Next Generation TB Diagnostics – An Update from BMGF

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November 2012

BILL & MELINDA GATES *foundation*

Presentation Outline

- Foundation Strategic Context
- Next Generation TB Diagnostics Program
- TB Diagnostics Forum

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TB Strategy 2011-2016: Goal and vision

Impact goal	**Accelerate the reduction of global TB incidence**
Vaccines	1 vaccine candidate in phase 3
Drugs	1 TB drug regimen in phase 3
Diagnostics	• 1 new TB biomarker identified • 2 new molecular diagnostics endorsed by WHO STAG
Country-level Innovation in TB Control	• Increase national TB budgets • Accelerated uptake of innovative TB control • New products with frugal engineering
Global Access and Market Dynamics	• Reduced costs of FDC and second-line drugs • Accelerated uptake of innovation in target countries and globally
Advocacy	Funding secured for one TB vaccine and one TB drug phase 3 clinical trial

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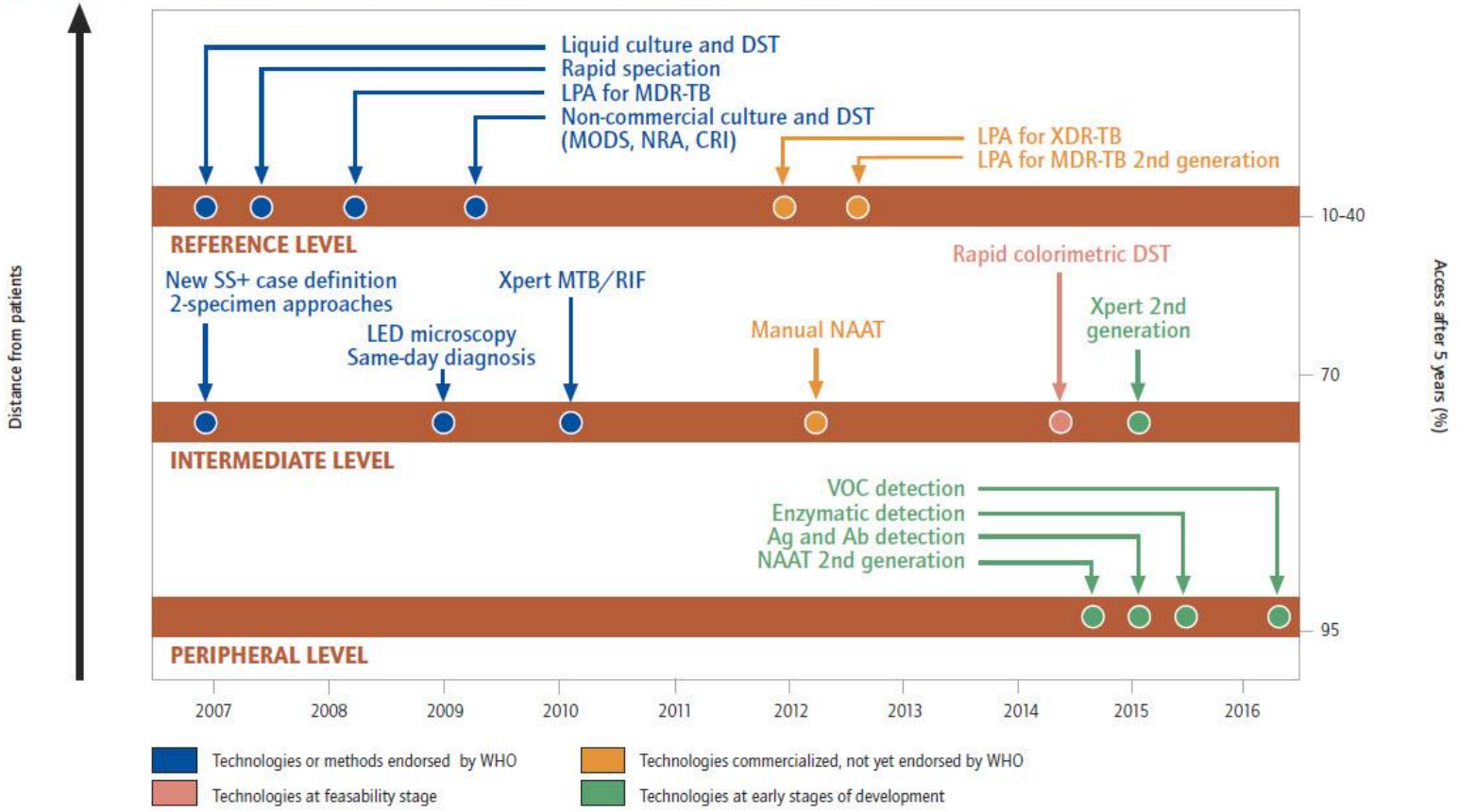
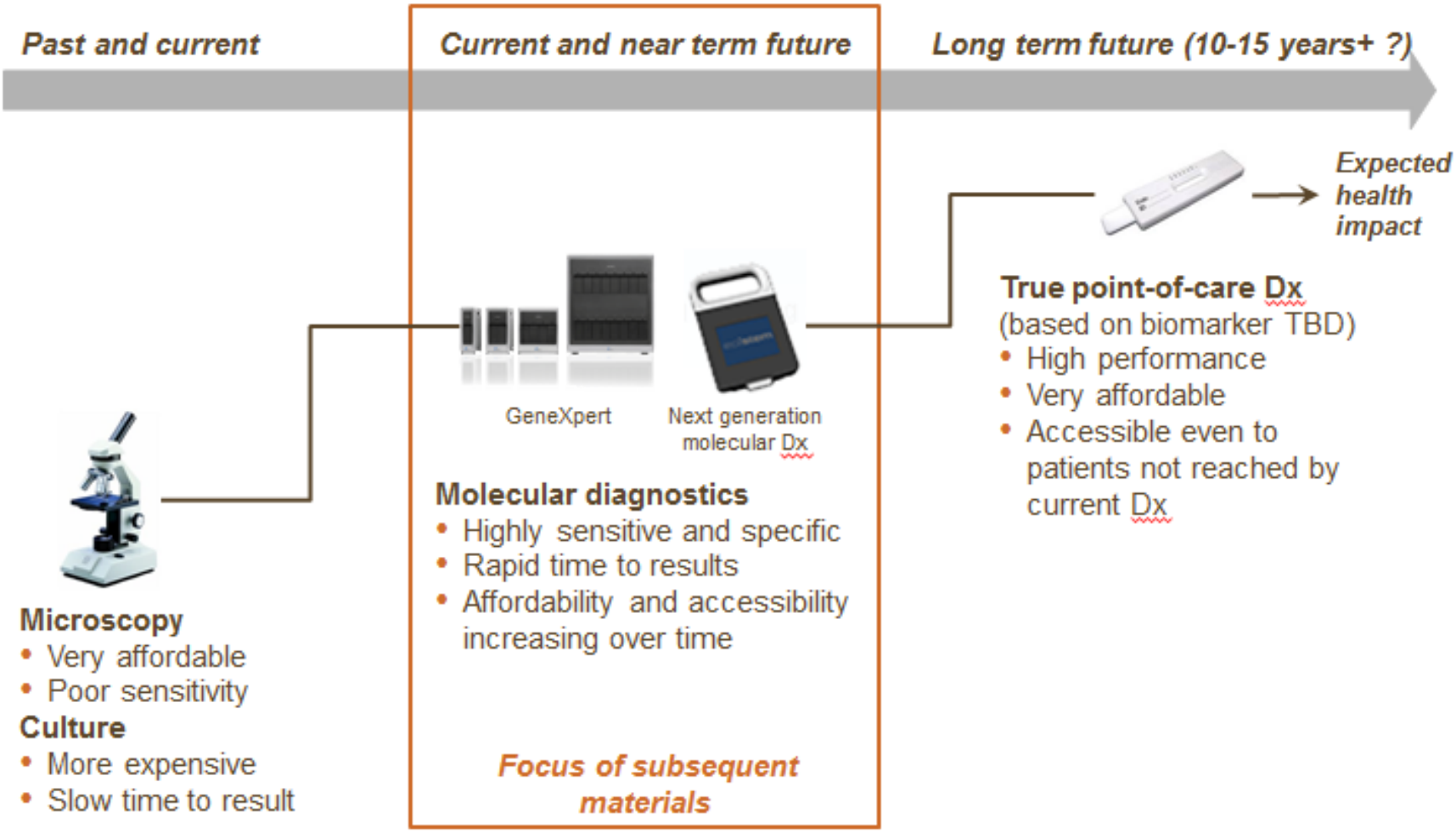
Significant Progress To Date in TB Diagnostics; Challenges Remain

