



INFECTIOUS DISEASE DIAGNOSTICS: POLICY CONSIDERATIONS

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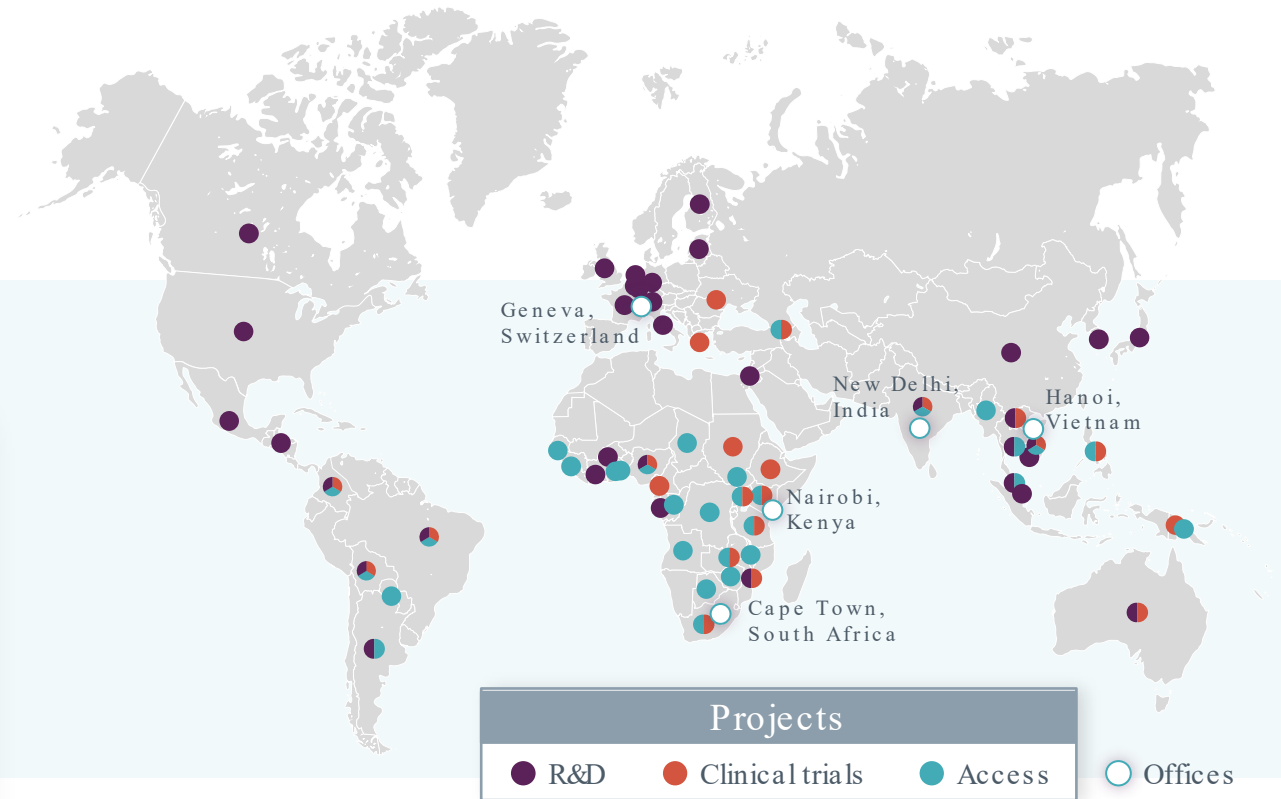


FIND ACCELERATES

EQUITABLE ACCESS TO RELIABLE DIAGNOSIS AROUND THE WORLD

In partnership with countries, WHO, and other global health agencies, we are driving progress towards **universal health coverage** and **global health security**

- ◆ Established in 2003 as a product development & delivery partnership
- ◆ Co-convener of the Access to COVID-19 Tools (ACT) Accelerator Diagnostic Pillar
- ◆ WHO Collaborating Centre for Laboratory Strengthening & Diagnostic Technology Evaluation
- ◆ WHO SAGE-IVD member



Tuberculosis
Malaria & Fever
Antimicrobial resistance
Neglected Tropical Diseases

Pandemic threats
Hepatitis C & HIV
Non-communicable diseases

TARGET PRODUCT PROFILE (TPP) FOR DIAGNOSTICS

COMPONENTS OF TPPs

- Intended use
- Target populations
- Performance (minimum and optimal)
- Operational characteristics (minimum and optimal)
- Costs (minimum and optimal)

WHO DEVELOPS TPPs?

