

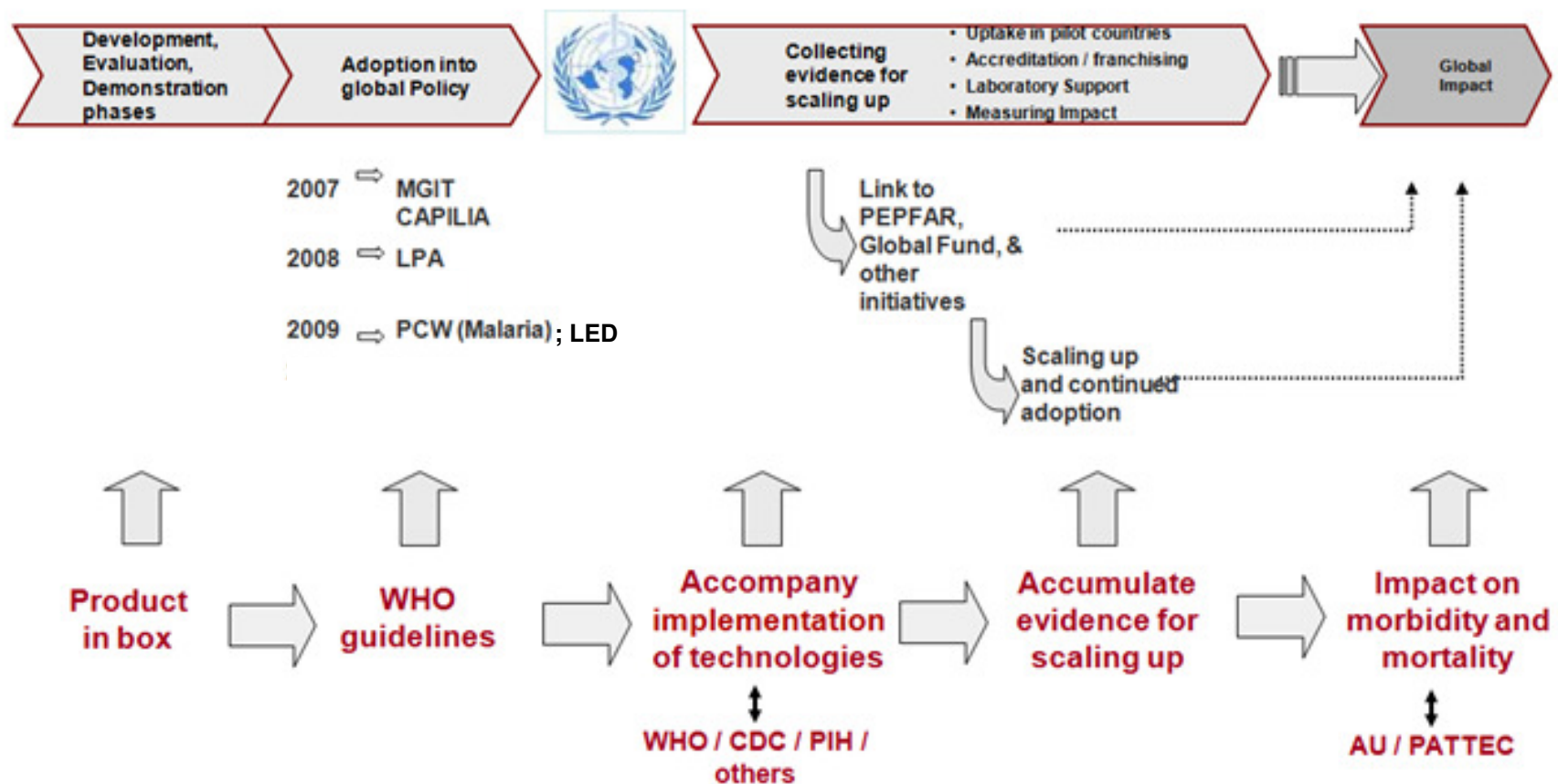


Progress in the Development & Implementation of New TB Diagnostic Tools

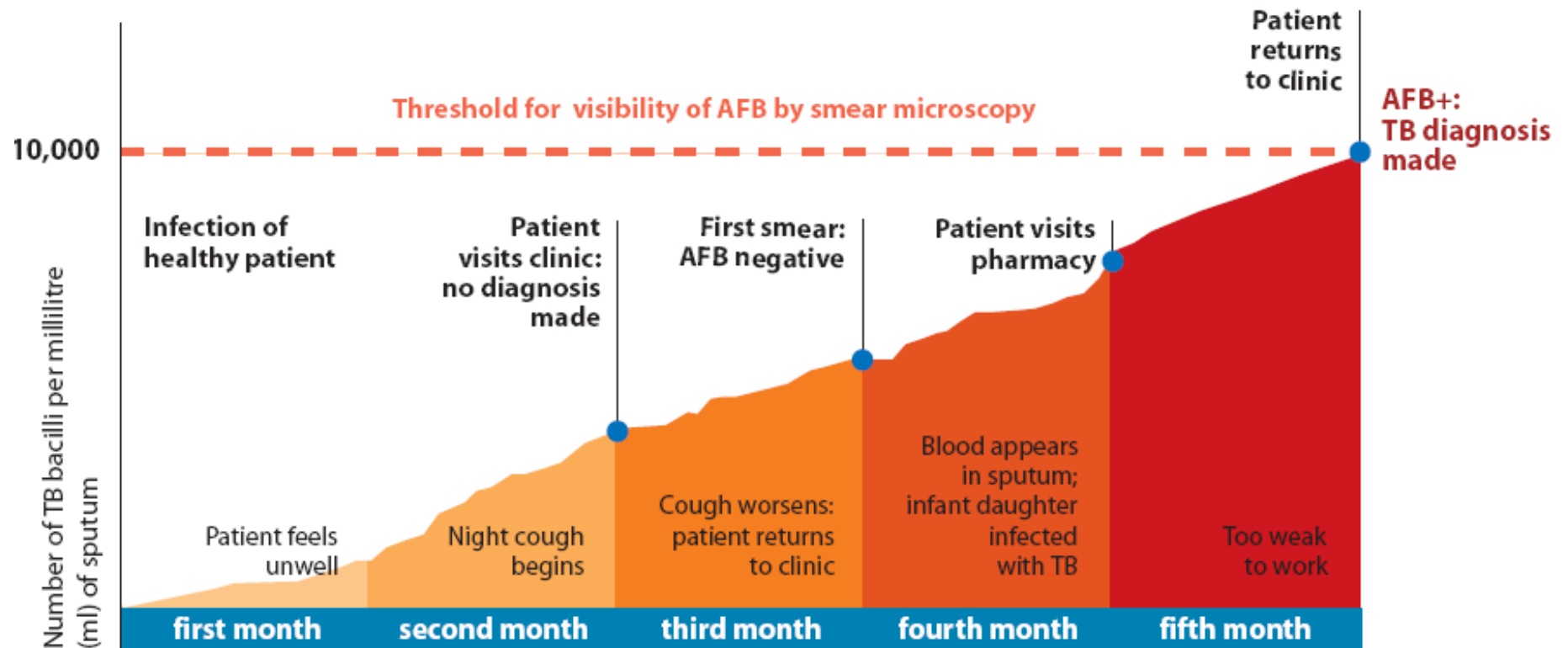
Giorgio Roscigno
Co-Chair of NDWG
Stop TB Partnership
Coordinating Board Meeting

