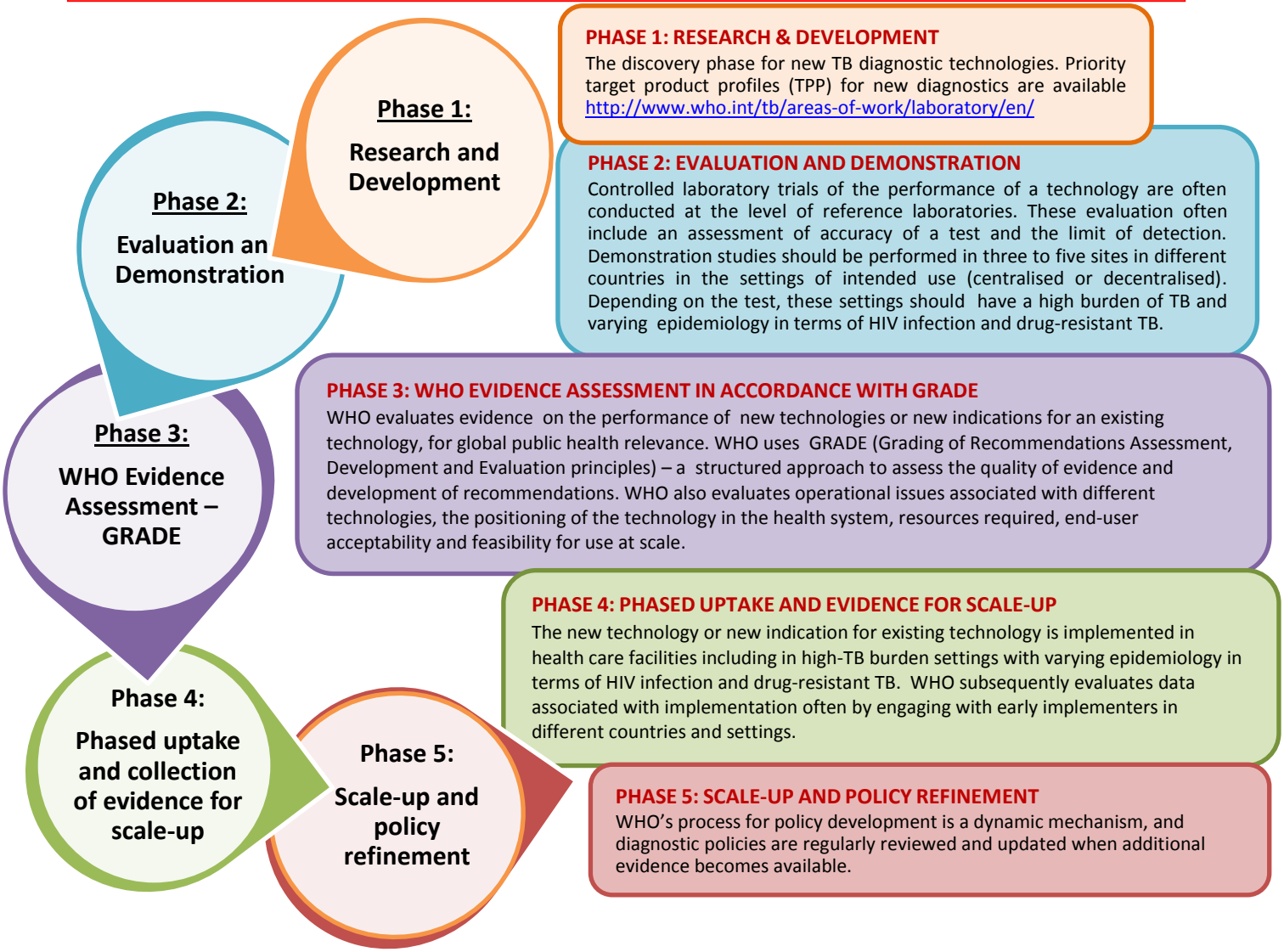
World Health Organization

DEVELOPMENT OF TUBERCULOSIS DIAGNOSTICS
ADVICE TO MANUFACTURERS

DEVELOPMENT AND ASSESSMENT OF TB DIAGNOSTICS



PHASE 1: RESEARCH & DEVELOPMENT
The discovery phase for new TB diagnostic technologies. Priority target product profiles (TPP) for new diagnostics are available http://www.who.int/tb/areas-of-work/laboratory/en/

PHASE 2: EVALUATION AND DEMONSTRATION
Controlled laboratory trials of the performance of a technology are often conducted at the level of reference laboratories. These evaluation often include an assessment of accuracy of a test and the limit of detection. Demonstration studies should be performed in three to five sites in different countries in the settings of intended use (centralised or decentralised). Depending on the test, these settings should have a high burden of TB and varying epidemiology in terms of HIV infection and drug-resistant TB.

PHASE 3: WHO EVIDENCE ASSESSMENT IN ACCORDANCE WITH GRADE
WHO evaluates evidence on the performance of new technologies or new indications for an existing technology, for global public health relevance. WHO uses GRADE (Grading of Recommendations Assessment, Development and Evaluation principles) – a structured approach to assess the quality of evidence and development of recommendations. WHO also evaluates operational issues associated with different technologies, the positioning of the technology in the health system, resources required, end-user acceptability and feasibility for use at scale.