WHO:
 When there is significant unmet health need for the product in question, potential for high public health impact and suitable for use in low to middle-income countries.
<https://www.who.int/tools/target-product-profile-database>

EXAMPLE

Page | 1




Target Product Profiles for improved antimicrobial stewardship for gonococcal infection

Others:
 UNICEF, PATH, GAVI, MSF, FIND...

FIND created **27 TPPs in 2022** in close collaboration with WHO, for diagnostic tools for poverty-related diseases.
<https://www.finddx.org/tools-and-resources/rd-and-innovation/target-product-profiles/>

WHO PREQUALIFICATION/PQ



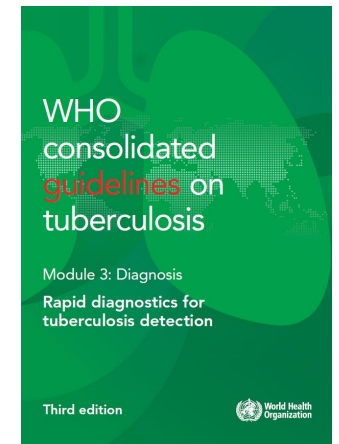
- WHO prequalification is a WHO assessment service for health/medicinal products for priority diseases.
- Every year, billions of US dollars worth of health products are purchased by international procurement agencies for distribution in resource-limited countries.
- Prequalification is intended to give these agencies the choice of a wide range of **quality** health products for a bulk purchase.
- Today, there are almost 1,500 WHO prequalified products – in vitro diagnostics (IVDs), vaccines, immunization devices, cold chain equipment, and vector control products – that have assisted in improving public health in low- and middle-income countries (LMICs).
- WHO prequalification has become a trusted and reputed symbol for *safety, quality and efficacy* across stakeholders.

IVDs in scope (not all include molecular)

- HIV
- HCV
- HBV
- Malaria
- G6PD
- HPV
- Cholera
- Syphilis
- COVID-19
- TB*

WHO TB DIAGNOSTIC GUIDELINES

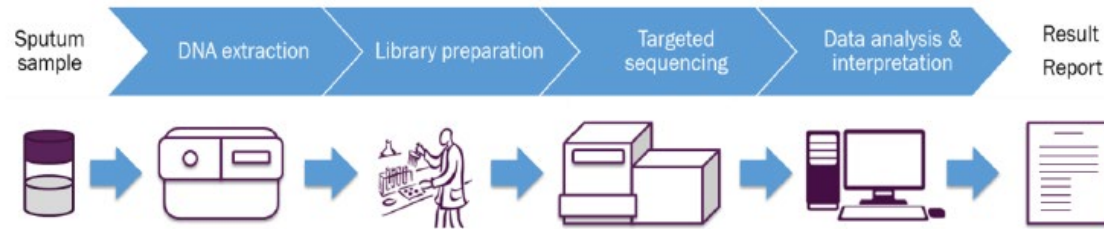
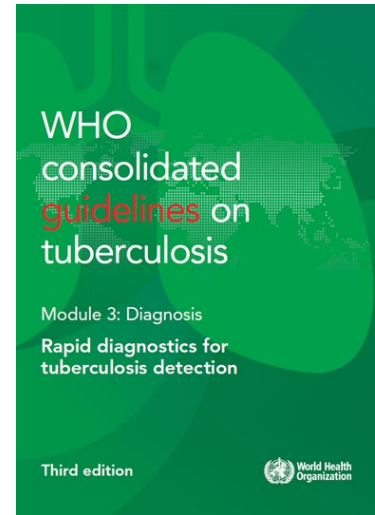
- WHO policy recommendations uses a systematic process with a public health view to guide decision making and inform country level policies
- WHO diagnostic guidelines are based on evidence and recommendations are developed following a standardized **GRADE** process
 - Grading of Recommendations Assessment, Development and Evaluation
 - Systematic search for evidence
 - Assessment of the certainty of evidence
 - Structured transition from evidence to recommendations, covering standard domains (Dx accuracy, end-user values and preferences, economic aspects, feasibility, acceptability)
- What is the question (**PICO**) and is the evidence addressing the question (performance)
 - Population
 - Intervention
 - Comparators
 - Outcomes



