

Standardization of diagnostics: FIND's experience

Meeting on Procurement of Laboratory Items

WHO, October 2008

Evan Lee, MD

Senior Medical Officer

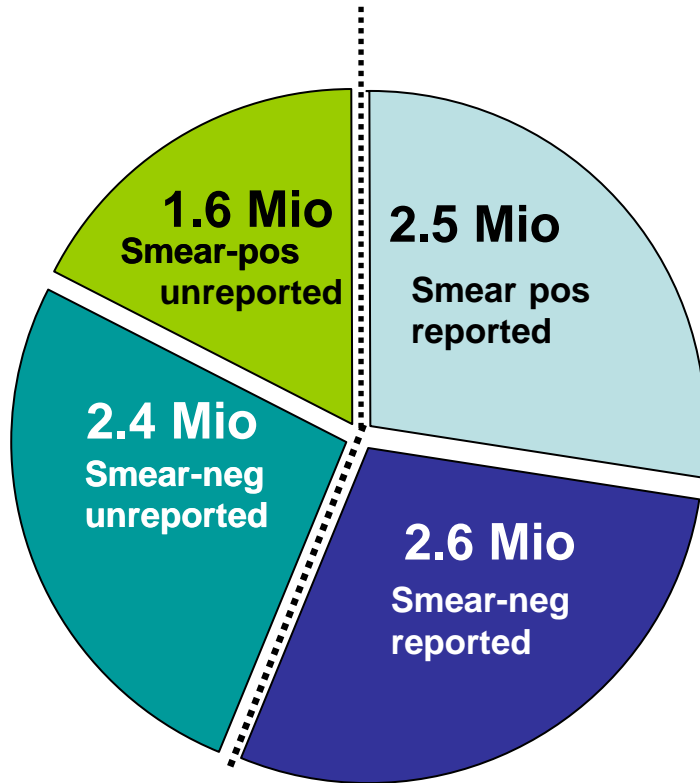
A non-profit Swiss Foundation

(Geneva, New Delhi, Kampala)

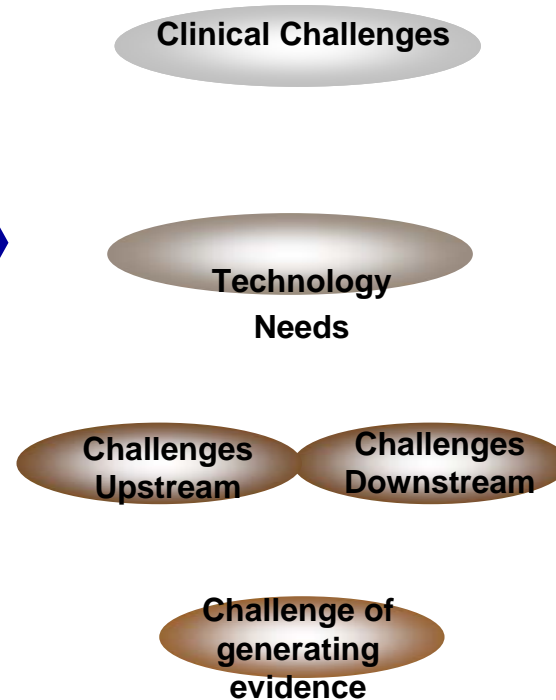
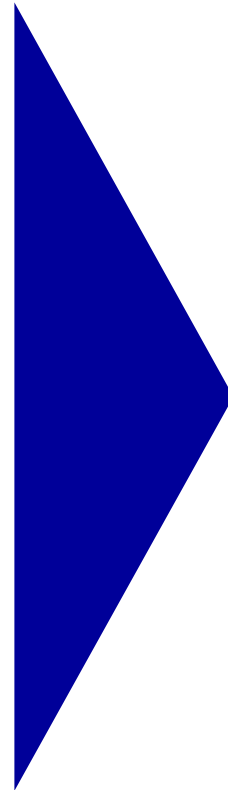


- **Founded in 2003** (WHO World Health Assembly):
Partnering for better diagnosis for all
- **Vision:** *A world where patients will have equitable access to high quality diagnosis*
- **Mission:** *FIND drives the development and implementation of accurate and affordable diagnostic tests, that are appropriate to patient care in low-resource settings*

