FIND

INFECTIOUS DISEASE DIAGNOSTICS: POLICY CONSIDERATIONS

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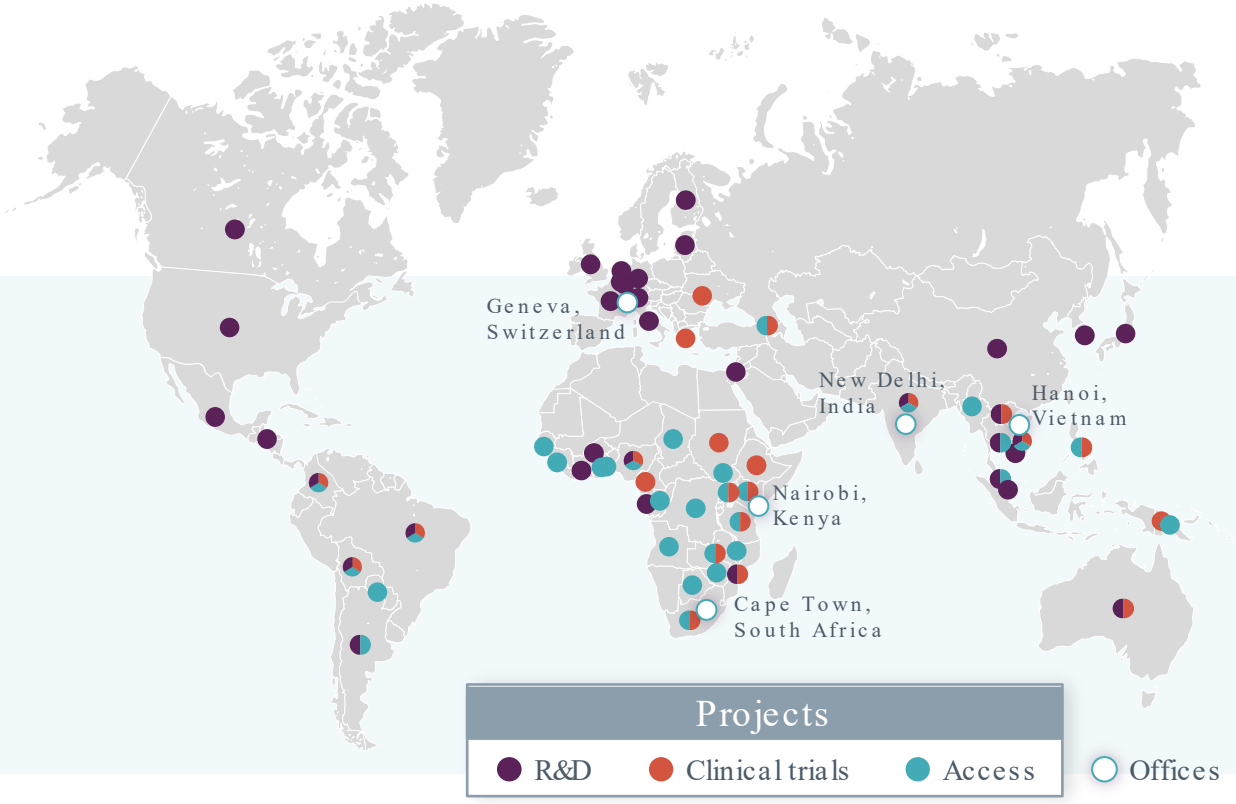
FIND ACCELERATES

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)

EXAMPLE

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

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.

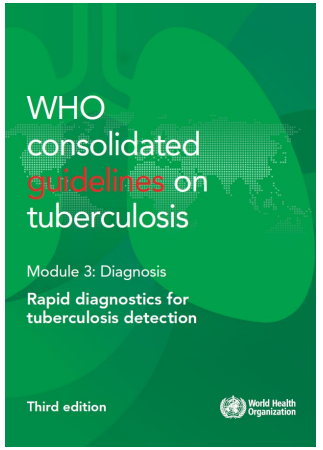
IVDs in scope (not all include molecular)

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

In Vitro Diagnostics Eligible for WHO Prequalification | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

