

РЕГИОНАЛЬНЫЙ СЕМИНАР ПО ВОПРОСУ УСКОРЕННОГО ВНЕДРЕНИЯ РУКОВОДСТВА ВОЗ ПО ПРОФИЛАКТИКЕ И ДИАГНОСТИКЕ ТУБЕРКУЛЕЗА И ЛЕЧЕНИЮ ТУБЕРКУЛЕЗА С ЛЕКАРСТВЕННОЙ УСТОЙЧИВОСТЬЮ (ЛУ-ТБ)

REGIONAL WORKSHOP ON ACCELERATED IMPLEMENTATION OF WHO GUIDELINES ON TB PREVENTION, DIAGNOSIS, AND DRUG-RESISTANT TB (DR-TB) TREATMENT

Technical resources to support the implementation of WHO recommendations

EURO workshop to plan the accelerated implementation of new WHO policies

Almaty 28-30 April, 2025

Alexei Korobitsyn Soudeh Ehsani Patricia Hall-Eidson

Diagnostic Team Global TB Programme and WHO EURO





Technical resources to support the implementation of WHO recommendations

- WHO GTB resources
 - Operational handbook
 - WHO standard
 - Mutations catalogue
 - Training package
 - Regional resources

- WHO PQ resources
 - TSS series
 - Performance evaluating protocols
- Partners:
 - GLI
 - GDF
 - FIND
- Other resources
 - Manufacturers
 - Regulatory agencies





Operational handbook

- Describes the WHO-recommended tests for detecting TB and DR-TB and the most recent WHO policy guidance for their use
- Describes the processes and steps needed for implementing a diagnostic test for routine use within the TB diagnostic network
- Describes the steps that need to be taken to implement a new diagnostic tool
- Outlines TB diagnostic model algorithms that incorporate the most recent WHO recommendations for detecting and treating TB and DR-TB, and considerations for the implementation of a new algorithm.



WHO operational handbook on tuberculosis

Module 3: Diagnosis

Rapid diagnostics for tuberculosis detection

2021 update

World Health Organization

https://extranet.who.int/tb knowledge/en/node/720



New Diagnostic Cascade Diagram Guides Users







New Algorithm 1 Highlights Populations & Consolidates Tests







WHO standard: universal access to rapid tuberculosis diagnostics

- Sets benchmarks to achieve universal access to WHO-recommended rapid diagnostics (WRDs), increase bacteriologically confirmed tuberculosis and drug resistance detection, and reduce the time to diagnosis.
- WHO-recommended rapid diagnostics are highly accurate, cost-effective, reduce the time to treatment initiation, and impact patient-important outcomes.
- Comprises twelve benchmarks to be computed by countries in the four steps of the diagnostic cascade:
 - identifying presumptive tuberculosis,
 - accessing testing,
 - being tested, and
 - receiving a diagnosis.
- Mapping of enablers, approaches, and solutions to scale up the use of WRDs is provided to assist countries in meeting the standard and related benchmarks.
- Specific investment considerations are also provided, as well as two country case studies providing real-world examples of implementation Universal access to tuberculosis diagnostics will result in better health for all and reduce the unacceptably high mortality due to this curable and preventable disease.









The four-step cascade of care used to structure the WHO standard: universal access to rapid tuberculosis diagnostics









WHO Mutation Catalogue

- The catalogue provides a reference standard for the interpretation of mutations conferring resistance to all first-line and a variety of second-line drugs.
- The 2023 update includes the analysis of over 52 000 isolates with matched data on WGS and pDST from 67 countries for the 13 medicines. It lists more than 30 000 variants, their frequency and association with resistance and susceptibility and includes methods used, mutations identified and summaries of important findings for each drug.
- The additional isolates included in this update resulted in 86 variants associated with BDQ resistance (up from zero in the previous catalogue), eight variants associated with LZD resistance (up from one in the previous catalogue) and 24 variants associated with resistance to DLM (up from one in the previous catalogue).
- TB laboratories around the world can use the catalogue as a support in the interpretation of genome sequencing results.
- The catalogue can also guide the development of new molecular drug susceptibility tests, including next-generation sequencing.
- Currently the third edition is being developed, planned for release: Q4, 2025









Catalogue of mutations in Mycobacterium tuberculosis complex and their association with drug resistance



WHO Prequalification program

- The World Health Organization (WHO), through its Prequalification Unit (PQ) and Global Tuberculosis Programme (GTB), jointly work to determine procurement eligibility for tuberculosis (TB) in vitro diagnostics (IVDs).
- The TB diagnostic assessment process for TB IVDs has evolved into a mechanism which focuses on the evaluation of classes of TB diagnostic technologies for WHO recommendation through WHO GTB while the WHO prequalification team evaluates each specific product brand for quality, safety and performance within the product intended use.
- WHO prequalification of IVDs is a comprehensive quality assessment of individual IVDs through a standardized procedure aimed at determining whether the product meets WHO prequalification requirements.
- Prequalification assessment consists of the review of a product dossier, an independent performance evaluation, inspection of the manufacturing site(s) and labelling review.









