet	145	16	11,0	158	7	4,4	91	14	15,4	66	5	7,6	112	5	4,5	142	10	7,0	61	13	21,3
SR Falesti	450	38	8,4	468	32	6,8	301	21	7,0	166	21	12,7	134	15	11,2	229	25	10,9	323	43	13,3
SR Floresti	476	66	13,9	490	28	5,7	245	28	11,4	92	18	19,6	247	39	15,8	111	26	23,4	279	57	20,4
SR Glodeni	395	20	5,1	393	20	5,1	322	17	5,3	143	11	7,7	183	10	5,5	143	16	11,2	284	13	4,6
SR Hincesti	120	38	31,7	743	63	8,5	349	50	14,3	138	28	20,3	201	28	13,9	299	36	12,0	104	16	15,4
SR Ialoveni	466	41	8,8	1023	35	3,4	405	32	7,9	214	12	5,6	391	27	6,9	320	15	4,7	285	22	7,7

SR Leova	35	28	80,0	264	34	12,9	231	29	12,6	72	13	18,1	146	22	15,1	149	22	14,8	182	21	11,5
SR Nisporeni	623	52	8,3	692	32	4,6	338	28	8,3	270	22	8,1	322	23	7,1	363	23	6,3	307	23	7,5
SR Ocnita	346	20	5,8	434	18	4,1	302	11	3,6	76	6	7,9	148	24	16,2	217	7	3,2	164	9	5,5
SR Orhei	939	76	8,1	710	48	6,8	478	58	12,1	193	44	22,8	179	30	16,8	490	59	12,0	453	51	11,3
SR Rezina	513	27	5,3	535	31	5,8	327	29	8,9	179	19	10,6	363	26	7,2	256	0	0,0	389	29	7,5
SR Riscani	847	19	2,2	850	18	2,1	541	17	3,1	87	9	10,3	152	13	8,6	267	3	1,1	62	16	25,8
SR Singerei	45	27	60,0	430	30	7,0	330	22	6,7	112	5	4,5	80	23	28,8	551	20	3,6	132	25	18,9
SR Soroca	459	29	6,3	444	27	6,1	186	19	10,2	351	24	6,8	216	27	12,5	446	0	0,0	387	26	6,7
SR Straseni	556	39	7,0	418	25	6,0	308	40	13,0	88	19	21,6	239	31	13,0	354	31	8,8	413	33	8,0
SR Soldanesti	270	23	8,5	149	15	10,1	318	22	6,9	210	25	11,9	222	24	10,8	292	25	8,6	281	24	8,5
SR Stefan Voda	338	23	6,8	625	27	4,3	268	14	5,2	117	15	12,8	228	16	7,0	605	17	2,8	542	21	3,9
SR Taraclia	359	14	3,9	349	8	2,3	321	8	2,5	154	5	3,2	136	4	2,9	175	3	1,7	191	8	4,2
SR Telenesti	28	24	85,7	244	24	9,8	315	28	8,9	138	18	13,0	19	16	84,2	192	13	6,8	89	32	36,0
SR Ungheni	654	53	8,1	661	29	4,4	463	46	9,9	313	27	8,6	378	35	9,3	519	31	6,0	1059	62	5,9
SR Comrat	615	22	3,6	472	23	4,9	456	18	3,9	96	4	4,2	66	4	6,1	31	8	25,8	114	9	7,9
SR Ceadir-Lunga	123	14	11,4	348	9	2,6	367	12	3,3	104	6	5,8	190	7	3,7	376	15	4,0	280	8	2,9
SR Vulcanesti	111	5	4,5	122	6	4,9	7	0	0,0	47	4	8,5	38	4	10,5	72	3	4,2	67	4	6,0
Districts right bank	**16589**	**1140**	**6,9**	**21135**	**1041**	**4,9**	**14730**	**946**	**6,4**	**6464**	**567**	**8,8**	**8431**	**708**	**8,4**	**12002**	**674**	**5,6**	**11233**	**801**	**7,1**
SM Tiraspol	842	55	6,5	1036	73	7,0	814	102	12,5	497	66	13,3	340	9	2,6	547	34	6,2	1036	59	5,7
DFP Bender	309	14	4,5	229	9	3,9	247	17	6,9	178	18	10,1	208	19	9,1	201	27	13,4	201	46	22,9
SR Camenca	216	6	2,8	381	8	2,1	202	8	4,0	203	8	3,9	204	5	2,5	239	12	5,0	508	16	3,1
DFP Dubasari (SN)	187	22	11,8	220	26	11,8	182	28	15,4	80	8	10,0	108	16	14,8	229	30	13,1	188	35	18,6
SR Grigoriopol	487	28	5,7	624	41	6,6	420	18	4,3	262	13	5,0	234	26	11,1	376	13	3,5	273	11	4,0
SR Ribnita	764	9	1,2	986	35	3,5	863	34	3,9	553	26	4,7	820	6	0,7	431	20	4,6	868	31	3,6
SR Slobozia	392	11	2,8	459	32	7,0	363	22	6,1	172	20	11,6	82	5	6,1	225	20	8,9	302	18	6,0
Penit, Transnist	345	9	2,6	437	15	3,4	269	9	3,3	149	5	3,4	188	5	2,7	292	5	1,7	193	13	6,7