WHO TB DIAGNOSTIC GUIDELINES

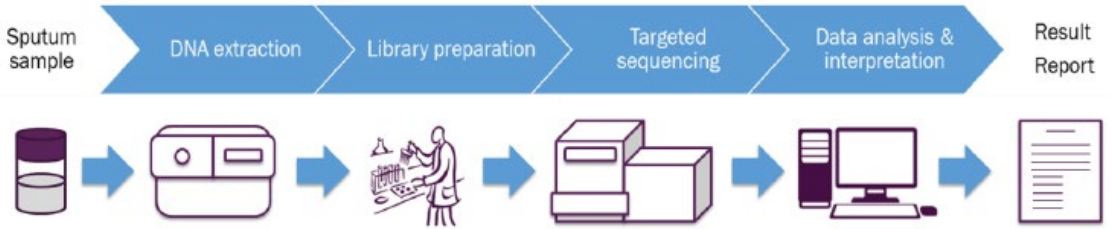
- WHO policy recommendations uses a systematic process with a public health view to guide decision making and inform country level policies
- WHO diagnostic guidelines are based on evidence and recommendations are developed following a standardized **GRADE** process
  - Grading of Recommendations Assessment, 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

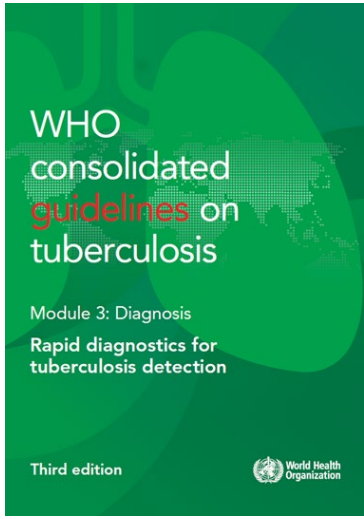


TNGS POLICY RECOMMENDATION, 20 MAR 2024

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)

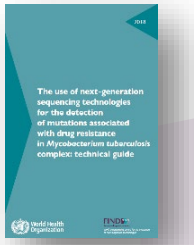
Remarks

- 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



ReSeqTB

CRyPTIC

Unitaid

Seq&Treat

1a: Analytical Validation Phase I

1b: Clinical Evaluation Phase II

2: Mutations Catalogue & WHO TB Knowledgebase

1+2: Inform WHO Policy on use of tNGS Solutions

3: Assess NGS Implementation Models

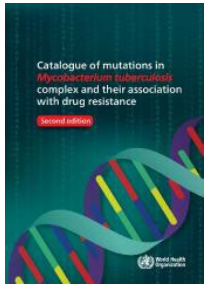
4: Prepare for Scale

2019 2020 2023 2024

Blinded reference panel

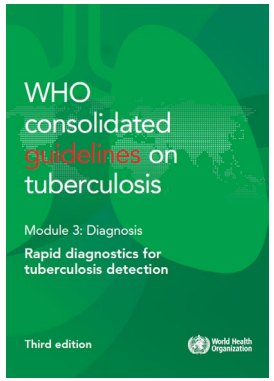
Prospective diagnostic accuracy

Mutation interpretation



WHO GDG New guidelines!

World Health Organization



Cost effectiveness analysis

Implementation models

https://www.finddx.org/what-we-do/projects/seqtreat/

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

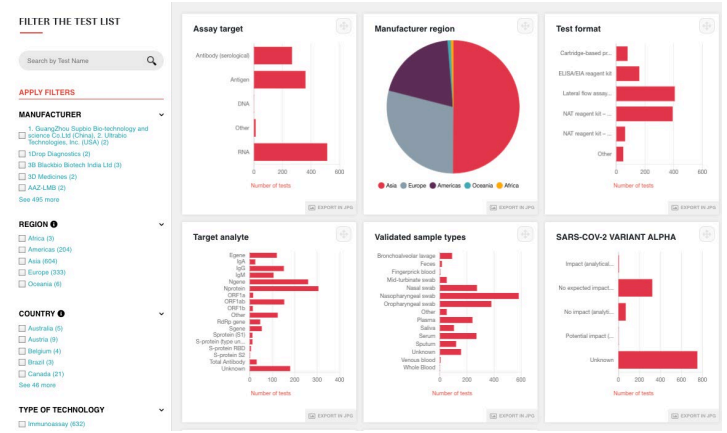
Fever, hepatitis, malaria, neglected tropical diseases, COVID-19, tuberculosis

