How to interpret discordant results from genotypic and phenotypic DST tests for DR-TB diagnosis

Latest WHO recommendations and ELI overview

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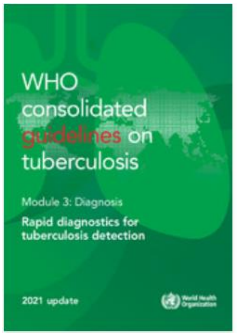
World Health Organization
European Region

Key principles of modern laboratory diagnostics of social significant infectious diseases
Part 1: **Tuberculosis**



- Shifting from focusing on the evaluation of specific products towards **classes of TB diagnostic technologies**.
- For the latest guidelines update, the three classes of technologies evaluated were defined by the **type of technology**, the **complexity of the test** for implementation and the **target conditions**.
- The level of complexity is only one of the elements that should be considered to guide implementation; others include **diagnostic accuracy**, the **epidemiological and geographical setting**, **operational aspects**, **economic aspects** and **qualitative** aspects of **acceptability, equity**, and **end-user values and preferences**.

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https://www.who.int/publications/i/item/9789240029415

Key principles of modern laboratory diagnostics of social significant infectious diseases
Part 1: **Tuberculosis**

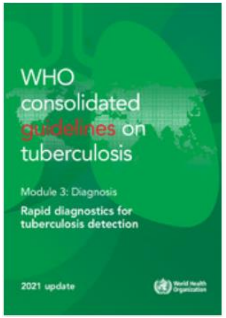

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Table 1.1. Classes of technologies and associated products included in current guidelines

Technology class	Products included in the evaluation
	Xpert® MTB/RIF and Xpert® MTB/RIF Ultra (Cepheid)*
	Truenat™ (Molbio) *;
Moderate complexity automated NAATs for detection of TB and resistance to rifampicin and isoniazid	Abbott RealTi*m*e MTB and Abbott RealTi*m*e MTB RIF/INH (Abbott) BD MAX™ MDR-TB (Becton Dickinson) cobas® MTB and cobas MTB-RIF/INH (Roche) FluoroType® MTBDR and FluoroType® MTB (Hain Lifescience/Bruker)
	TB-LAMP (Eiken) *
Antigen detection in a lateral flow format (biomarker-based detection)	Alere Determine™ TB LAM Ag (Alere)
Low complexity automated NAATs for the detection of resistance to isoniazid and second-line anti-TB agents	Xpert® MTB/XDR (Cepheid)
Line probe assays (LPAs)	GenoType® MTBDR*plus* v1 and v2; GenoType® MTBDR*sl*, (Hain Lifescience/Bruker), Genoscholar™ NTM+MDRTB II; Genoscholar™ PZA-TB II (Nipro)

*These recommendations are currently product specific but will be changed to class-based to align with the other recommendations.

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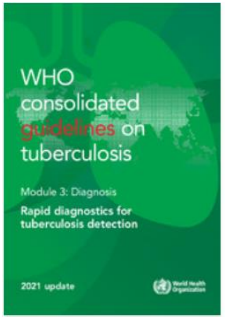

TB Regional Action Plan 2023-2030 – Rational on diagnosis related activities by Member States and WHO

- **Delayed diagnosis of TB and DR-TB**, and the consequent **late initiation of appropriate therapy**, is a major factor leading to **poor treatment outcomes and ongoing transmission**.
- To increase the **access to rapid molecular diagnostic tools** and **decrease the turn-around time** from sample collection to result, especially in settings with moderate-to-high TB incidence, priority should be given to **decentralization either by placing mWRDs at peripheral health centres** or connecting settings, via **efficient sample referral systems and sample transport mechanisms**, with the closest mWRD site.
- **Universal DST for all**, using molecular techniques for the rapid detection of resistance to all medications used for the treatment of TB and DR-TB and ensuring reliable access close to the point-of-care, should be prioritized and implemented.
- In low-burden settings, **access for vulnerable groups** (high-risk groups and remote settings) must be ensured, which will help reduce the time to diagnosis confirmation and lead to timely initiation of appropriate treatment

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

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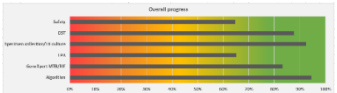
Focusing on major elements that will lead to well and safely functioning laboratories that provide quality assured and timely test results

- Laboratory biosafety / Well functioning and safe equipment
- Policies and implementation of WHO recommendations

- Technical guidance in line with WHO global recommendations and the countries capacities and needs
- Strengthening quality assurance



- Well trained human resources in all key aspects

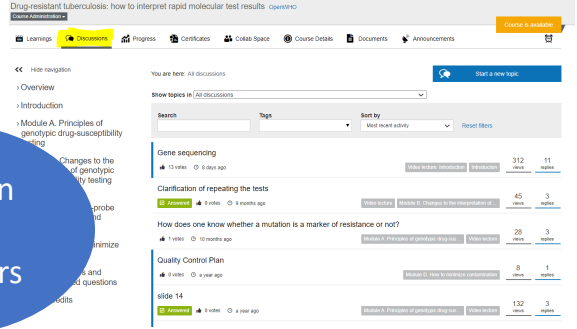
- Moving towards integrated services

- Developing a sequencing strategy planning tool

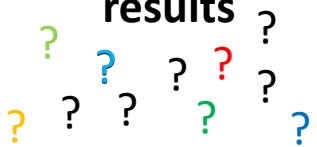
https://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/publications/2017/subregional-training-on-tuberculosis-laboratory-biosafety-cabinet-maintenance.-tbilisi,-georgia-29-august6-september-2017
https://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/news/news/2016/10/subregional-training-of-engineers-and-technicians-in-bsc-maintenance,-yerevan,-armenia,-26-september-5-october-2016
https://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/areas-of-work/laboratory-diagnosis https://openwho.org/courses/multi-drug-resistant-tb