	Mycobacterium Tuberculosis complex and resistance to first and/or second line anti-TB drugs Tests						
TSS 17 - In vitro diagnostic	Product name	Product code(s)	Manufacturer name	Dossier review	Quality Management System review	Product performance evaluation	Labelling review
gualitative detection of	BD MAX MDR-TB	443878	Becton, Dickinson and Company, BD Biosciences (USA)	•	٠	Ŋ	þ
Mycobacterium tuberculosis	Truenat MTB Plus	601130020, 601130005, 601130025, 601130050, 6011301100, and 601130200	Molbio Diagnostics Private Limited	R	•		
associated with drug-	Truenat MTB-RIF Dx	601210200, 601210005, 601210020, 601210100, 601210025, and 601210050	Molbio Diagnostics Private Limited	R	•		
resistant tuberculosis	cobas MTB-RIF/INH	09040617190, 09040625190, 09051953190, 08185476001	Roche Diagnostics GmbH	þ	s	Alternative laboratory evaluation pathway	
TSS 23 - Rapid diagnostic	cobas MTB	09040579190, 09040587190, 09051953190, 08185476001	Roche Diagnostics GmbH	R	S	Alternative laboratory evaluation pathway	
tests to detect mycobacterial	Loopamp MTBC Detection Kit	972000, 970000, 971000	Eiken Chemical Co., Ltd.	R			
lipoarabinomannan (LAM)	Xpert MTB/XDR	GXMTB/XDR-10	Cepheid AB	R	Ŋ	Alternative laboratory evaluation pathway	•
antigen in urine	In Vitro Diggnostics Under Assessmen	t WHO - Pregualification of Medical F	Products (IVDs. Medicines. V	accines and	Immunizati	ion Devices. Vec	tor Control)

- WHO PQ evaluates each specific diagnostic product brand for quality, safety and performance within the product intended use
- Prequalification Technical Specification Series and Performance Evaluation protocols available for NAATs
- Xpert MTB/RIF Ultra prequalified as the first TB diagnostic
- Prequalification Technical Specification Series available for LF-LAM + Performance Evaluation protocol publication in 2025
- At least 7 additional low and moderate complexity products undergoing evaluation





WHO/PQ main reference documents

- The Technical Specifications Series (TSS) set out the performance evaluation criteria for meeting prequalification requirements.
- Each TSS document provides information on the minimum performance requirements for WHO prequalification that should be met by a manufacturer to ensure that the in vitro diagnostic that is being submitted for prequalification is safe and performs optimally.
- TSS-17: In vitro diagnostic medical devices used for the qualitative detection of Mycobacterium tuberculosis complex DNA and mutations associated with drug-resistant tuberculosis
- Protocol for performance evaluation intended to help assist IVD manufacturers understand the requirements for WHO prequalification assessment and/or procurement by WHO and other UN agencies.









Training

Android -

https://play.google.com <u>/store/apps/details?id=c</u> om.whotbksp



iOS -

https://apps.apple.com/ us/app/who-tbguide/id1569546750



Consolidated Guidelines Operational Handbooks Training Catalogue Quick Search Recommendations Log in

WHO TB KNOWLEDGE SHARING PLATFORM

Access the modular WHO guidelines on tuberculosis, with corresponding handbooks and training materials.

Consolidated Guidelines

WHO guidelines provide the latest evidenceinformed recommendations on TB prevention and care to help countries achieve the Sustainable Development Goals (SDGs) and the targets of the End TB Strategy.

Operational Handbooks

The WHO Operational Handbooks on tuberculosis provide users with practical "how to" guidance, with details essential for the proper implementation of the corresponding WHO guidance.

https://extranet.who.int/tbknowledge

Training

Catalogue

training materials to help users implement the corresponding WHO guidance.