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

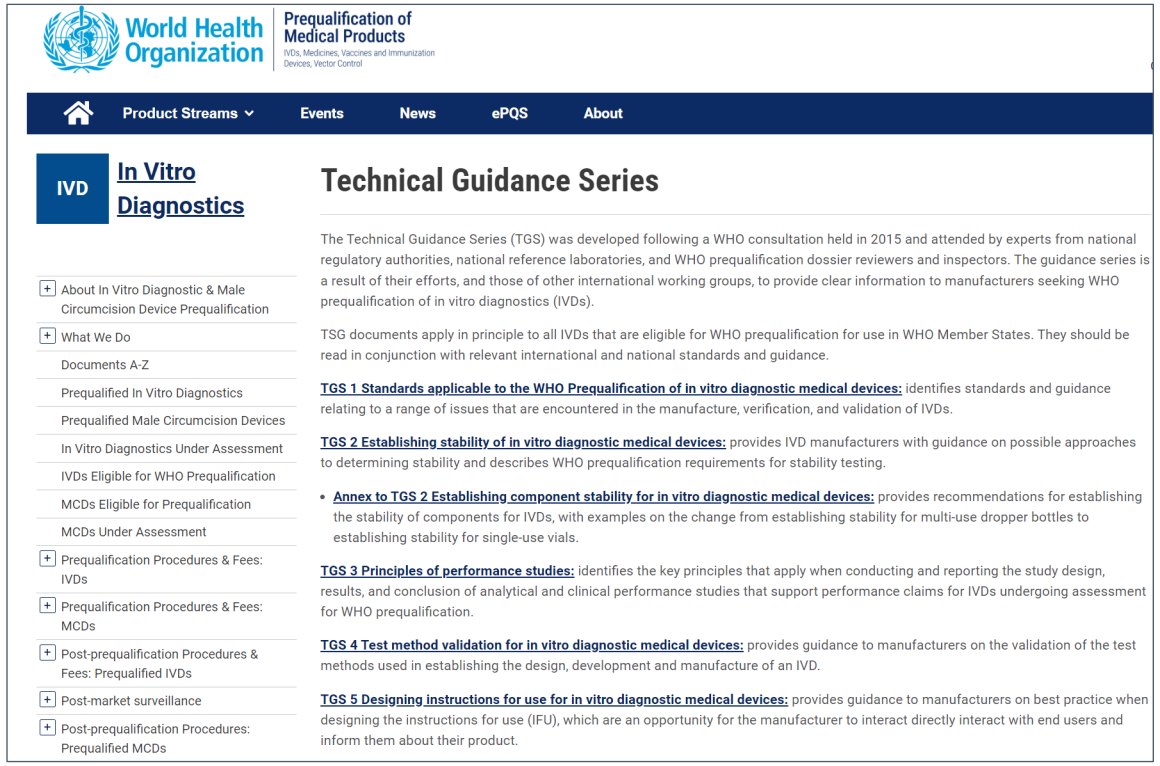
OTHER RESOURCES

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

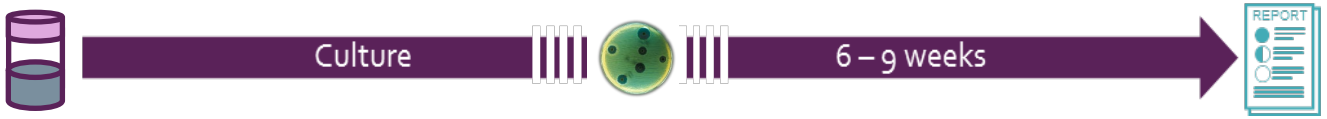
Technical Guidance Series (TGS) contain valuable information on a range of issues that are encountered in the manufacture, verification, and validation of specific categories of IVD. TGS apply in to all IVDs that are eligible for WHO PQ.

