An overview of progress in the development of TB diagnostics, August 2020

TECHNOLOGIES IN DEVELOPMENT

Molecular detection of TB and drug resistance
- Gendrive MTB/RIF ID, Epistem, UK
- TruArray MDR-TB, Akkoni, USA
- INFINITIMTB Assay, AutoGenomics, USA
- FluoroType XDR-TB assay, Hain Lifescience, Germany
- MeltPro TB assay, Zeesan Biotech, China
- QuantuMDx, POC, UK
- Truenat MTB-INH/MTB-FQ, Molbio, India
- AccuPower XDR-TB RT PCR, Bioneer, Republic of Korea

Interferon gamma release assays (IGRAs) for TB infection
- Access QuantiFERON®-TB, QIAGEN, USA
- IP-10 IGRA elisa/lateral flow, rBioPharm, Germany
- ichroma™ IGRA-TB, Boditech Med Inc., Republic of Korea
- T-Track(R) TB, Lophius Biosciences GmbH, Germany
- VIDAS TB-IGRA, bioMérieux, France

Skin tests for TB infection
- c-Tb skin test, Serum Institute of India, India
- EC-Test, Anhui Zhifei Longcom Biopharmaceutical Co. Ltd, China

ON THE MARKET (NOT YET EVALUATED BY WHO)

Molecular detection of TB and drug resistance
- iCubate System, iCubate, USA
- Genechip, TB drug resistance array, Capital Bio, China
- EasyNAT TB Diagnostic kit, Ustar Biotechnologies, China
- Amplification-based tNGS assays: Next Gen-RDST assay, TGen, USA; Deeplex-MycTB assay, GenoScreen, France

Interferon gamma release assays (IGRAs) for TB infection
- Lioferon TB/LTBI, LIONEX Diagnostics & Therapeutics GmbH, Germany
- STANDARD E TB-Feron ELISA, SD Biosensor, Republic of Korea
- Advansure TB IGRA, LG chem, Republic of Korea

Skin tests for TB infection
- Diaskintest, JSC Generium, Russian Federation

TECHNOLOGIES ENDORSED BY WHO

Molecular detection of TB and drug resistance
- Xpert MTB/RIF and Xpert Ultra as the initial diagnostic test for TB and rifampicin resistance, Cepheid, USA
- Line probe assays for the detection of *Mycobacterium tuberculosis* (MTB), isoniazid and rifampicin resistance in acid-fast bacilli smear positive sputum or MTB cultures (FL-LPA), Hain Lifescience, Germany and Nipro, Japan
- Line probe assays for the detection of resistance to fluoroquinolones and second-line injectable agents (SL-LPA), Hain Lifescience, Germany
- TB LAMP for detection of TB, Eiken, Japan
- Truenat MTB, MTB Plus and MTB-RIF Dx assays as initial diagnostic tests for TB and rifampicin resistance, Molbio Diagnostics, India

Interferon gamma release assays (IGRAs) for TB infection
- T-SPOT.TB, Oxford Immunotec, UK
- QuantiFERON-TB Gold Plus (QFT-Plus), Qiagen, USA

Culture-based technologies
- Commercial liquid culture systems and rapid speciation
- Culture-based phenotypic DST using 1% critical proportion in LJ,7H10,7H11 and MGIT media

Microscopy
- Light and light-emitting diode microscopy (diagnosis and treatment monitoring)

Biomarker based assays
- Alere Determine TB-LAM, Alere, USA for TB detection in HIV infected people

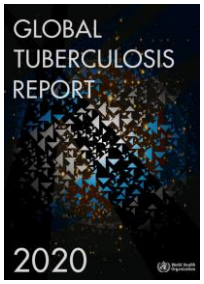
UNDER EVALUATION BY WHO

Molecular detection of TB and drug resistance
- Molecular technologies for genotypic drug resistance testing (including sequencing technologies)
- FluoroType MTBDR, Hain Lifescience, Germany
- *m*2000 RealTi*me* MTB System, Abbott, USA
- BD Max MDR-TB, Becton Dickinson, USA
- Roche cobas® MTB system, Roche Diagnostics, Switzerland
- AccuPower TB & MDR RT PCR, Bioneer, Republic of Korea
- Genoscholar PZA TB II, Nipro, Japan
- Xpert XDR-TB cartridge, Cepheid, USA

Computer-aided detection (CAD) for digital chest radiography
- CAD4TB, Delft Imaging, Netherlands
- Lunit INSIGHT CXR, Lunit, South Korea
- qXR, qure.ai, India
- DxTB, Deeptek, USA
- XrayAME, Epcon, Belgium
- InterRead DR Chest, Inter VISION, China
- T-Xnet, Artelius, India
- Dr CADx, Dr CADx, Zimbabwe
- RediSen, AXIR, South Korea
- JF CXR-1, JF HEALTHCARE, China

Culture-based drug susceptibility testing
- Sensititre™ MYCOTBI plate; ThermoFisher Scientific Inc., USA

XDR-TB = combined resistance to rifampicin, isoniazid, a fluoroquinolone and an injectable agent



The global clinical development pipeline for new anti-TB drugs and drug regimens to treat TB disease, August 2020

Phase I[a]

- BTZ-043[b]
- Macozinone[b]
- OPC-167832[b]
- SPR720[b]
- TBAJ-876
- TBI-166
- TBI-223
- ACTG A5312

Phase II[a]