Transnistria total	**3542**	**154**	**4,3**	**4372**	**239**	**5,5**	**3360**	**238**	**7,1**	**2094**	**164**	**7,8**	**2184**	**91**	**4,2**	**2540**	**161**	**6,3**	**3569**	**229**	**6,4**
Districts All RM	**20131**	**1294**	**6,4**	**25507**	**1280**	**5,0**	**18090**	**1184**	**6,5**	**8558**	**731**	**8,5**	**10615**	**799**	**7,5**	**14542**	**835**	**5,7**	**14802**	**1030**	**7,0**
LNR Chisinau	9193	1300	14,1	10116	1329	13,1	9332	1066	11,4	3551	582	16,4	6888	1114	16,2	8877	1321	14,9	11404	1500	13,2
LRR Balti	2295	329	14,3	2308	293	12,7	2116	265	12,5	909	185	20,4	1358	246	18,1	1886	241	12,8	2398	292	12,2
LRR Vorniceni	2435	498	20,5	3286	529	16,1	2751	498	18,1	1784	320	17,9	2966	442	14,9	3478	376	10,8	4141	396	9,6
LRR Bender	1589	131	8,2	1934	166	8,6	992	132	13,3	627	127	20,3	598	92	15,4	866	221	25,5	857	306	35,7
Total LNR&RRL	**15512**	**2258**	**14,6**	**17644**	**2317**	**13,1**	**15191**	**1961**	**12,9**	**6871**	**1214**	**17,7**	**11810**	**1894**	**16,0**	**15107**	**2159**	**14,3**	**18800**	**2494**	**13,3**
Total RM	**35643**	**3552**	**10,0**	**43151**	**3597**	**8,3**	**33281**	**3145**	**9,4**	**15429**	**1945**	**12,6**	**22425**	**2693**	**12,0**	**29649**	**2994**	**10,1**	**33602**	**3524**	**10,5**

Key Observations

1. **Real-Time Data Integration:**
    - The cloud-based tool implemented by the NRL facilitates real-time data reporting from all Level 1 laboratories, enhancing oversight and decision-making.
    - This system ensures that diagnostic trends are closely monitored, enabling rapid responses to outbreaks or resource shortages.
2. **Widespread Coverage:**
    - Moldova's Level 1 laboratories ensure universal diagnostic coverage across the country, with laboratories in all districts and municipalities.
    - This geographic reach ensures that diagnostic services are accessible to even the most remote populations.
3. **Effective Use of Molecular Diagnostics in Some Regions:**
    - Laboratories like SR Ialoveni, SR Nisporeni, SR Rezina demonstrate strong collaboration with local TB doctors, achieving positivity rates close to the national average (7.7% in 2023).
4. **Underperforming Laboratories**:
    - Laboratories such as **AMT Ciocana (1.0%)**, **AMT Centru (1.4%)**, and **AMT Botanica (2.1%)** had positivity rates far below the national average of **7.0% (Table 3)**.
    - The low positivity rates reflect inefficiencies in patient selection, poor collaboration with healthcare providers, and limited active case-finding efforts.
5. **Links to TB Doctors**:
    - Field visits revealed that many laboratories lack strong partnerships with TB clinicians, limiting effective case-finding and suspect referrals.
    - **Example of Weak Link**: AMT Botanica, with a positivity rate of **2.1%**, highlights the absence of coordinated case-finding efforts.
    - **Example of Strong Link**: SR Ialoveni demonstrated effective collaboration with TB doctors, achieving a positivity rate of **7.7%**, close to the national average.
6. **Inefficient Resource Utilization**:
    - Many patients diagnosed at Level 1 laboratories are re-tested at higher-level laboratories, leading to duplication of tests and unnecessary resource consumption.
    - Smear microscopy remains over-utilized for diagnostic purposes, even when molecular diagnostics are available.
7. **Infrastructure gaps**:

- Some laboratories lack adequate climate control, e.g. Orhei, Cahul.

8. **Data management**:
    - GeneXpert machines did not have integration with SimiTB or Siams systems.