TNGS POLICY RECOMMENDATION, 20 MAR 2024

In people with bacteriologically confirmed RIF-Res pulmonary TB, targeted NGS may be used on respiratory samples to diagnose resistance to INH, Fq, Bdq, Lzl, Cfz, Z, E, Amk and S **rather than** culture-based pDST.

(Conditional recommendation, certainty of evidence high [INH, Fq and Z], moderate [E], low [Bdq, Lzl, Cfz and S], very low [Amk])



Products

Deeplex® Myc-TB (GenoScreen)

AmPORE-TB® (Oxford Nanopore Tech)

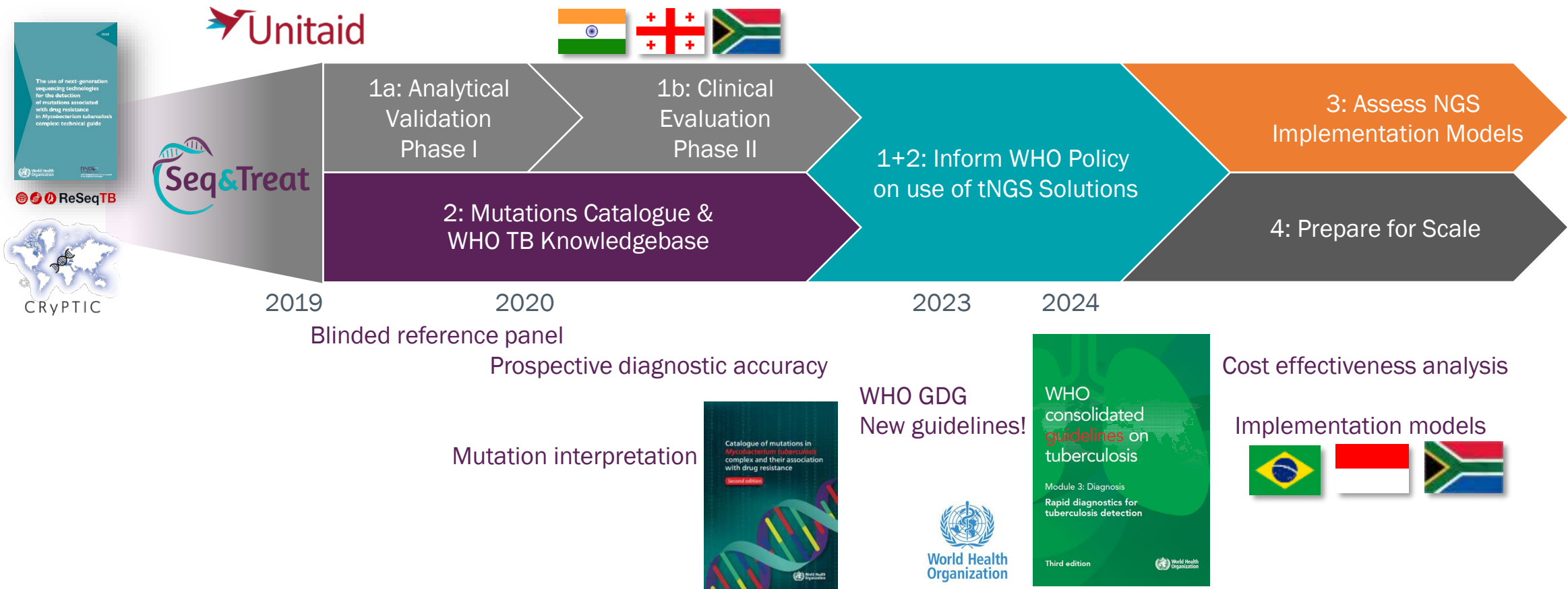
TBseq® (ShengTing Biotech)