Partnering for better diagnosis for all

Challenges of Implementing New Diagnostics – the Value Chain

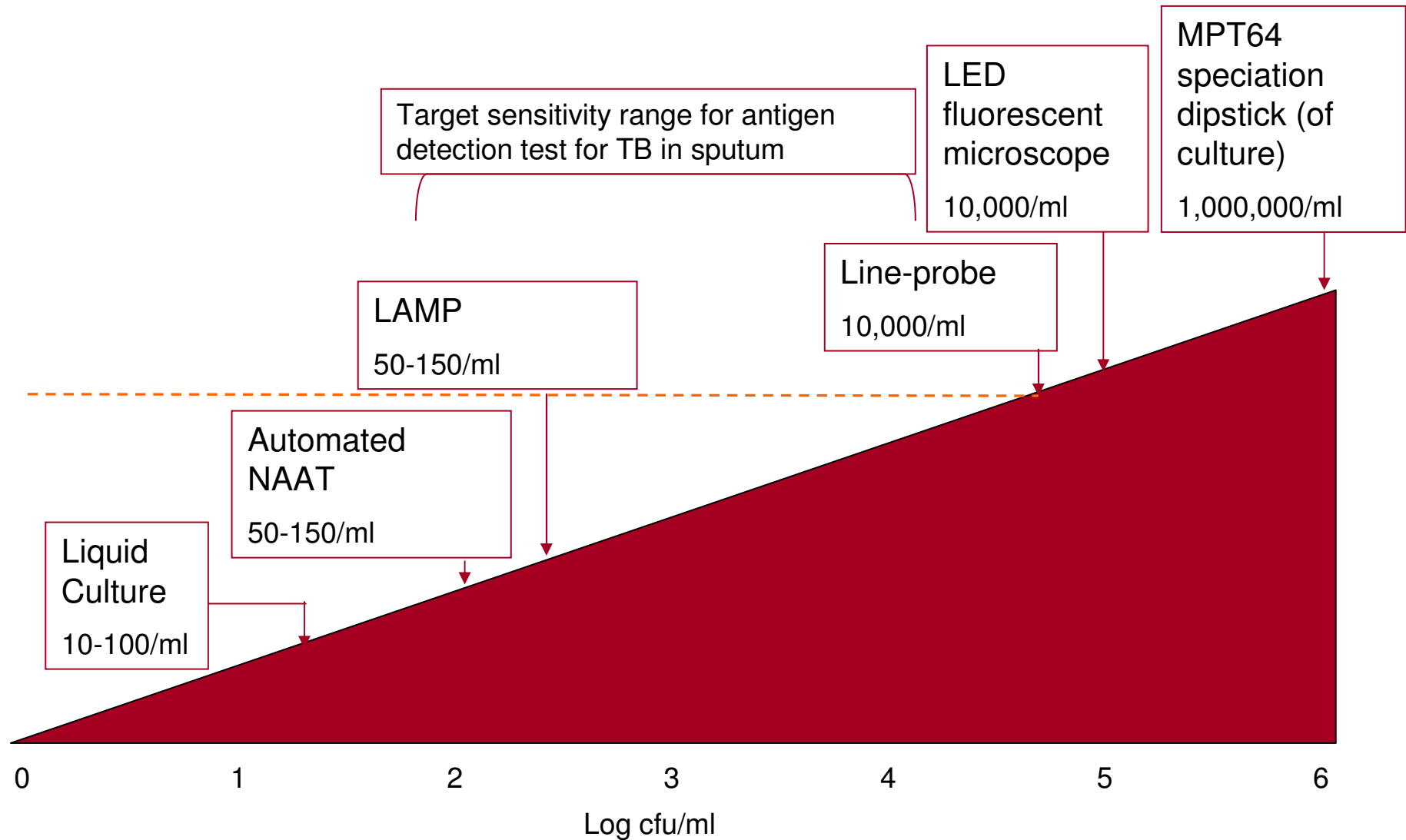


The slow road to TB diagnosis



Importance of early diagnosis

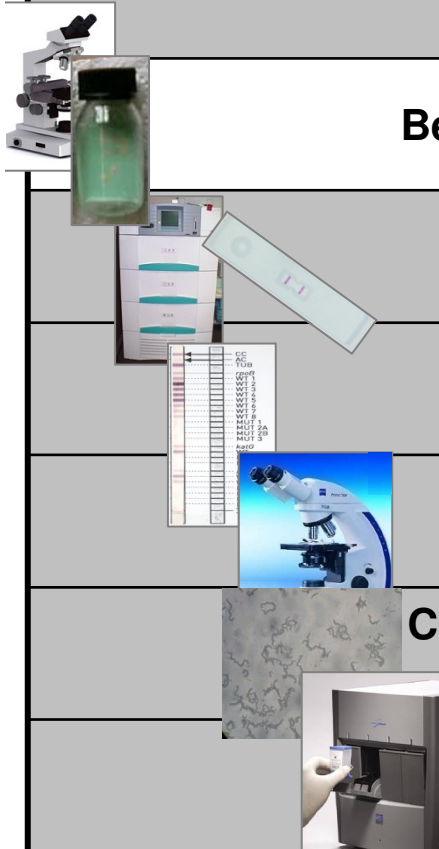
Sensitivity (cfu/ml) of pulmonary TB tests in portfolio