PHASE 4: PHASED UPTAKE AND EVIDENCE FOR SCALE-UP
The new technology or new indication for existing technology is implemented in health care facilities including in high-TB burden settings with varying epidemiology in terms of HIV infection and drug-resistant TB. WHO subsequently evaluates data associated with implementation often by engaging with early implementers in different countries and settings.

PHASE 5: SCALE-UP AND POLICY REFINEMENT
WHO's process for policy development is a dynamic mechanism, and diagnostic policies are regularly reviewed and updated when additional evidence becomes available.

GUIDELINE DEVELOPMENT PROCESS FOR TUBERCULOSIS DIAGNOSTICS

- For the development of guidelines on TB diagnostics WHO uses the **GRADE** (Grading of Recommendations Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, and to develop and report recommendations.
- The detailed policy recommendations referred to in guidelines qualify their strength as well as the certainty of the evidence on which they are based.
- Four main factors determine the direction and strength of a recommendation in public health
  - The quality of the evidence
  - Values and preferences related to the outcomes of an intervention or exposure
  - The balance of evidence and harms
  - Resource implications

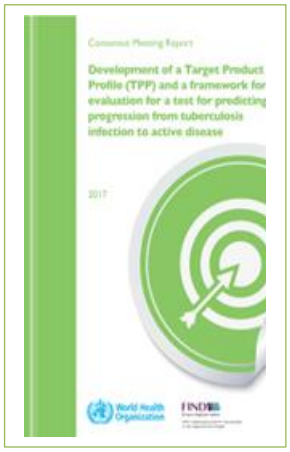
GENERAL ADVICE

- Engage with WHO early in the development process to ensure that design-locked products meet WHO requirements
- WHO provides information on reference standards, which samples should be tested, how the evaluation of diagnostics differs from that of medicines, and provides general guidance on study design.
- FIND as a WHO Collaborating Center facilitates independent evaluation.
- WHO will consider an evaluation of any new test that meets the minimal performance characteristics of any of the priority TPPs.
- WHO evaluates different diagnostics in the settings of intended use including centralised, decentralised and near point-of care settings, as relevant.
- WHO, FIND, UNITAID, StopTB Partnership, McGill University all play a role in accelerating TB diagnostic through the TB diagnostic critical pathway http://www.tbdxpathway.org/

WHO MECHANISMS AND PROCESSES

Technical Guidelines	GRADE assessment of evidence overseen by **Guidelines Review** Committee	Recommendation Policy implementation guides
Complementary mechanisms	**SAGE-IVD** **Prequalification programme**	WHO Essential Diagnostics List WHO List of Prequalified Products
Support for policy uptake	TB Supranational Reference Laboratory Network Global Laboratory Initiative	Policy implementation documents; reports of monitoring and technical assistance

TARGET PRODUCT PROFILES



- Sputum based, smear replacement
- Biomarker-based, non sputum
- Rapid drug susceptibility testing
- Triage/rule-out test
- Predictive test of disease progression
- Sample transport solutions

DO TB DIAGNOSTICS NEED WHO PRE-QUALIFICATION (PQ)?

Currently PQ is not applicable to TB diagnostic tests

- All WHO recommended TB diagnostics are automatically included in the Essential Diagnostics List
- Most TB diagnostics have single source manufacturers employing unique technologies
- TB diagnostic guidelines specify the use of TB tests in specific patients populations
- TB diagnostics usually involve a multi-step laboratory-based process (with pre-analytical, analytical and post-analytical phases)

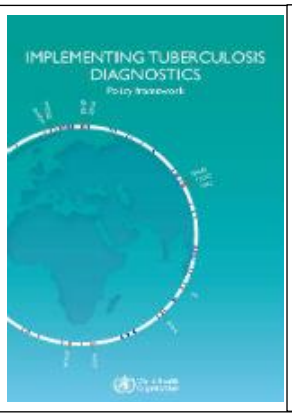
The PQ process currently applies to *in-vitro* diagnostics (IVDs) for HIV, Malaria and other infectious diseases, and involves:

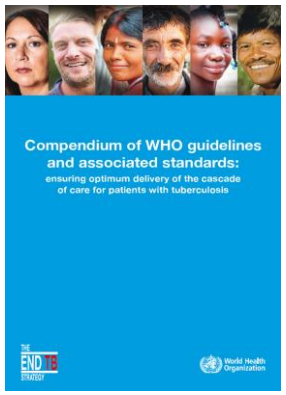
- Review of the product dossier
- Performance evaluation including operational characteristics
- Inspection of manufacturing sites and
- Labelling review

CONSOLIDATED GUIDELINES ON TB DIAGNOSTICS, TREATMENT AND CARE

The WHO Policy Framework: Implementing TB diagnostics available (click here).

This document consolidates all TB diagnostic guidelines into a single document.





The Compendium of WHO guidelines and associated standards are available (click here)

This document consolidates all TB diagnostic, treatment and care guidelines and standards into a single document.

For more information please visit:
http://www.who.int/tb