Remarks

- Priority should be assigned to those at higher risk of resistance to first-line treatment medications
- Conditional due to lack of data on health benefits, the variable certainty of evidence on diagnostic accuracy, and the fact that accuracy is suboptimal for certain drugs.
- In addition, because this is a new technology that has not yet been widely implemented, there is still limited and variable evidence on costs, cost-effectiveness and feasibility of implementation.

RAPID, COMPREHENSIVE tNGS SOLUTIONS FOR DR-TB DIAGNOSIS IN LMICS SEQ&TREAT – FROM EVIDENCE TO POLICY

Generate evidence and boost in-country capacity to support the global adoption of end-to-end solutions for targeted NGS for comprehensive diagnosis of DR-TB

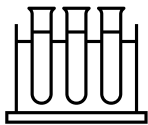


IN ADDITION TO DIRECT INDUSTRY PARTNERSHIPS, WE ALSO PROVIDE OPEN DATA, RESOURCES AND INSIGHTS

Target product profiles to inform product development

27 TPPs co-created between 2015 and 2020 to inform the development of diagnostic tests that are **fit-for-purpose** for local contexts and needs of end-users.

Biobank services to speed up development and evaluations



~500,000 samples available to developers
Fever, hepatitis, malaria, neglected tropical diseases, COVID-19, tuberculosis

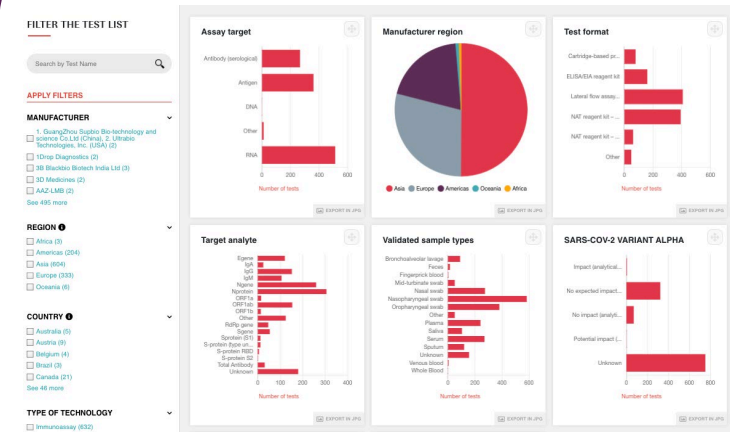
<https://www.finddx.org/biobank-services/>

Market insights and technology landscape



<https://www.finddx.org/reports-and-guidance/>

Test directory to increase visibility of diagnostics



<https://www.finddx.org/covid-19/test-directory/>

Independent test evaluations

More than **100 COVID-19 tests** were assessed in 2021 through FIND-qualified partner sites.

ACKNOWLEDGEMENTS

Our work is made possible by our donors alongside significant contributions from our private sector partners



our country partners



...and the FIND sequencing team



www.finddx.org/sequencing

FIND 



BACKUP

OTHER RESOURCES

Technical Specification Series (TSS) describe WHO's interpretation of the minimum validation and verification studies to be undertaken by the manufacturer in support of in vitro diagnostic (IVD) performance claims

<https://extranet.who.int/prequal/vitro-diagnostics/technical-specifications-series>

Technical Guidance Series (TGS) contain valuable information on a range of issues that are encountered in the manufacture, verification, and validation of specific categories of IVD. TGS apply in to all IVDs that are eligible for WHO PQ.