Achievements as per WHO endorsements 2007-2010

Importance of

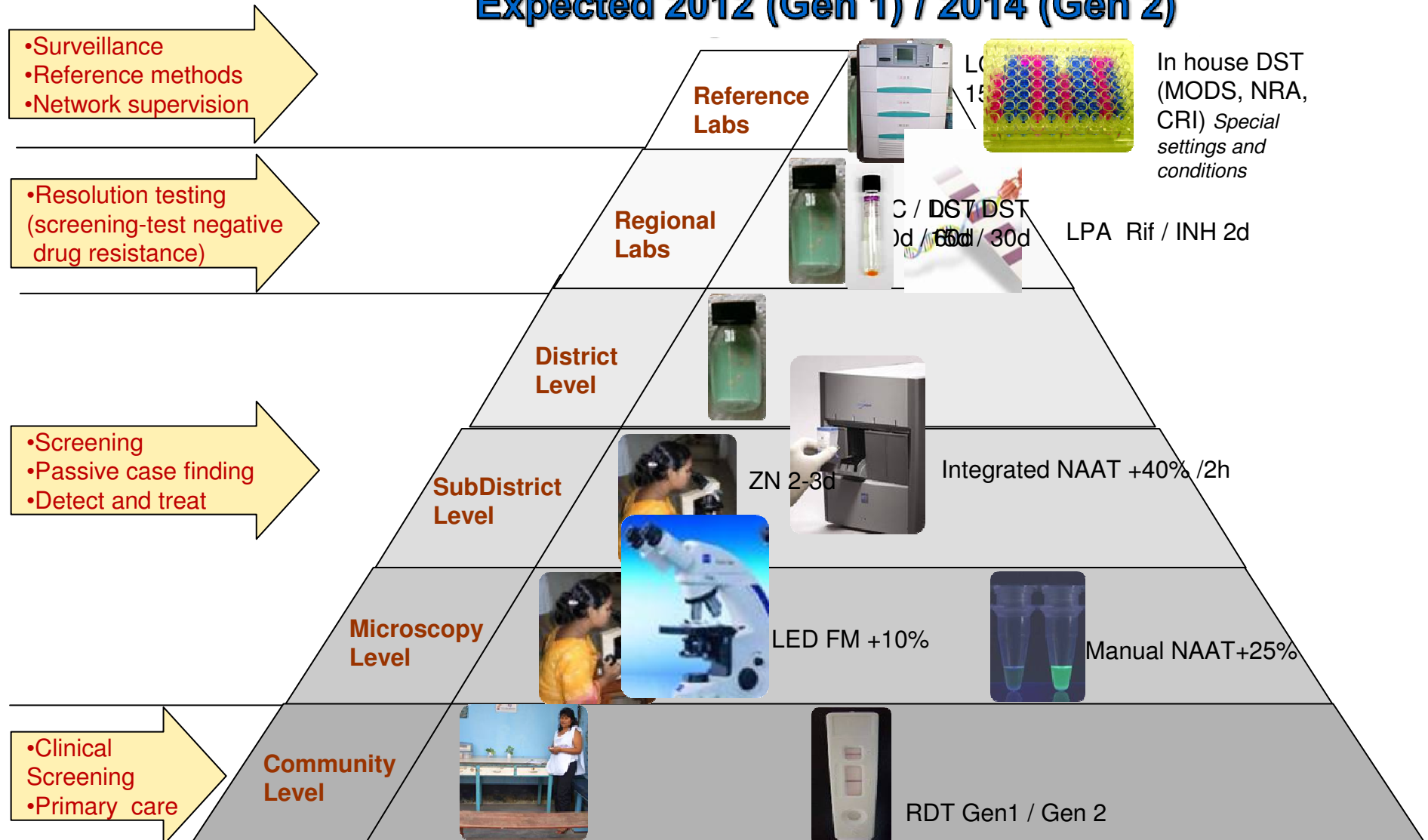
a) early diagnosis & care; b) smear-negative TB; c) rapid MDR/XDR detection





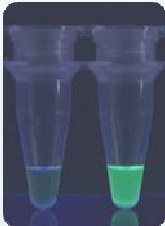

Year	Technology	Turnaround time	Sensitivity gain
Before 2007	ZN microscopy Solid Culture	2-3 days 30-60 days	Baseline
2007	Liquid Culture / DST Rapid speciation	15-30 days	+10% compared to LJ
2008	Line Probe Assay (1st line, Rif & INH)	2-4 days	At this time for S+ only
2009	LED-based FM	1-2 days	+10% compared to ZN
Conditional 2009	In house DST (MODS, CRI, NRA)	15-30 days	1 st line only
Expected 2010	Integrated NAAT (TB, Rif)	90 minutes	+40% compared to ZN

Integration of new tools in the tiered health system

Expected 2012 (Gen 1) / 2014 (Gen 2)



Increasing cost-effectiveness: Technology platform expansion

Technology		“Menu”
Regional Laboratories		<ol style="list-style-type: none"> 1. TB Rif / INH 2. TB Fluoroquinolones/Inject Aminoglycosides 3. EID/HIV
District/Subdistrict Laboratories		<ol style="list-style-type: none"> 1. TB Rif 2. TB Fluoroquinolones/Inject Aminoglycosides 3. STD 4. Viral load HIV 5. Others: Hepatitis B/C
Microscopy Centres		<ol style="list-style-type: none"> 1. TB 2. Malaria 3. HAT 4. EID/HIV
Microscopy Centres		<ol style="list-style-type: none"> 1. TB 2. HAT 3. Malaria