Recommendations

1. **Streamline Diagnostic Pathways**:
    - Eliminate unnecessary re-testing at higher-level laboratories by building trust in results from Level 1 laboratories.
    - Revise national diagnostic algorithms to clarify roles and responsibilities, ensuring that Level 1 laboratory results are accepted unless quality concerns are validated.
2. **Strengthen Links to TB Doctors**:
    - Conduct regular joint workshops between laboratories and TB clinicians to improve patient referrals and case-finding.
    - Use successful models like SR Ialoveni to replicate effective practices across other laboratories.
3. **Enhance Active Case-Finding**:
    - Deploy TB doctors in underperforming regions to conduct community outreach, contact tracing, and workplace screenings.
    - Provide incentives for TB doctors to collaborate actively with laboratory staff in identifying high-risk individuals.
4. **Prioritize Molecular Diagnostics**:
    - Transition Xpert MTB/RIF as the primary diagnostic tool for TB suspects, minimizing reliance on smear microscopy for initial diagnosis (see recommendation in chapter **Diagnostic Algorithm**).
    - Ensure consistent availability of Xpert MTB/RIF cartridges, including Ultra cartridges, across all Level 1 laboratories.
5. **Address Infrastructure and Staffing Gaps**:
    - Improve laboratory layouts to separate smear microscopy and molecular testing areas.
    - Invest in ventilation systems to enhance biosafety.
    - Recruit additional technicians for high-volume laboratories to reduce reliance on a single-technician model.

6. **Optimize Resource Utilization**:
    - Monitor test positivity rates and referral volumes to identify inefficiencies and improve resource allocation.
    - Use Laboratory Information Management Systems (LIMS) to integrate data across laboratory levels, preventing duplicate testing.
7. **Monitor and Evaluate Laboratory Performance**:
    - Establish regular performance reviews to identify underperforming laboratories and provide targeted support.
    - Use performance indicators, such as positivity rates and test volumes, to guide resource allocation and training priorities.

Summarizing comments

The review of Moldova's TB diagnostic network highlights both significant achievements and critical challenges that require attention to enhance the network's efficiency and effectiveness. The tiered structure of the laboratory network—comprising the National Reference Laboratory (NRL), three Level 2 Regional Reference Laboratories, and 56 Level 1 Peripheral Laboratories—provides comprehensive geographic coverage and a strong foundation for TB diagnostics. Noteworthy accomplishments include the implementation of a cloud-based data collection system by the NRL, high diagnostic coverage rates with WHO-recommended rapid diagnostics, and robust quality assurance systems.

However, several gaps persist, hindering optimal TB control. Resource inefficiencies, such as duplicate testing across laboratory levels, and the continued reliance on smear microscopy for primary diagnosis, limit the impact of advanced diagnostic tools like Xpert MTB/RIF. Infrastructure and biosafety deficiencies, particularly in Level 2 laboratories, coupled with aging equipment and workforce shortages, further constrain diagnostic capacity. Weak collaboration between laboratories and TB clinicians in some regions undermines active case-finding and timely diagnosis.

To address these challenges, a revised diagnostic algorithm is recommended to minimize reliance on smear microscopy and streamline diagnostic pathways, with Xpert MTB/RIF as the primary tool for TB detection. Strengthening partnerships with TB clinicians, optimizing laboratory layouts, upgrading biosafety measures, and introducing advanced molecular diagnostics, such as next-generation sequencing, are critical steps for improvement. Additionally, conducting a Diagnostic Network Optimization (DNO) study will provide a strategic roadmap for reorganizing underperforming laboratories and enhancing specimen logistics.

With targeted investments and strategic realignment, Moldova's TB diagnostic network can build on its successes to achieve greater efficiency and accuracy, contributing significantly to the country’s TB elimination goals. These enhancements will ensure timely and accurate diagnosis, optimize resource utilization, and strengthen the foundation for addressing the challenges of multidrug-resistant and extensively drug-resistant TB.

Acknowledgements

The successful completion of this assessment of Moldova's TB laboratory network would not have been possible without the collaboration, support, and dedication of many individuals and organizations.

I extend my gratitude to the Ministry of Health of the Republic of Moldova for their leadership and commitment to strengthening TB diagnostic services. Special thanks go to the team at the National Reference Laboratory (NRL) for their guidance, technical expertise, and efforts to coordinate data collection and field visits.

I would like to express my sincere appreciation to the Center for Health Policies and Studies (PAS) for funding this important assessment and supporting efforts to enhance TB diagnostics and control in Moldova. Their financial and strategic contributions have been pivotal to this work.

I am grateful for the support and partnership of international stakeholders, including the World Health Organization (WHO), Principal Recipient of Global Fund to Fight AIDS, Tuberculosis, and Malaria (UCIMP), and other technical and financial partners, whose contributions have been vital to Moldova's efforts in combating TB.

Annex 1

List of mission reports and national policies reviewed in preparation for the mission

- **National Strategic Plan 2022-2025**

- **Ministry of Health Order no. 970/2023**
Protocol for TB diagnostics and management.