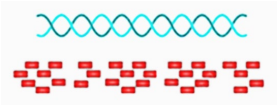
https://extranet.who.int/prequal/vitro-diagnostics/technical-guidance-series



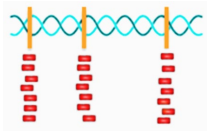
TARGETED NGS FOR FAST & COMPREHENSIVE TB SUSCEPTIBILITY TESTING

Phenotypic DST (current standard of care)





Whole-genome sequencing



Targeted sequencing

Why Targeted NGS for TB AMR?

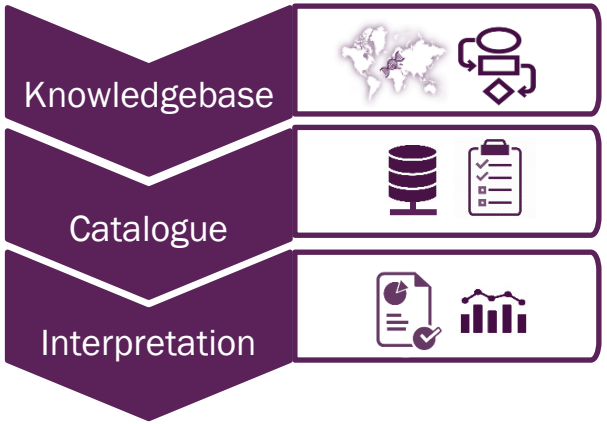
- Strong genotype → phenotype correlations in TB
- High-throughput, scalable, lower biosafety requirements
- Faster results to inform clinical decision-making
- Adaptable to new genes and mutations
- Multi-disease platform

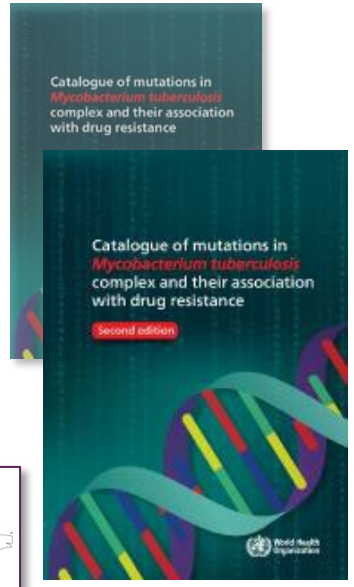
A PARADIGM SHIFT

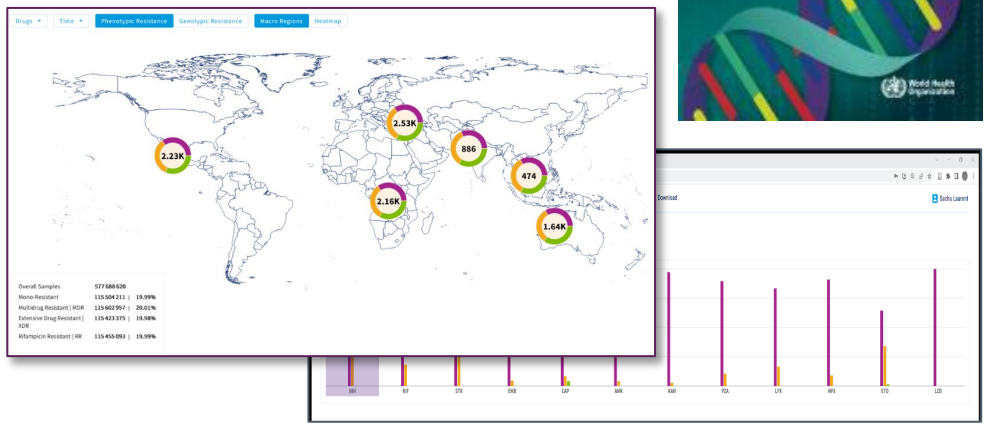
Targeted NGS-based diagnosis of DR-TB direct from clinical samples