FIGURE 8.1 **The development pipeline for new TB diagnostics, July 2012**

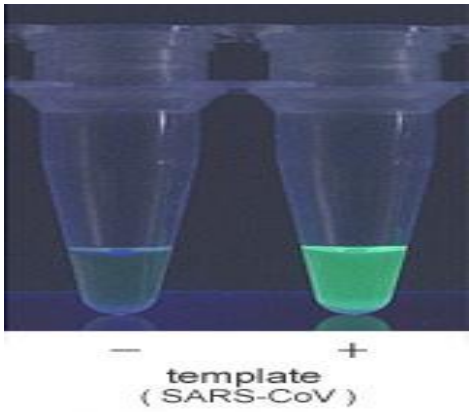


Abbreviations: **DST** Drug susceptibility test; **NAAT** Nucleic acid amplification test; **LTBI** Latent TB infection; **Ag** Antigen; **Ab** Antibody; **MODS** Microscopic observation drug-susceptibility; **NRA** Nitrate reductase assay; **CRI** Colorimetric redox indicator assay; **LED** Light-emitting diode; **LPA** Line probe assay; **VOC** Volatile organic compound.

Molecular diagnostics improve upon current tools, providing a bridge to true point-of-care Dx



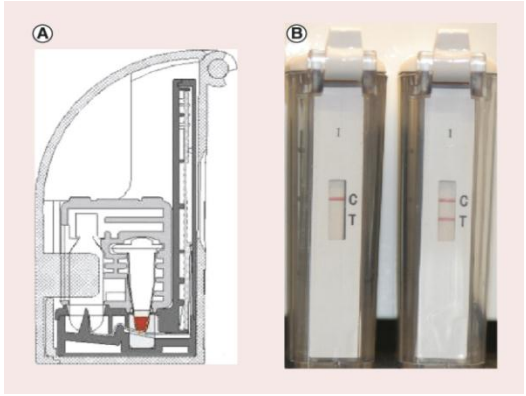
Fast-follower NAATs are rapidly entering the market