Appropriateness of new diagnostics

Example Xpert™ MTB/RIF; Khayelitsha CT



Xpert MTB/RIF assay performance

Case detection; single Xpert S3, per patient

	Sensitivity in S+C+	Sensitivity in S-C+	Specificity in Non-TB
UPCH, Peru	98.0% (193 / 197)	66.7% (8 / 12)	100.0% (101/101)
STI & Borstel, Azerbaijan	97.3% (73 / 75)	68.8% (44 / 64)	97.2% (69/71)
UCT, South Africa	96.8% (92 / 95)	86.3% (44 / 51)	99.5% (185/186)
SAMRC, South Africa	96.6% (28 / 29)	57.1% (8 / 14)	98.6% (215/218)
Hinduja, India	98.8% (159 / 161)	69.2% (18 / 26)	100.0% (35/35)
Total	97.8% (545 / 557) [96.3% - 98.8%]	73.1% (122 / 167) [65.9% - 79.2%]	99.0% (605/611) [97.9% - 99.5%]

- Overall sensitivity in culture pos patients for single Xpert 667/724 (92.1%)
- Reference standard composed of 3 smears and 4 cultures

Reducing time to diagnosis of MDR

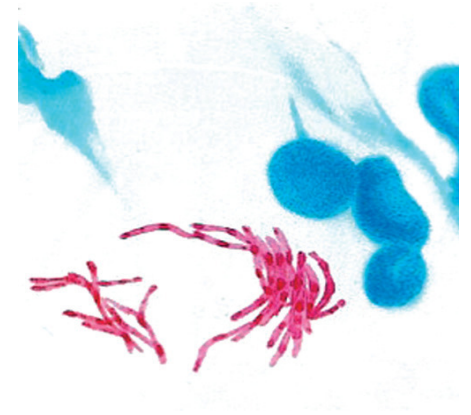
	Micro- scopy	Specimen transport or patient transfer	Test 1	MDR Treatment decision	Test 2	Total time to MDR diagnosis
Solid Culture / 1st line DST	24 h	Yes	SC 6-8 w	No	1 st line DST 3– 4 w	9-12 w (plus transfer time and reporting of result)
Liquid Culture / 1st line DST	24 h	Yes	LC 2-3 w	No	1 st line DST 1– 3 w	3-6 w (plus transfer time and reporting of result)
Line Probe Assay / Liquid Culture DST	24 h	Yes	Sm+ LPA 24 h	Yes	Full DST where required	2 d (plus transfer time and reporting of result)
			Sm- LC 2-3 w	No	1 st line DST LPA/LC 24 h – 3 w	2-6 w (plus transfer time and reporting of result)
Integrated NAAT / Liquid Culture DST	No	No	NAAT 2 h	Yes	Full DST where required	2 h



Moving Diagnostics into Countries: Activities of the Global Laboratory Initiative

Dr John Ridderhof (CDC)
Chair, Global Laboratory Initiative WG
May 4, 2010
Hanoi, Vietnam

TB CAP Toolbox

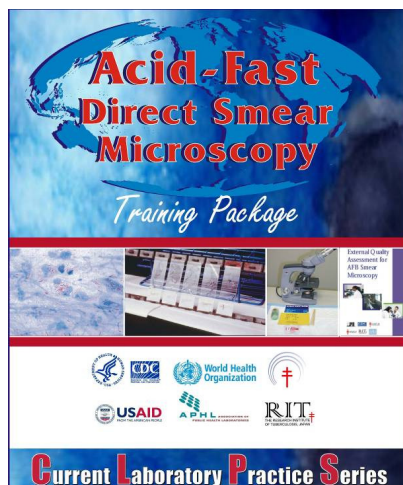


- ❖ Standard Operating Procedures (SOPs)
- ❖ Management Information System (MIS)
- ❖ Logistics/supply management tool
- ❖ Culture and DST training ("workshop in a box")
- ❖ EQA training ("workshop in a box")

- ❖ TBCAP = KNCV, RIT/JATA, IUATLD, WHO, CDC.....



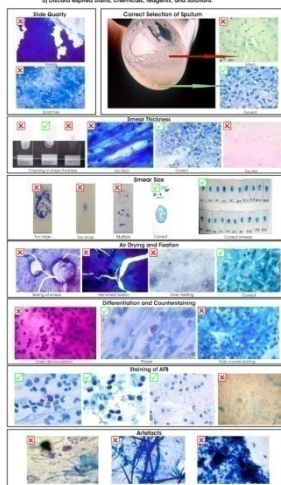
GLI Guidance, Tools, Programs



SRLN
TB SUPRANATIONAL REFERENCE LABORATORY NETWORK

Quality Issues of AFB Smear Preparation and Staining Technique

Important: 1) Always use good quality stains, chemicals, reagents, and new slides.
2) Prepare and label staining solutions as per standard operating procedures.
3) Verify quality and maintain the record.
4) Store all stains, chemicals, reagents, and solutions under appropriate conditions.
5) Discard expired stains, chemicals, reagents, and solutions.



External Q quality
Assessment for
AFB Smear
Microscopy



GLI Partners

- American Society for Microbiology (ASM)
- Association of Public Health Laboratories (APHL)
- Bill & Melinda Gates Foundation
- Centers for Disease Control and Prevention (CDC)
- CDC Global AIDS Programme (GAP)
- Fondation Merieux
- Foundation for Innovative New Diagnostics (FIND)
- International Union Against TB and Lung Disease (Union)
- PEPFAR
- USAID
- KNCV
- Merieux Alliance
- Management Sciences for Health (MSH)
- Medecins Sans Frontiers
- Stop TB Partnership Working Groups (New Diagnostics, MDR-TB, Retooling Task Force, DOTS Expansion)
- National TB Programmes
- SRLs/SRLN
- WHO
- UNITAID
- *and growing...*

First Issue
20th January 2010

**A Roadmap for Ensuring Quality Tuberculosis Diagnostics
Services within National Laboratory Strategic Plans**

Prepared by

The Global Laboratory Initiative
Advancing TB Diagnosis



USAID
FROM THE AMERICAN PEOPLE

Stepwise approach

❖ Phase 1: Laboratory preparedness

- Assessment of TB laboratory networks and diagnostic policies
- Upgrade of laboratory infrastructure and biosafety
- Development and implementation of GLP, SOPS, QA, etc.
- Training of core laboratory staff
- **Initiation of NTP policy reform on diagnostics**