BASIS FOR PREDICTING RESISTANCE FROM MUTATIONS

MUTATIONS CATALOGUE AND WHO TB KNOWLEDGEBASE





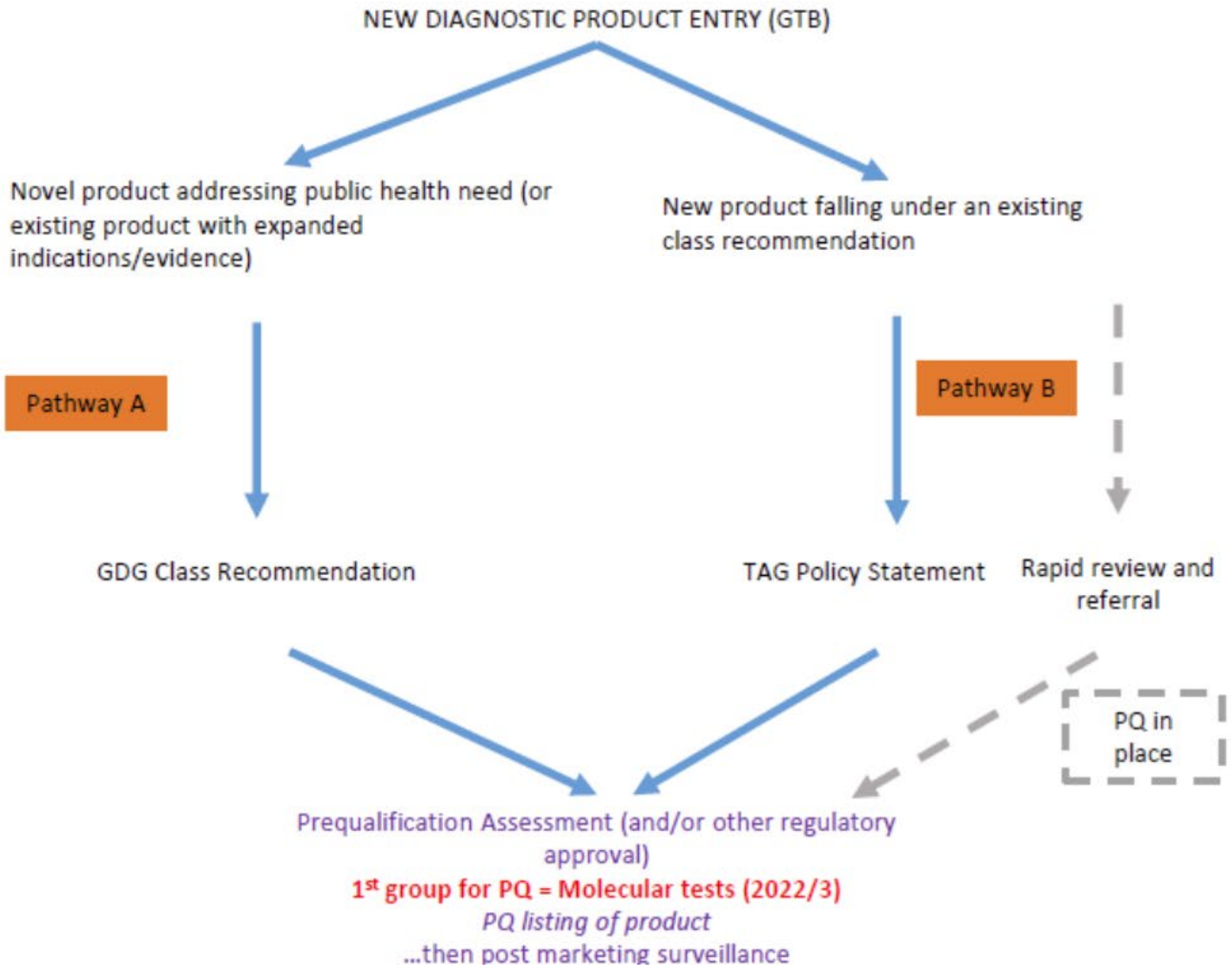


- **Catalogue of resistance-associated mutations in TB** - Standardized analysis and interpretation of genetic data for prediction of drug-resistance
- **v1** mutations catalogue in 2021
  - Data from **38,000 isolates, 40 countries**
- **v2** released Nov 2023
  - **+ 15,000 isolates**
  - **+ geographic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

https://www.who.int/publications/i/item/9789240028173

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.