Loopamp® by Eiken, Japan

TrueLab® by Molbio, India

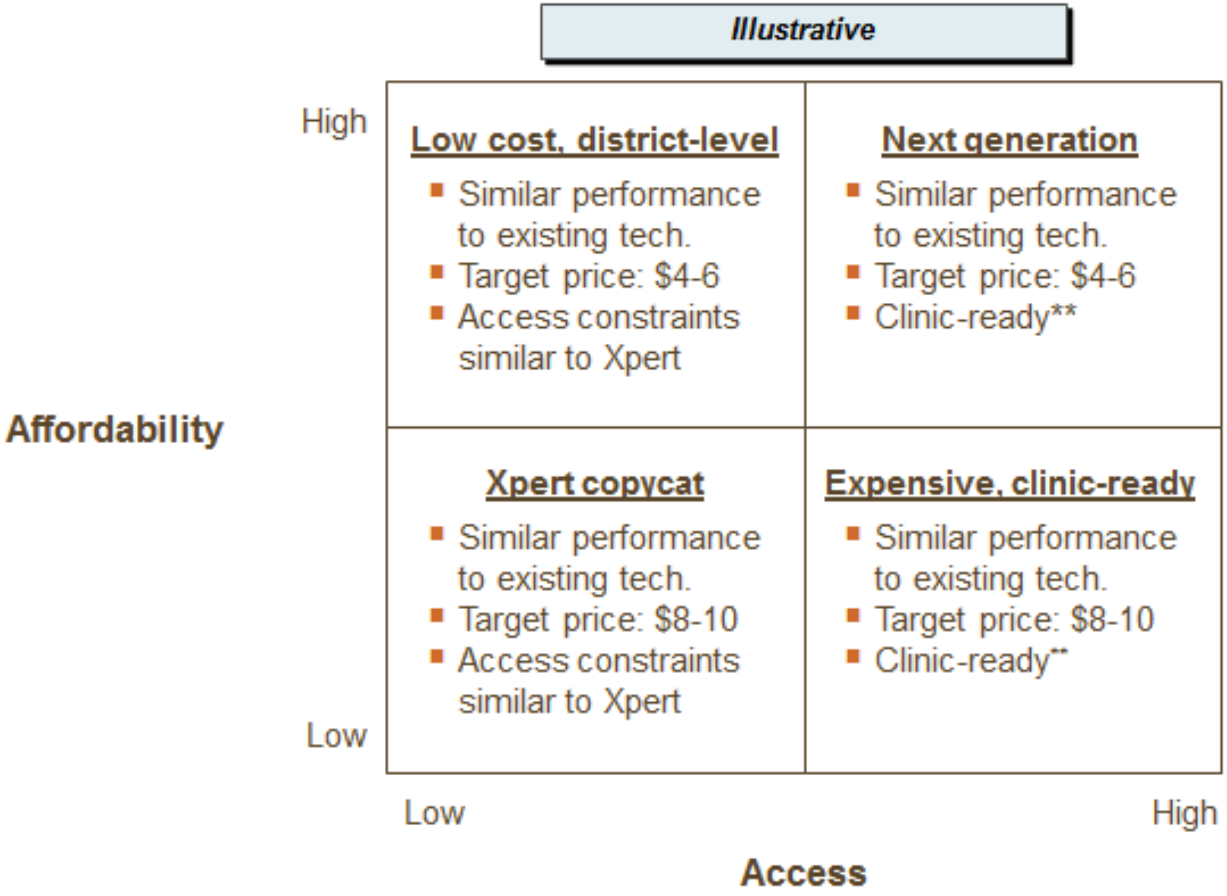
GeneDrive® by Epistem, UK



NATeasy® by Ustar, China

Potential visions for next generation of molecular Dx...

Key trade-off between affordability and access



**e.g., Battery powered, heat stable, substantially lower cost instrument, etc.

Simple and Affordable Molecular Testing for Tuberculosis

“To support the creation of a validated, low-cost, nucleic-acid assay for clinical TB detection on platforms capable of operation in rudimentary laboratories in low-resource settings. It is our intention for these assays to be to created and validated for use within 24-36 months”

Target Product Profile – Key Characteristics

Characteristic	Optimal	Minimal
Cost of consumables	< $4	< $8
Cost of instrument	< $5,000	< $10,000
Time to market	< 24 mos	< 36 mos
Specificity	> 99%	> 97%
Sensitivity	> 98% smear-positive and 80% smear-negative patients	95% of smear-positive and 65% smear-negative patients
Sample Prep & processing	Integrated	Minimal, < 5 steps
Time to result	< 1 hour	< 2 hours
Sample type	Sputum	Sputum
Drug resistance screening	Detection of Rif, FQ, and INH resistance testing via a separate cartridge with additional consumable cost (Reflex Testing)	Rifampin drug resistance testing via a separate cartridge with additional consumable cost (Reflex Testing)
Training	< .5 day	< 1 day

Full TPP Available: http://tbevidence.org/wp-content/uploads/2012/09/TPP-for-Simple-and-Affordable-Molecular-Testing-for-TB.pdf

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Problem Statement

- Progress is accelerating on drug regimens (REMox, PaMZ)
- Desire to save new drugs from resistance
- Historic underinvestment in TB R&D has led to significant unknowns, specifically related to DST for key regimen components
- Lack of coordination between researchers, drug developers, and the public health community that will be needed to achieve a common goal

Background and Purpose

- **TB Diagnostics Forum established in 2012 in collaboration with NIH**

- **Overall purpose is to facilitate:**
  - **Communication and discussion of research priorities, research gap areas, and new relevant data**
  - **Coordination of research and research funding**
  - **Collaboration on select projects**

- **The Diagnostics Forum has identified rapid drug susceptibility testing as an initial topic of focus.**