- GSK-3036656[b]
- Telacebec (Q203)[b]
- TBA-7371[b]
- Delpazolid (LCB01-0371)
- SQ109
- Sutezolid
- High-dose rifampicin for drug-susceptible TB **(PanACEA)**
- Bedaquiline and delamanid **(ACTG 5343 DELIBERATE trial)**
- Bedaquiline and pretomanid with existing and re-purposed anti-TB drugs for MDR-TB **(TB PRACTECAL Phase II/III trial)**
- Shorter regimens including clofazamine and rifapentine for drug-susceptible TB **(CLO-FAST trial)**
- Pretomanid-containing regimens to shorten treatment for drug-susceptible TB **(APT trial)**
- Delamanid–linezolid–levofloxacin–pyranzimamide for fluoroquinolone-susceptible MDR-TB **(MDR-END trial)**
- Levofloxacin with OBR[c] for MDR-TB **(Opti-Q)**
- 4-month treatment for drug-susceptible TB **(PredicTB trial)**
- High-dose rifampicin for TB meningitis **(ReDEFINe)**
- Multiple adjunctive host-directed TB therapies for drug-susceptible TB **(TBHDT)**

Phase III[a]

- Bedaquiline (TMC-207)[b]
- Delamanid (OPC-67683)[b]
- Pretomanid
- Clofazimine
- High-dose rifampicin for treatment of drug-susceptible TB
- Rifapentine for treatment of drug-susceptible TB
- Bedaquiline–delamanid–linezolid–levofloxacin–clofazimine (6-month oral regimen for RR-TB) or bedaquiline–delamanid–linezolid–clofazimine (6–9 month oral regimen for pre-XDR and XDR-TB) **(BEAT TB trial)**
- Bedaquiline–pretomanid–moxifloxacin–pyrazinamide (BPaMZ) **(SimpliciTB trial)**
- Bedaquiline–pretomanid–linezolid **(NiX-TB trial)**
- Bedaquiline–pretomanid–linezolid **(ZeNix trial)** - Linezolid optimization
- Bedaquiline with two OBRs[c] (all-oral, 9 months; with injectable, 6 months) **(STREAM trial)**
- Bedaquiline–linezolid–levofloxacin with OBR[c] for MDR-TB **(NExT trial)**
- Bedaquiline and delamanid with various existing regimens for MDR-TB and XDR-TB **(endTB trial)**
- Bedaquiline-delamanid-linezolid-clofazamine for fluoroquinolone-resistant MDR-TB **(endTB-Q)**
- Rifapentine–moxifloxacin for treatment of drug-susceptible TB **(TB Trial Consortium Study 31/A5349)**
- Several 2-month regimens for drug-susceptible TB **(TRUNCATE-TB trial)**

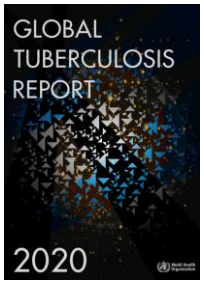
XDR-TB = combined resistance to rifampicin, isoniazid, a fluoroquinolone and an injectable agent

[a] New drug compounds are listed first, followed by repurposed drugs and then by regimens.

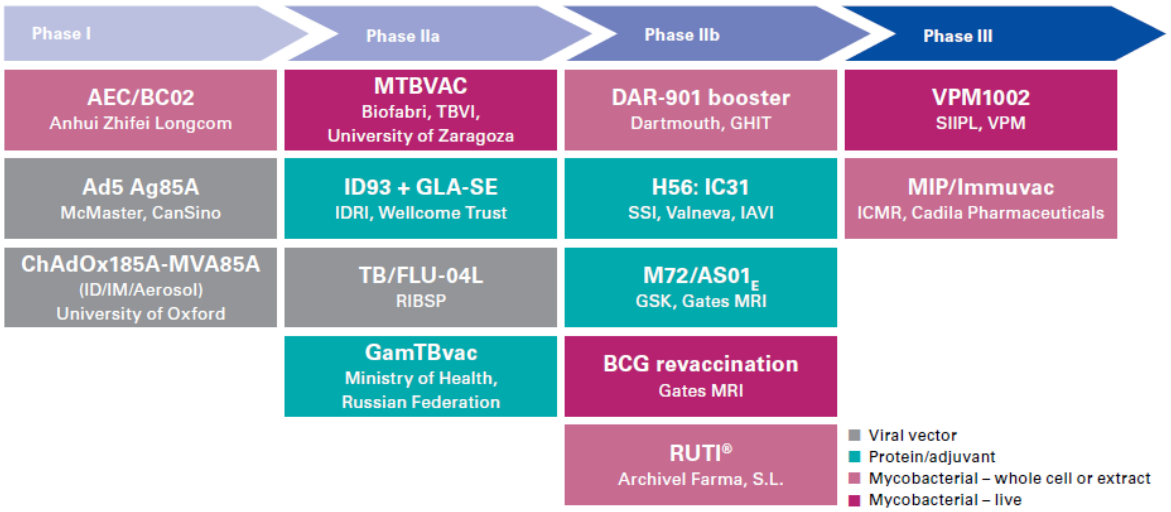
[b] New chemical class.

[c] Optimized background regimen.

Source: Adapted from the Working Group on New TB Drugs pipeline. More information on these products and other ongoing projects can be found at http://www.newtbdrugs.org/pipeline.php



The global clinical development pipeline for new TB vaccines, August 2020[a]



[a] Information was self-reported by vaccine sponsors, and the Stop TB Partnership Working Group on New TB Vaccines supported the review of the pipeline.