<https://extranet.who.int/prequal/vitro-diagnostics/technical-guidance-series>

World Health Organization
Prequalification of Medical Products
IVDs, Medicines, Vaccines and Immunization Devices, Vector Control

Product Streams ▾ Events News ePQS About

IVD In Vitro Diagnostics

Technical Specifications Series

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. (A transition period is being applied for those products prequalified before the relevant TSS document was issued. Manufacturers must comply with the technical specifications in the relevant TSS document within three years of its publication.)

Compliance with prequalification technical specifications is verified during re-inspection. Failure to comply with the relevant technical specifications will result in the delisting of the product concerned from the WHO List of Prequalified IVDs.

- [TSS 1 - Human immunodeficiency virus \(HIV\) rapid diagnostic tests for professional and/or self-testing](#)
- [TSS 2 - In vitro diagnostic medical devices to identify glucose-6-phosphate dehydrogenase \(G6PD\) activity](#)
- [TSS 3 - Malaria rapid diagnostic tests](#)
- [TSS 4 - In vitro diagnostic medical devices used for the detection of high-risk human papillomavirus \(HPV\) types in cervical cancer screening](#)
- [TSS 5 - Rapid diagnostic tests used for surveillance and detection of an outbreak of cholera](#)
- [TSS 6 - Syphilis rapid diagnostic tests](#)
- [TSS 7 - see 2021 version update TSS 16 below](#)
- [TSS 8 - Immunoassays to detect hepatitis C antibody and/or antigen](#)
- [DRAFT TSS 9 - Immunoassays to detect HIV antibody and/or antigen](#)
- [TSS 10 - In vitro diagnostic medical devices used for the qualitative and quantitative detection of hepatitis C RNA](#)
- [TSS 11 - In vitro diagnostic medical devices used for the quantitative detection of HIV-1 nucleic acid](#)
- [TSS 12 - In vitro diagnostic medical devices used for the qualitative detection of HIV-1 and HIV-2 nucleic acid](#)
- [TSS 13 - Rapid diagnostic tests to detect hepatitis B surface antigen](#)
- [TSS 14 - Immunoassays to detect hepatitis B virus surface antigen](#)
- [TSS 15 - In vitro diagnostic medical devices used for the quantitative detection of hepatitis B DNA](#)
- [TSS 16 - Hepatitis C rapid diagnostic tests for professional use and/or self-testing, 2021 update](#)
- [TSS 17 - In vitro diagnostic medical devices used for the qualitative detection of Mycobacterium tuberculosis complex DNA and mutations associated with drug-resistant tuberculosis](#)

Navigation menu: Home, Product Streams ▾, Events, News, ePQS, About

Left sidebar menu: About In Vitro Diagnostic & Male Circumcision Device Prequalification, What We Do, Documents A-Z, Prequalified In Vitro Diagnostics, Prequalified Male Circumcision Devices, In Vitro Diagnostics Under Assessment, IVDs Eligible for WHO Prequalification, MCDs Eligible for Prequalification, MCDs Under Assessment, Prequalification Procedures & Fees: IVDs, Prequalification Procedures & Fees: MCDs, Post-prequalification Procedures & Fees: Prequalified IVDs, Post-market surveillance, Post-prequalification Procedures: Prequalified MCDs, Prequalification Reports

World Health Organization
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Product Streams ▾ Events News ePQS About

IVD In Vitro Diagnostics

Technical Guidance Series

The Technical Guidance Series (TGS) was developed following a WHO consultation held in 2015 and attended by experts from national regulatory authorities, national reference laboratories, and WHO prequalification dossier reviewers and inspectors. The guidance series is a result of their efforts, and those of other international working groups, to provide clear information to manufacturers seeking WHO prequalification of in vitro diagnostics (IVDs).

TSG documents apply in principle to all IVDs that are eligible for WHO prequalification for use in WHO Member States. They should be read in conjunction with relevant international and national standards and guidance.

TGS 1 Standards applicable to the WHO Prequalification of in vitro diagnostic medical devices: identifies standards and guidance relating to a range of issues that are encountered in the manufacture, verification, and validation of IVDs.

TGS 2 Establishing stability of in vitro diagnostic medical devices: provides IVD manufacturers with guidance on possible approaches to determining stability and describes WHO prequalification requirements for stability testing.