❖ Phase 2: Introduction of new diagnostics

- Integration of new diagnostics into NTP policies and procedures
- Procurement and installation of instruments, reagents, supplies
- Validation of new tools and laboratory performance
- **Adjustment of NTP policy based on local data**

❖ Phase 3: Impact assessment

- Continued mentoring, technical support and oversight
- Assessment of impact on NTP outcomes

GLI Biosafety Projects

❖ Biosafety guidance for TB lab procedures

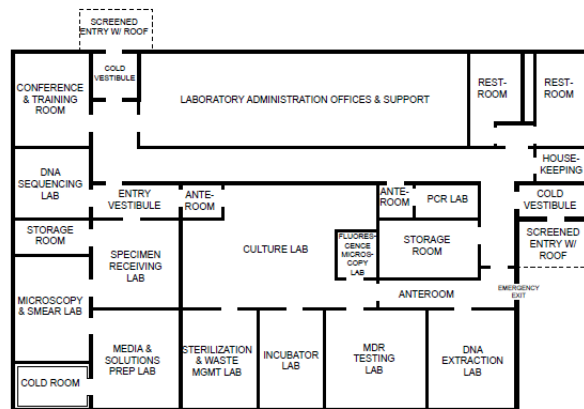
- technical consultation in Sept. 2008
- expert meeting in April 2009

❖ Specifications for a ventilated work station suitable for direct AFB-smear microscopy

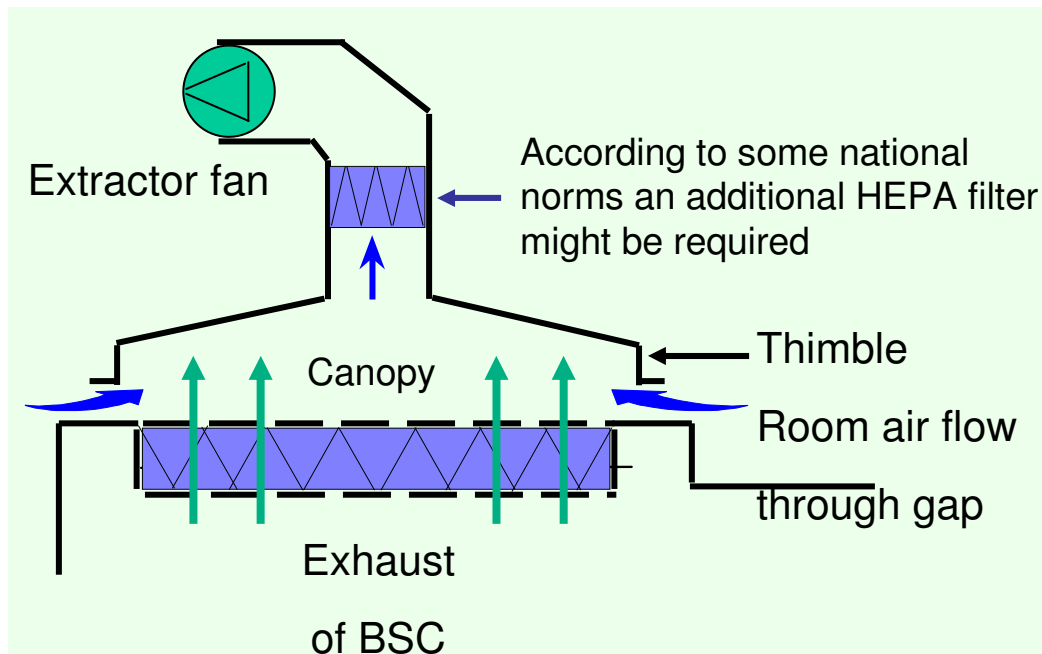
- Expert consultation in Sept. 2009

❖ WHO TB Laboratory Biosafety Manual

- Laboratory design and layout
- Risk assessment and procedures



CENTRAL LAB 3A: cold conditions
[combined lab & office building]



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Find businesses, addresses and places of interest.

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GLI TB Supra-National and National Reference Labs