Proposed Structure

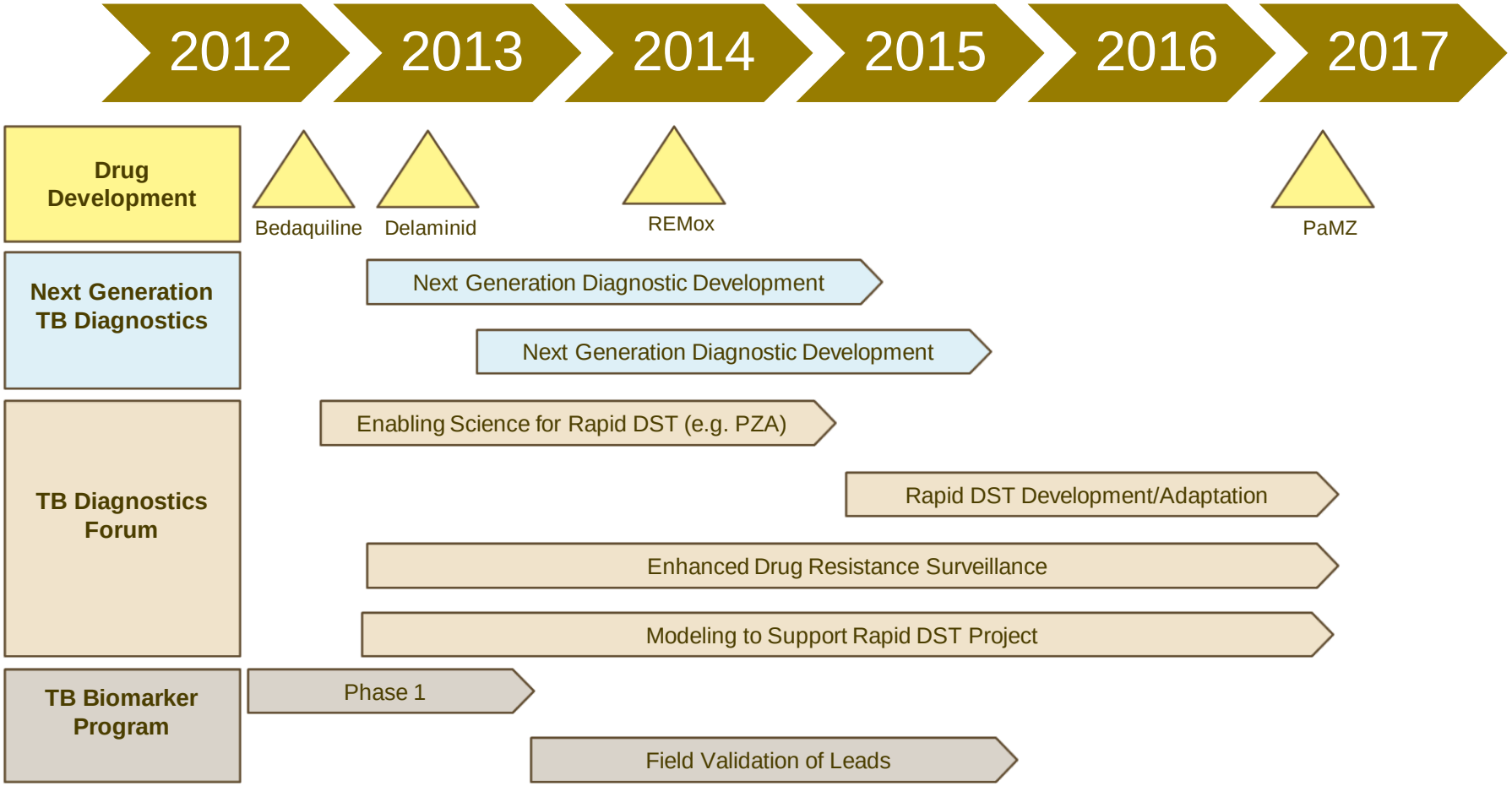
TB Diagnostics Research Forum Coordinating Committee
NIH, CDC, BMGF, WHO, EDCTP

Forum Coordinator

Enabling Science Workgroup Chair: David Sherman (Seattle Biomed)	Modeling Workgroup Chair: David Dowdy (JHU)	Surveillance Workgroup Chair: Bonnie Plikaytis (CDC)	Assay Development Workgroup Chair: Mark Perkins (FIND)

Program Management Support

Coordinated timeline – BMGF Activities



Grand Challenge: Biomarkers for the Diagnosis of TB

- **$7.7M invested in 10 projects, 24 month grants**
- **Program Goal:** support innovative research to facilitate development of a low-cost, simple-to-use tool that can quickly and accurately diagnose TB in developing countries
- **Investigators are evaluating both host and pathogen markers in highly characterized clinical samples through partnership with FIND**
- Concurrent development of TPPs for POC diagnostics to inform decisions

grandchallenges.org/biomarkers

Thank You