Diagnostic algorithms should start with appropriate screening policies to identify persons at risk.

New, rapid WHO-recommended tests should be prioritised in persons with risk factors for drug resistance and/or persons with HIV co-infection.

One size does not fit all: Recommended diagnostics are not mutually exclusive and should be combined based on country epidemiology, the existing laboratory network (see Figure 1), and available resources.

Implementation of any recommended diagnostic requires all core laboratory components to be in place (see Box).

Drug susceptibility testing (DST) is accurate and reproducible for detection of multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR) TB. For other drugs, DST is problematic and the clinical relevance of results are unclear.

Even with new, rapid diagnostics, conventional laboratory capacity (microscopy, culture and DST) must be maintained for monitoring patient response to treatment and detecting resistance to drugs other than rifampicin.

Scale-up of diagnostic capacity must be matched with access to appropriate treatment and care.

**Core Laboratory Components for Uptake of Diagnostics**

- Sufficient funding.
- Adequate human resources and training.
- Country-specific diagnostic algorithms.
- Appropriate infrastructure and biosafety.
- Specimen transport and referral mechanisms.
- Equipment validation and maintenance.
- Management of laboratory commodities.
- Laboratory information management systems.
- Laboratory quality management systems.

**Figure 1:** Currently recommended TB diagnostics require different levels of laboratory sophistication due to technical complexity and biosafety concerns
WHO-RECOMMENDED DIAGNOSTIC TOOLS

RECOMMENDED FOR USE (detailed policy guidance: http://www.who.int/tb/laboratory/en/)
- LED microscopy: For use at all laboratory levels as replacement of conventional fluorochrome and light microscopy.
- Commercial liquid culture and DST systems: For use at central/regional reference laboratory level, as current reference standard.
- Rapid speciation strip technology: For use with conventional culture and DST at central/regional reference laboratory level, to identify Mycobacterium tuberculosis.
- Commercial molecular line probe assays for 1st-line anti-TB drugs: For use at central/regional reference laboratory level for rapid detection of rifampicin (alone or with isoniazid) resistance. Suitable for use on smear-positive specimens or culture isolates.
- Selected non-commercial DST methods: MODS*, NRA**, CRI***: For conditional use at central/reference laboratory level for detection of rifampicin resistance only. MODS and NRA suitable for use on smear-positive specimens or culture isolates, CRI suitable for use on culture isolates only.
- Automated real-time nucleic acid amplification - Xpert MTB/RIF system: For rapid detection of pulmonary and extrapulmonary TB and rifampicin resistance in adults and children at decentralised laboratory and health care centres.
- LF-LAM**** assay may be used to assist in the diagnosis of TB in HIV positive adult in-patients with signs and symptoms of TB who have a CD4 cell count ≤ 100 cells/µL, or HIV positive patients who are seriously ill regardless of or with unknown CD4 count.

NOT RECOMMENDED DUE TO CURRENT INSUFFICIENT EVIDENCE
- Sputum concentration and decontamination methods.
- Phage-plaque technology for rapid rifampicin resistance.
- Thin-layer agar methods for rapid culture and DST.
- Interferon-gamma release assays as replacement for the tuberculin skin test for detection of latent TB in low- and middle-income (typically high TB and/or HIV) settings.
- Molecular line probe assays for 2nd-line anti-TB drugs.
- Loop-mediated isothermal amplification test kit for TB.

RECOMMENDED NOT TO USE (detailed policy guidance: http://www.who.int/tb/laboratory/en/).
- Commercial TB serodiagnostic tests.
- Interferon-gamma release assays for detection of active TB (all settings).
- Except as specifically described above for persons with HIV infection with low CD4 counts or who are seriously ill LF-LAM assay should not be used for the diagnosis of TB.

*MODS: microscopic observation of drug susceptibility; **NRA: nitrate reductase assay; ***CRI: colorimetric redox indicator; ****LF-LAM: Lateral flow urine lipoarabinomannan assay.

PHASES OF TB DIAGNOSTIC POLICY DEVELOPMENT

Phase 1: Research and development
The discovery phase for new diagnostic technologies. Priority target product profiles (TPP) for new diagnostics, developed following a consensus building process, are described in the TPP meeting report.*

Phase 2: Evaluation and demonstration
Controlled laboratory trials, or evaluation studies, are often conducted at the level of reference laboratories and should be performed in three to five sites in different countries that have a high burden of TB and varying epidemiology in terms of TB, HIV infection and MDR-TB.

Phase 3: Evidence assessment by WHO
WHO evaluates a dossier about new technologies or new indications for an existing technology, provided the technology is not intended for use only in a specific country.

Phase 4: Phased uptake and evidence for scale-up
The new technology is implemented in routine TB services including in high burden TB and HIV settings. WHO subsequently evaluates operational issues associated with implementation, as well as the cost effectiveness of a new technology, 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*