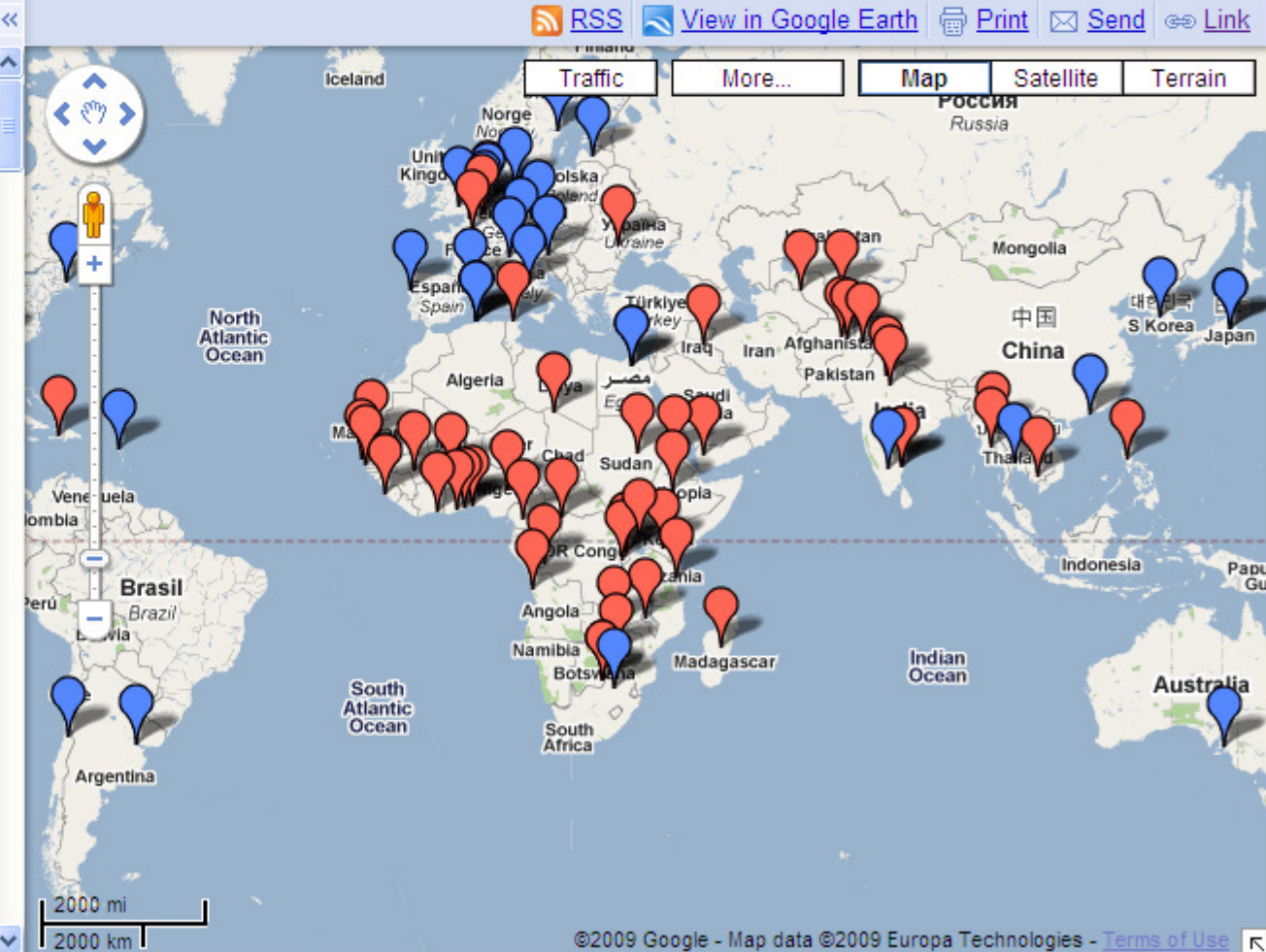
Global Laboratory Initiative (GLI)
Tuberculosis Reference Laboratories

Map Key:
Blue: Supra-National TB Reference Labs
Red: National TB Reference Labs

Contact:
United States Agency for International Development
(USAID)/Washington DC
USAIDTB@gmail.com
<http://glitblabs.blogspot.com/>

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-  [Algeria](#)
Laboratoire national de reference pour la Tuberculose
-  [Argentina](#)



http://www.stoptb.org/wg/gli/default.asp

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TB Stop TB Partnership | Global Laboratory Initiative

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What's new?

[Narrowing the Gap: Expanding and accelerating access to diagnostics for patients at risk of multi-drug resistant tuberculosis \(MDR-TB\)](#)

<< April 2010 >>						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

Welcome to the website of the Global Laboratory Initiative (GLI)!

The Global Laboratory Initiative (GLI) is a network of international partners dedicated to accelerating and expanding access to quality assured laboratory services in response to the diagnostic challenges of TB, notably HIV-associated and drug-resistant TB. The GLI provides a focus for TB within the framework of a multi-faceted yet integrated approach to laboratory capacity strengthening.

Organizationally, the GLI is one of seven main Working Groups of the Stop TB Partnership (STP) with the GLI secretariat provided by WHO-HQ in Geneva. Functionally, the GLI serves as an independent, technical expert advisory group to WHO, the STP, development agencies and countries. Structurally, the GLI consists of individuals with expertise in multiple disciplines, representing constituencies of stakeholders and/or institutions involved in global, regional and country-level laboratory strengthening.



Moving TB diagnostics into countries

Karin Weyer, WHO-STB
on behalf of EXPAND_x-TB

EXPAND-TB is a collaboration between WHO, GLI, FIND and GDF,
funded by UNITAID and other partners