- **Annex to TGS 2 Establishing component stability for in vitro diagnostic medical devices:** provides recommendations for establishing the stability of components for IVDs, with examples on the change from establishing stability for multi-use dropper bottles to establishing stability for single-use vials.

TGS 3 Principles of performance studies: identifies the key principles that apply when conducting and reporting the study design, results, and conclusion of analytical and clinical performance studies that support performance claims for IVDs undergoing assessment for WHO prequalification.

TGS 4 Test method validation for in vitro diagnostic medical devices: provides guidance to manufacturers on the validation of the test methods used in establishing the design, development and manufacture of an IVD.

TGS 5 Designing instructions for use for in vitro diagnostic medical devices: provides guidance to manufacturers on best practice when designing the instructions for use (IFU), which are an opportunity for the manufacturer to interact directly with end users and inform them about their product.

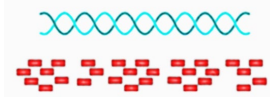
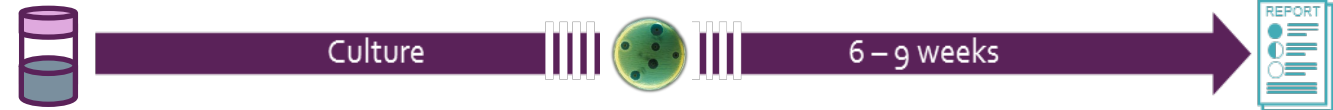
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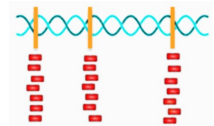
TARGETED NGS FOR FAST & COMPREHENSIVE TB SUSCEPTIBILITY TESTING



Phenotypic DST
(current standard of care)



Whole-genome sequencing



Targeted sequencing



Why Targeted NGS for TB AMR?

- Strong genotype → phenotype correlations in TB
- High-throughput, scalable, lower biosafety requirements
- Faster results to inform clinical decision-making
- Adaptable to new genes and mutations
- Multi-disease platform