- Training toolkit on **Drug-resistant tuberculosis: how to interpret rapid molecular test results (in ENG and RUS)**

More than 20.000 active users



Discordant results



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

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

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ONLINE TRAINING TOOLKIT ON DRUG-RESISTANT TUBERCULOSIS: HOW TO INTERPRET RAPID MOLECULAR TEST RESULTS

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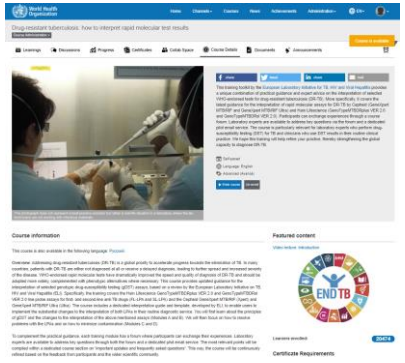

Course contents

Module A. Principles of genotypic drug-susceptibility testing:

By the end of this module, participants should understand how mutations cause drug-resistance, the strength and limitations of gDST testing, and the reasons for the changes to the interpretation of WHO-endorsed gDST assays.

Module B. Changes to the interpretation of genotypic drug-susceptibility testing assays:

By the end of this module, participants should understand the minor changes to the interpretation of Xpert and Ultra and how to use the ELI interpretation guide and ELI interpretation templates to implement the major changes to the interpretation of the FL-LPA and SL-LPA.

Module C. Hain line-probe assays: ramp rate and troubleshooting:

By the end of this module, participants should understand the importance of using the correct ramp rate for the LPAs and how to resolve other problems with these assays.

Module D. How to minimize contamination:

By the end of this module, participants should understand the different approaches to minimize contamination in laboratories.

Important updates and frequently asked questions:

Notable findings from the scientific literature and frequent questions from participants will be shared in this section.

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

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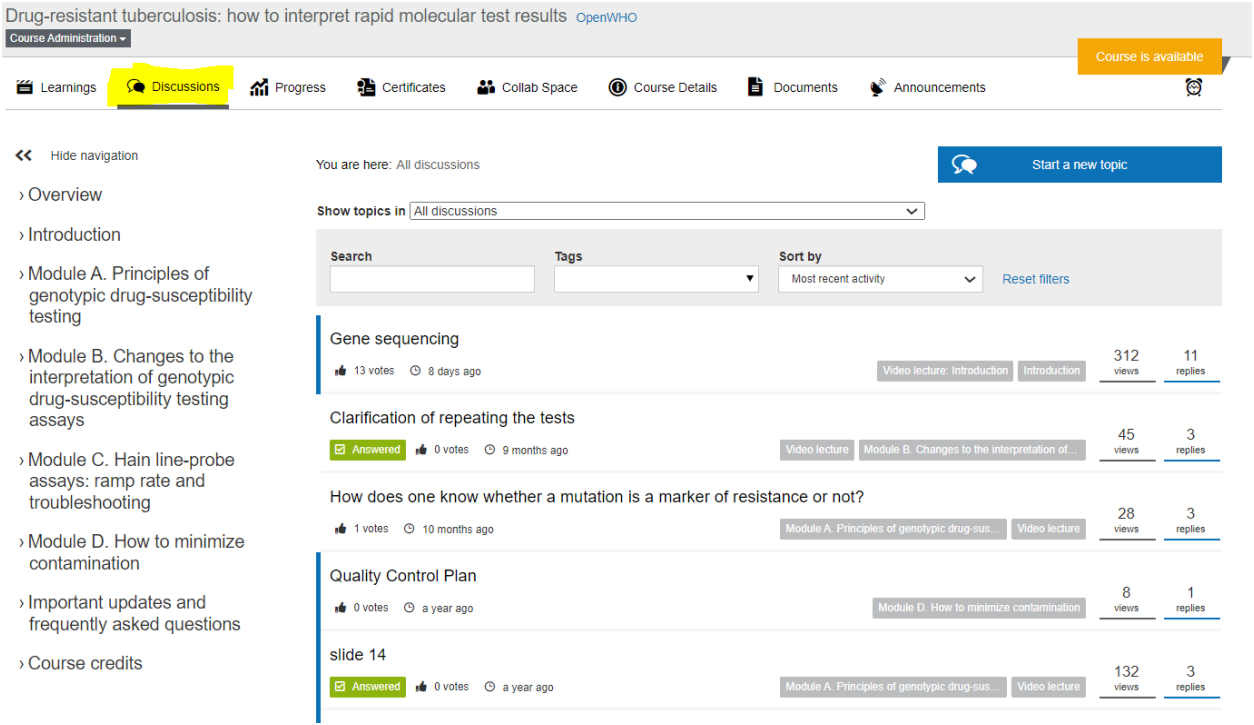

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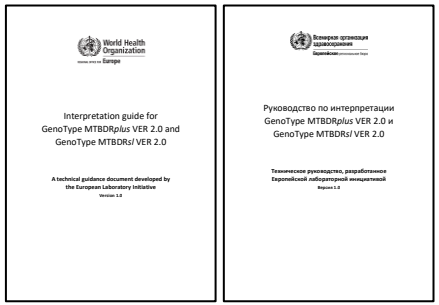
- Planned updates:
  - ELI LPA guide will be removed as Hain is due to update its instructions for use.
  - Inclusion of Cepheid XDR and other WHO-endorsed gDST assays.
  - Module about discordant DST results



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Thank you for your attention

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