*Stop-TB Partnership Coordinating Board Meeting
Hanoi: 4 - 5 May 2010*

AIMS

Reduce the MDR-TB diagnostic gap

Ensure rapid, effective technology transfer in upgraded laboratories

Support 27 countries, ~100 laboratories

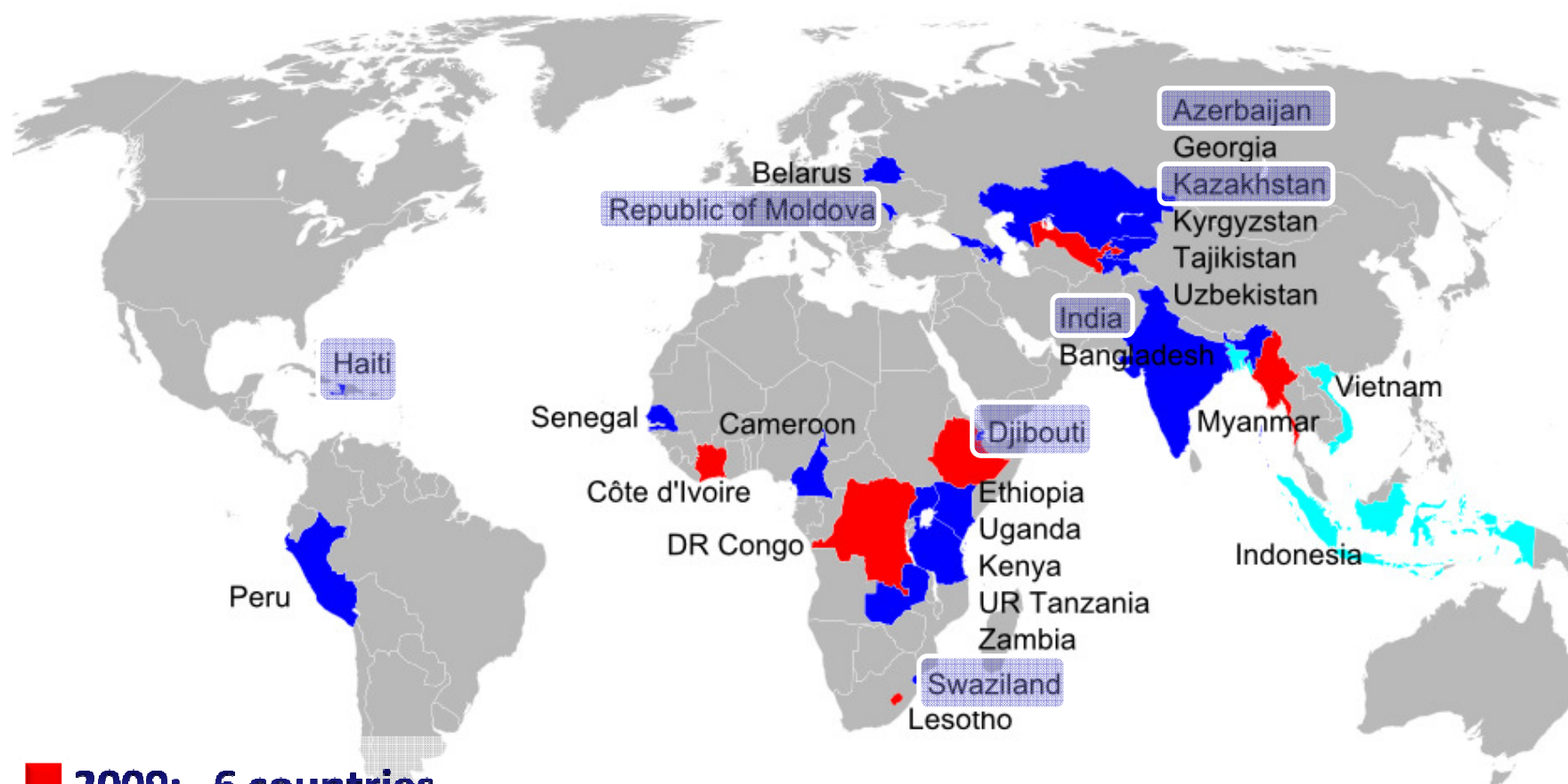
Detect ~130,000 MDR patients (and ~950,000 drug-susceptible TB patients)

Leverage UNITAID funding to secure other core components of laboratory strengthening

Positively impact MDR-TB Dx market dynamics



WORLDWIDE COMMITMENT 2009-13



- **2009: 6 countries**
- **2010: 18 countries, including India (>40 labs)**
- **2011: 3 countries**