TB is vastly underdiagnosed



WHO Global TB Report 2008



FIND Project Management: Milestones and Deliverables

Feedback: Market Vigilance and Surveillance

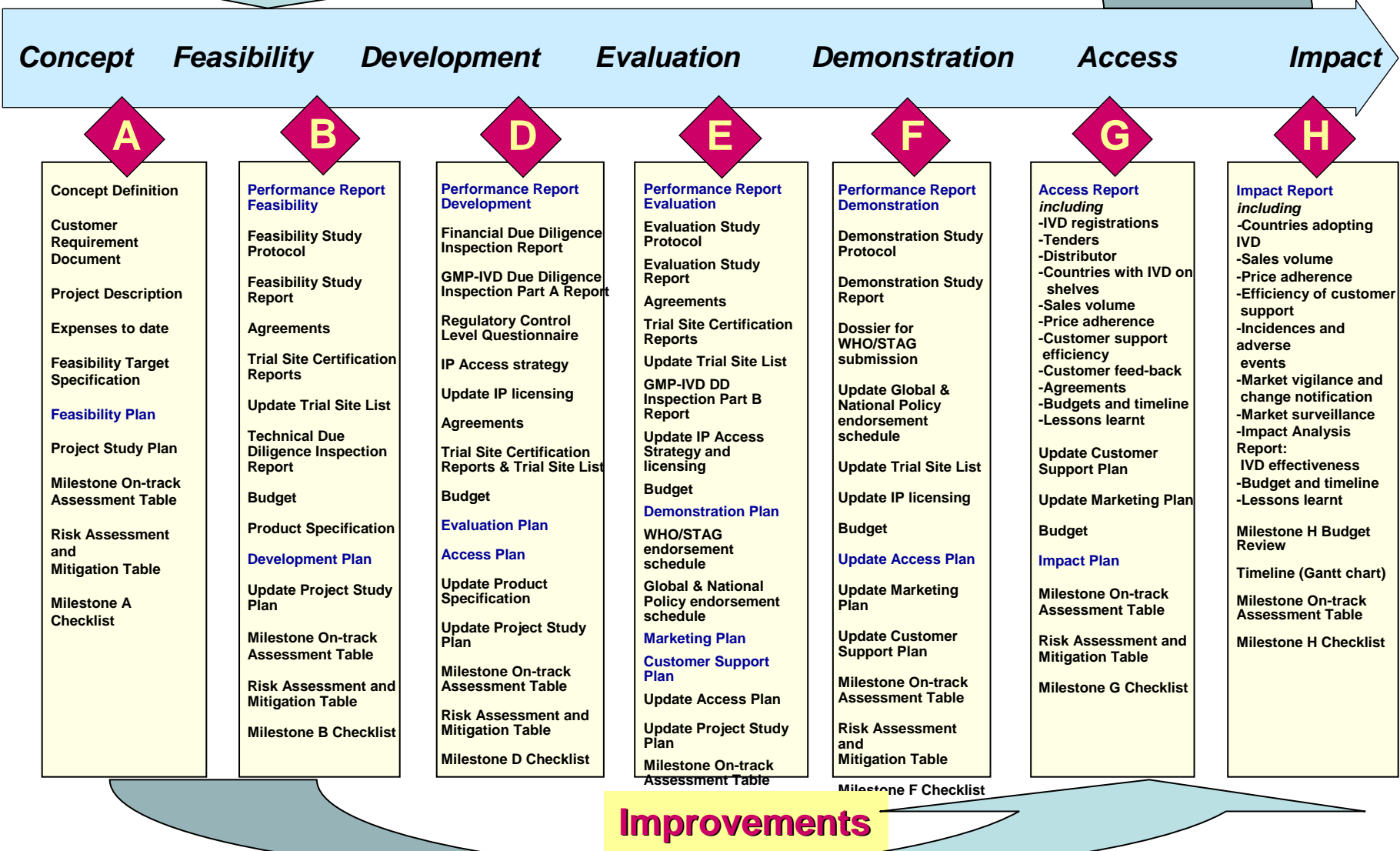


Figure 1: Project phases, milestones and deliverables

Investment in trials increases as products move through pipeline

Study type	Feasibility	Evaluation	Demonstration
Endpoints	“Proof-of-principle”: <ul style="list-style-type: none"> Analytical performance Operational performance Ballpark clinical performance New potential applications 	<ul style="list-style-type: none"> Efficacy Clinical performance Registration 	<ul style="list-style-type: none"> Impact Cost-Effectiveness Definition of requirements for implementation Awareness
Nr. of patients	300 - 600	1,000 – 3,000	5,000 – 10,000
Nr. of sites	1 - 3	3 - 6	4 - 10
PMM Targets	Feasibility target specifications	Product specifications	Customer requirements
Average costs per patient <small>(equipment/reagents for new method not included)</small>	LOW (e.g. Bangladesh): 30-50 \$ Standard (e.g. Peru, Vietnam): 100 \$ High (e.g. South Africa): 300 – 500 \$	Low: 150 \$ Standard: 200 \$ High: 500 – 1000 \$	Low: 50 \$ Standard: 100 – 150 \$ High: 250 -350 \$