English

World Health Organization





EUROPEAN LABORATORY INITIATIVE (ELI) ON TB HIV AND VIRAL HEPATITIS





Network for TB (ERLTB-Net)

Enter your keyword(s) Training and tools v Tuberculosis Disease Network **European Reference Laboratory Network for TB** European Reference Laborator (ERLTB-Net)

- Strengthening TB laboratory capacities in the WHO **European Region**
- ELI platform for experience and knowledge exchange
- Supporting countries in the implementation and where necessary tailoring of the global recommendations to the region's needs and capacities

Q

About ECDC 🗸

In 2018 ELI's mandate was expanded to support **TB**, **HIV** and viral hepatitis laboratories

SUPPORTING LABORATORY SERVICES IN A COMPREHENSIVE WAY IN LINE WITH THE LATEST WHO EURO TB ACTION PLAN



Сосредоточение внимания на основных элементах, которые приведут к эффективному и безопасному функционированию лабораторий, предоставляющих качественные и своевременные результаты испытаний

- Laboratory biosafety / Well functioning and safe equipment
 - Strengthening quality assurance
- Technical guidance in line with WHO global recommendations and the countries capacities and needs

DST QAAD

ntegrated use of la nfectious diseases i

https://openwho.org/courses/multi-drug-resistant-tb

Implementation of WHO recommendations



× ° ° ×

Well trained human resources in all key aspects



- Moving towards integrated services
- Developing a sequencing strategy planning tool















Governance and Operating Procedures



Global Laboratory Initiative

- Coordinated by the GLI Core Group (CG) with support from the Secretariat (WHO)
- The mission of the GLI and its network of international partners is to serve as a collaborative platform for the development and uptake of practical guidance and tools for building and sustaining high-quality TB diagnostic networks, in the areas of:
 - Implementation of WHO policy guidance on TB diagnostics and laboratory strengthening
 - Health system solutions and innovations for ensuring rapid, accurate testing and linkage to appropriate patient management
 - Continuous quality improvement (CQI) at all levels of the laboratory network
 - Integration of laboratory diagnostic networks
 - Human resource capacity development
 - Advocacy and resource mobilization











Global Laboratory Initiative

Examples of available resources











Global Drug Facility

- Facilitates global access to qualityassured, affordable TB diagnostics and treatments
- Is a one-stop bundled procurement and supply mechanism providing a unique package of services that combine strategic procurement of TB products and coordination of market activities, with technical assistance and capacitybuilding for TB programmes.
- This unique approach has made GDF the largest global provider of qualityassured TB products to the public sector











FIND >>> DIAGNOSTIC NETWORK OPTIMIZATION GUIDE

- The guide provides an overview of diagnostic network optimization (DNO), a geospatial analytics approach to analyze and optimize diagnostic networks to enable the greatest access to services, while maximizing the overall efficiency of the system.
- It includes a description of the concepts of DNO, the process to conduct a DNO analysis, data requirements, software solutions for conducting DNO and how outputs from DNO analyses can be used to inform decision-making.
- DNO is an approach that helps to understand the diagnostic networks needed to achieve national health goals and targets. It helps to identify areas for improvement in the diagnostic network design, examine alternative solutions to address the gaps, and consider trade-offs to enable selection of the preferred solution to implement.



- DNO enables decision-makers to utilize data and build evidence to identify the most impactful interventions for:
 - better network visualization facilitating enhanced coordination among programmes and partners and enabling better decision-making
 - improving access to diagnosis leading to reduced diagnostic delay and loss, resulting in more people diagnosed and treated; and
 - increasing network efficiency resulting in reduced procurement and operating costs, enabling better prioritization of available resources.









DIAGNOSTIC NETWORK OPTIMIZATION:

A network analytics approach to design patient-centred and cost-efficient diagnostic systems



Other resources:

- Manufacturers
- Regulatory agencies (US FDA, CE-IVDR)





European Region







Conclusion:

- There are multiple resources provided by WHO and partners to implement WHO recommendations for the diagnosis of TB
- The technical resources provided by
 - WHO focus either on health systems/patient-oriented class-based implementation principles (GTB); quality, safety, performance principles (PQ) or regional aspects (EURO)
 - partners are either product specific implementation guides (GLI), procurement catalogues (GDF) or overarching laboratory system optimization oriented (FIND)
 - manufacturers are product oriented (IFU)
 - regulatory agencies provide regulatory aspects for specific diagnostic products







Acknowledgements

•WHO Global TB Programme Diagnostics Team and PCI Unit

- Patricia Hall-Eidson
- Alexei Korobitsyn
- Nazir Ismail
- Carl-Michael Nathanson
- WHO EURO
 - Soudeh Ehsani
- •Global laboratory initiative
- •Partners
- •Manufacturers
- •Regulatory agencies





THANK YOU! СПАСИБО!







TB | PLUS