A UNIQUE PARTNERSHIP MODEL

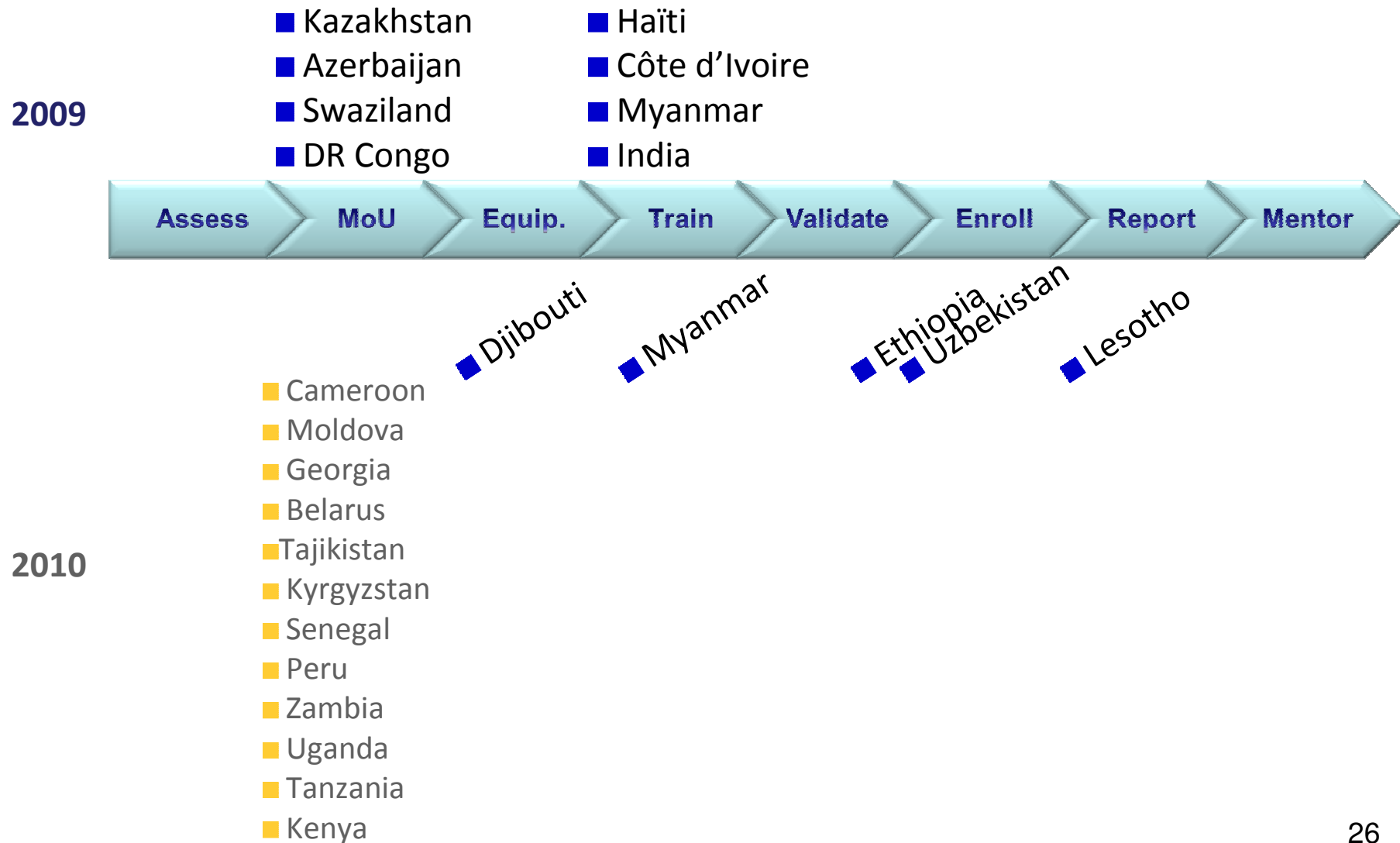


a

STRONG IN-COUNTRY PARTNERS

Ethiopia	Lesotho	Côte D'Ivoire	Uzbekistan	Myanmar	Haïti
<ul style="list-style-type: none"> • MOH, PEPFAR-CDC, GAP/ILB, JHU & ICAP, SRLN, GF 	<ul style="list-style-type: none"> • MOH, PIH, PEPFAR/CDC, WHO, URC, GF, BD, SAMRC 	<ul style="list-style-type: none"> • MOH, WHO, PNLT, IPCI; CAT Adjame, CeDReS, ASM, PEPFAR, EGPAF 	<ul style="list-style-type: none"> • MOH, WHO, KfW (EPOS), GF, USAID, Euro Lab Task Force 	<ul style="list-style-type: none"> • MOH, WHO, NTPL, AKK. JAICA, PSI, MSF, UNION 	<ul style="list-style-type: none"> • MOH, NTP, WHO, NPHL, NRLM, GHESKIO, Fondation Mérieux, CDC-PEPFAR, ASM, Cornell University

PROGRESS AT-A-GLANCE



LESOTHO – a model for rapid knowledge transfer

1 reference lab: QEII hospital

1 regional lab: Mafeteng government hospital

2006-2008: FIND, PIH and WHO renovated the NRL and reinforced microscopy services, streamlined culture and DST and introduced modern TB diagnostic methods

2007: BSL3, solid culture and DST, and EQA for smear microscopy established within 4 months

Liquid culture and DST introduced one month later

2008: LPA introduced for rapid detection of MDR-TB

2009: National TB/HIV Strategic Plan for 2008 – 2012 finalized by MOH

2009: FIND conducted retraining for laboratory technicians at the NRL

2009: Validation of new TB Dx algorithm finalised

2010: Regional laboratory is currently being renovated

2010: Patient enrolment has started under ExpTB – 116 patients reported Jan-Mar

INT J TUBERC LUNG DIS 14(1):59-64
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Experience establishing tuberculosis laboratory capacity in a developing country setting

C. N. Paramasivan,* E. Lee,* K. Kao,* M. Mareka,* G. Kubendiran,* T. A. Kumar,* S. Keshavjee,* H. Satti,* G. Alabi,* M. Raviglione,* G. Roscigno*

*Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland; †Ministry of Health, Maseru, ‡FIND, Maseru, §Partners in Health, Maseru, Lesotho; ¶Stop TB, World Health Organization, Geneva, Switzerland

SUMMARY

OBJECTIVE: To describe the experience of strengthening laboratory diagnosis of tuberculosis (TB) in a resource-limited country with high TB-HIV (human immunodeficiency virus) and multidrug-resistant TB (MDR-TB) prevalence.

METHODS: In the Kingdom of Lesotho, which is confronted with high levels of TB, MDR-TB and HIV prevalence, between 2006 and 2008 a coalition of the Foundation for Innovative New Diagnostics, Partners In Health and the World Health Organization renovated the National TB Reference Laboratory and reinforced microscopy services, streamlined conventional culture and drug susceptibility testing (DST) and introduced modern TB diagnostic methods.

FINDINGS: It was feasible to establish a biosafety level three facility for solid culture and DST and an external quality assessment programme for smear microscopy within 4 months, all in 2007. Liquid culture and DST

were introduced a month later. Preliminary results were comparable to those found in laboratories in industrialised countries. A year later, line-probe assay for the rapid detection of MDR-TB was introduced.

DISCUSSION: Through strong political commitment and collaboration, it is possible to rapidly establish quality assured TB diagnostic capacity, including current methods, in a resource-limited setting. Case detection and management for TB and MDR-TB have been greatly enhanced. From a low baseline, TB culture throughput in the laboratory increased ten-fold and has been sustained. This experience has served as a catalyst to translate policy into practice with new diagnostic technologies. It supports global policy setting to enhance and modernise laboratory work in developing countries.

KEY WORDS: TB laboratory capacity; liquid culture; line-probe assay; MDR-TB; low-income country



ETHIOPIA – a model for integration

8 sites supported:

2 central labs: EHNRI (NRL), St Peters Hospital and **6 regional labs:** Mekelle, Bahir Dar, Jimma, Awasa, Adama (Nazret), Harrar

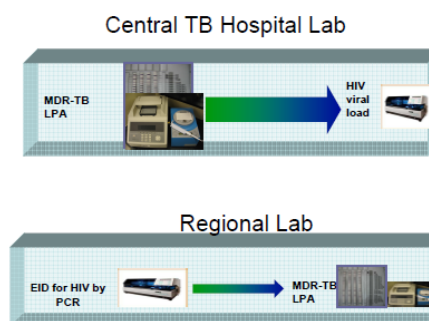
FIND involved since 2007 with full-time consultant

Integrated HIV viral load testing with Line Probe Assay at central and regional locations

Refresher training in 2 central labs

Technical proficiency validated (sputum processing, SC, LC, LPA)

Negative air pressure and equipment installed at 6 regional labs, training planned



Inauguration March 2009

INDIA – a model for scale-up

40 sites to be supported:

4 national reference lab , 27 intermediate reference state laboratories, 9 medical colleges

Joint project involving UNITAID (EXPTB) and GF (CTD-MoH)

In 2008, Collaboration Agreement GoI and FIND to demonstrate introduction of liquid culture, LPA and species ID

2010 FIND's role as a sub-recipient for India's GF R9:

- support of human resources in data management and lab support
- technical assistance and on-site training support for technology uptake.

Signing of Expand-TB MoU and start of activities April 2010



MYANMAR – a model for political commitment

2 sites

1 central lab, in Yangon and 1 regional lab in Mandalay

Equipment for 2 BSL3s shipped, installation completed

WHO country office acts as recipient of goods

MOH, Government of Myanmar in charge of customs clearance & shipping to sites

EXP-TB consultant coordinating all activities

Government of Myanmar has refurbished the laboratories

5 lab techs underwent 2-week training in Bangkok by FIND, with funding from WHO