Factors influencing trial costs	<ul style="list-style-type: none"> Cross-sectional vs longitudinal Clinical information needs (e.g. CD4 status) Required gold standard (e.g. blood culture, drug susceptibility testing) Specimen needs (e.g. serum) and volume Patient groups: paediatric TB, extrapulmonary or disseminated TB, contact persons Other donors/partners involved (e.g. CREATE, AERAS, Universities, MOH) 		

Quality Assurance

During the development process is key to ensuring a reliable, standardized diagnostic tool

- ISO 13485 & 9001 certificates received in 2007
- Surveillance audit successfully passed in 2008

ZERTIFIKAT ♦ CERTIFICATE ♦ 證書註冊 ♦ CERTIFIKAT ♦ CERTIFICADO ♦ CERTIFICAT

SWISS TS 

CERTIFICATE

The certification body of Swiss TS Technical Services AG hereby certifies that

FIND
FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS
Geneva, SWITZERLAND

has introduced and applies a quality management system for
**Project Management for Design, Development and Manufacturing of IVD.
Evaluation and Demonstration of IVD.**

according to:
ISO 13485 : 2003

Registration number: 07-268-006
Initial certification date: 29.06.2007
Valid until: 28.06.2010

Heinrich A. Bieler
Wallisellen, 29.06.2007
The certification centre of Swiss TS Technical Services AG
A SVTI and TÜV SÜD company



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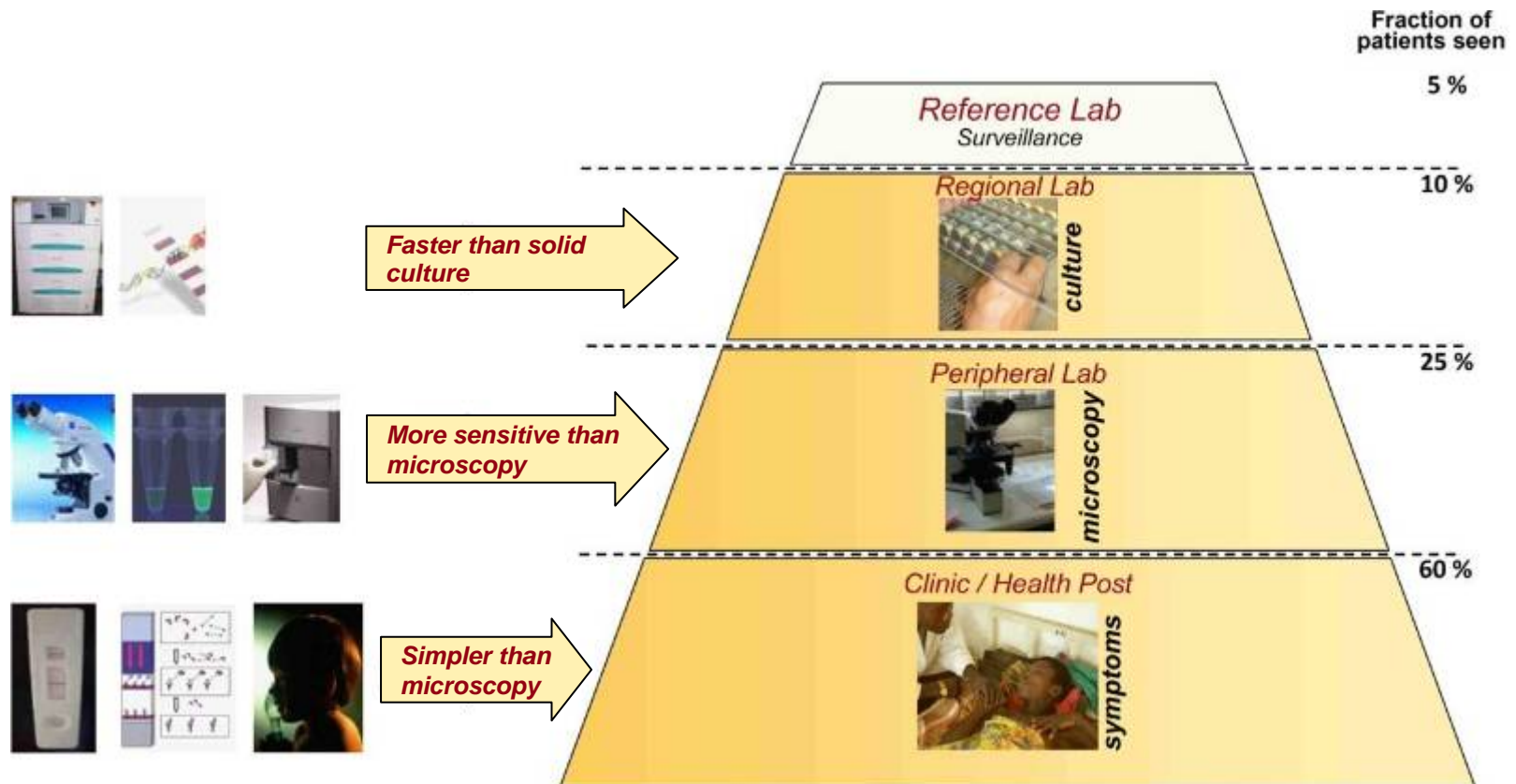
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TB Diagnostics have to meet the requirements at different health levels