A PARADIGM SHIFT

Targeted NGS-based **diagnosis** of **DR-TB** direct from clinical samples

BASIS FOR PREDICTING RESISTANCE FROM MUTATIONS

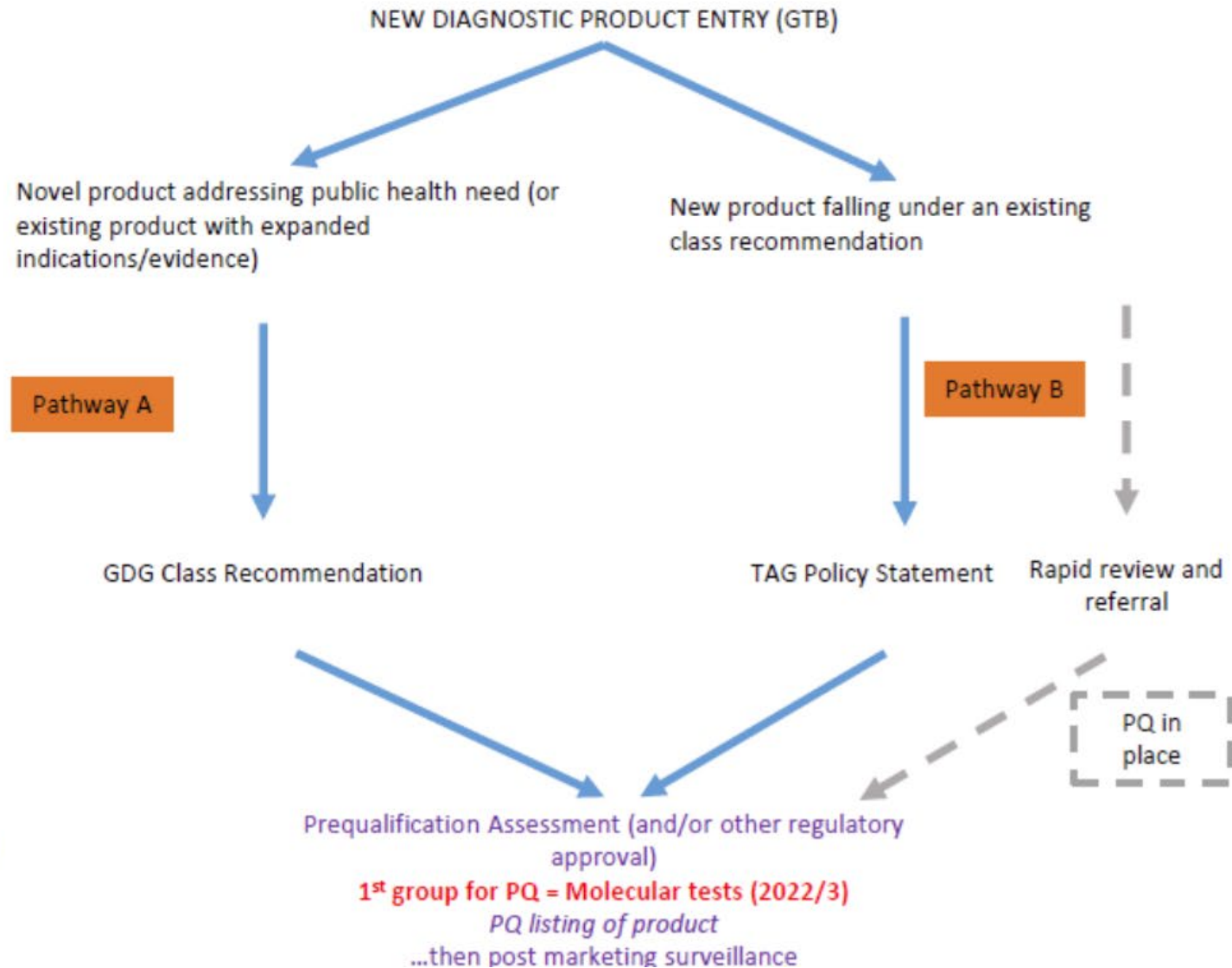
MUTATIONS CATALOGUE AND WHO TB KNOWLEDGEBASE



- ◆ Catalogue of resistance-associated mutations in TB - Standardized analysis and interpretation of genetic data for prediction of drug-resistance
- ◆ v1 mutations catalogue in 2021
 - Data from 38,000 isolates, 40 countries
- ◆ v2 released Nov 2023
 - + 15,000 isolates
 - + geographic and drug coverage: BDQ, DLM
- ◆ WHO TB knowledgebase for genotypic-phenotypic data for global *Mtb* strains

WHAT IS THE QUESTION (PICO) AND IS THE EVIDENCE ADDRESSING THE QUESTION (PERFORMANCE)

- Population
 - Is the intervention a primary test for all people or is it a follow-on test
 - Is there specific differences expected for sub populations (children, PLHIV)
- Intervention
 - Is the method standardized and quality assured with good reproducibility
 - What is the sample type and technology solution
- Comparator
 - If evaluating the accuracy, what is the reference standard/standard of care and are potential gaps sufficiently addressed
 - If evaluating patient-important outcomes, is the comparator well defined and mapped to the outcome
- Outcomes
 - On accuracy, is this comparable to existing tests, if not what is the evidence that justifies the tradeoff
 - On patient outcomes, is this comparable or if lower accuracy has it saved lives or had population impact



WHO Responsibility:
Global TB Programme

Pre-Qualification Team

TARGET PRODUCT PROFILE (TPP) FOR DIAGNOSTICS

WHAT IS IT?

Requirement documents for **products that are currently not available** on the market but that fulfil a priority need **in the context of Global Health**.
All TPPs are publicly available.

WHAT IS IT USED FOR?

To ensure that R&D activities are **focused on relevant products** and designed for the contexts and needs of end-users by researchers, developers and manufacturers.

HOW IS DONE?

It is a **consensus-based document** created by a large and diverse group of experts submitted to public consultation.