- **Ministry of Health Order no. 121/2024**
National Clinical Protocol "Tuberculosis in Adults," PCN-123, Edition VI.

- **GLC Mission Report (October–November 2021)**
Evaluation of the TB diagnostic network and services.

- **Regional GLC Technical Assistance Report (11–15 December 2023)**
Comprehensive assessment of diagnostic tools and laboratory efficiency.

- **GeneXpert Spot Check report, 2024**

- **OptimaTB Moldova 2023 Report**
Analysis of resource optimization and cost-effectiveness in TB control.

- **Guide: Principles for Interpreting Xpert MTB/RIF Results**
National Reference Laboratory, 2019 Edition.

- **Guide: Procedures for Collection and Processing of Biological Samples for TB Diagnosis**
Developed by the National Reference Laboratory, 2012 Edition.

- **Guide: Microbiological Diagnosis of Tuberculosis**
National Reference Laboratory, 2012 Edition.

Annex 2

Mission agenda, 21 – 31 July 2024

Time	Activities	Location
17.30	Arrival, Sunday, 21 July 2024	ZENTRUM Hotel, Chisinau
	Monday, 22 July 2024	
09.00-09.30	Departure from the hotel to National TB Reference Laboratory (NRL)	
09.30–10:30	Meeting with director of Institute of Phthisiopneumology (IPP)– Doina Rusu and NTP Coordinator – Valentina Vilc	Institute of Phthisiopneumology
11.00-12.30	Visit of National TB Reference Laboratory of IPP	NRL, IPP, Chisinau
12.30–14.00	Lunch	
14.00-15.30	National TB Reference Laboratory. Discuss & review the TB lab network	NRL, IPP, Chisinau
16.00-17.30	Meeting with Director of PCIMU (PR of GFATM) – Victor Burinschi	PCIMU, Chisinau
	Tuesday, 23 July 2024	
09.00–11.00	Visit the Level 1 Peripheral laboratory – district Botanica, Chisinau	AMT Botanica, Chisinau
11:00-13:00	Visit the Level 1 Peripheral laboratory – district Ciocani, Chisinau	AMT Ciocani, Chisinau
13.00–14.30	Lunch	
14.30-16.00	Prison Hospital Pruncul - Visit the Level 1 laboratory from Prison	Prison Hospital, Pruncul
16.30-17.30	National TB Reference Laboratory. Analysis of visiting sites	
	Wednesday, 24 July 2024	
8.30-10.00	Departure to Bender	
10.00-13.00	Visit the Level 2 Regional Reference Laboratory, Bender, Transnistria	Bender, TB Hospital
13.00–14.00	Lunch	
14.30-16.30	Visit the Level 1 Peripheral laboratory – mun. Tiraspol, Transnistria	Tiraspol, Mun. Hospital
16.30- 18.00	Departure to Chisinau	
	Thursday, 25 July 2024	
8.00-10.30	Departure to Falesti	
10.50-12.00	Visit the Level 1 Peripheral laboratory – district Falesti	Falesti, TB Office
12.00-14.30	Departure to Balti	
14.30-16.30	Visit the Level 2 Regional Reference Laboratory, Balti	Balti, Mun. Hospital
16.30–18.30	Departure to Chisinau	
	Friday, 26 July 2024	

08.00–10.30	Departure to Cahul	
10.30–12.00	Visit the Level 1 Peripheral laboratory – mun. Cahul	Cahul, Mun. Hospital
12.30-15.00	Departure to Chisinau, Lunch	
15.30–17.30	Meeting National TB Reference Laboratory. Summarizing 1 week of visits	NRL, IPP, Chisinau
	Monday, 29 July 2024	
8.45- 09.55	Departure to Orhei	
10.00-11.30	Visit the Level 1 Peripheral laboratory district Orhei, TB office district Orhei	Orhei, TB Office
11.00-14.00	Departure to Vorniceni, Lunch	
14.00-16.30	Visit the Level 2 Regional Reference Laboratory Vorniceni, of IPP	Vorniceni, Straseni
16.30-19.00	Departure to Chisinau	
	Tuesday, 30 July 2024	
9.00-11.00	SCBI "Toma Ciorba" Hospital, AIDS Center, National **HIV** Laboratory	AIDS Center, Codru
11.30-13.00	Meeting at National TB Reference Laboratory: Discuss and review the TB laboratory network, algorithm of investigations in Moldova.	NRL, IPP, Chisinau
13.00–14.30	Lunch	
14.30-16.30	Summarizing. Meeting with director of IPP – Doina Rusu and NTP Coordinator – Valentina Vilc, Director of PCIMU – Victor Burinschi	Institute of Phthisiopneumology
	Wednesday, **31 July 2024**	
10.00–12.30	Meeting with NRL and NTP Coordinator. SWOT analysis.	NRL, IPP, Chisinau
12.30–13.00	Departure to the Airport	