The Maputo Declaration on Strengthening of Laboratory Systems

Maputo, Mozambique, January 2008

“Call on academic institutions and research funders to accelerate efforts to develop new diagnostic tools applicable to resource-limited settings”

Challenges differ between levels of the lab network



High-volume Lab
with automated
analyzers



Small lab belonging
to doctor-run clinic



Point-of-care lab

Beyond Demonstration



WHO has an established mechanism for evaluating and reviewing new TB-related technologies for endorsement into global policy



Seventh Meeting

**STRATEGIC & TECHNICAL ADVISORY GROUP
FOR TUBERCULOSIS
(STAG-TB)**

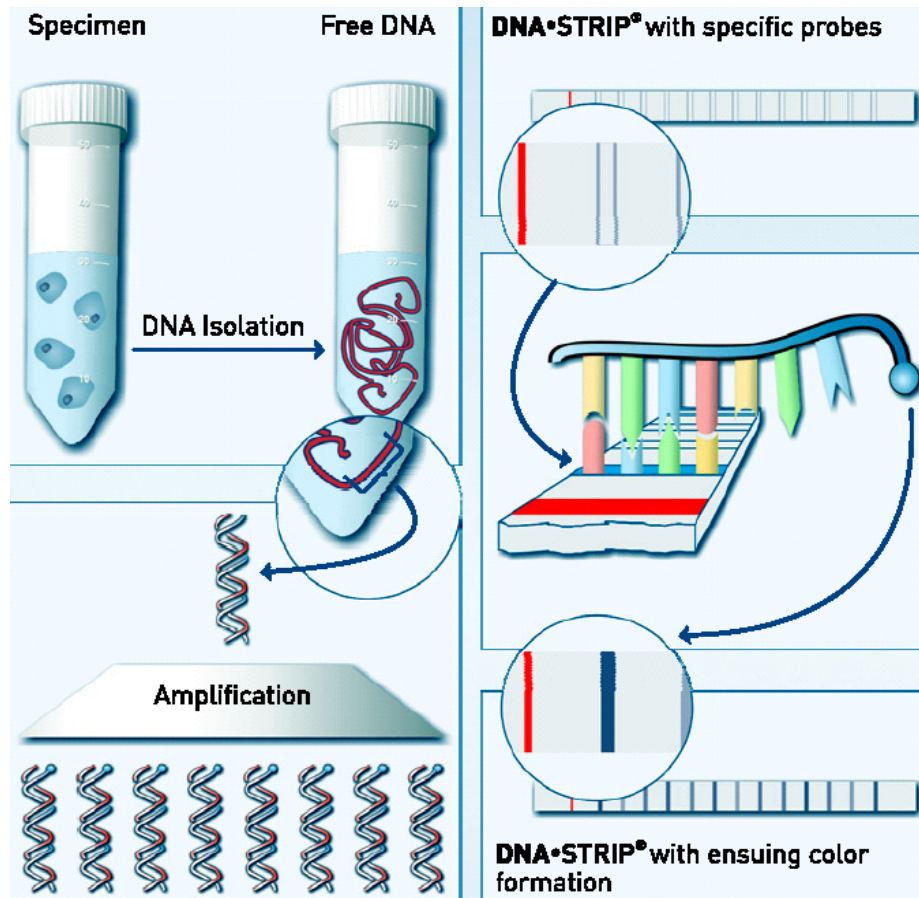
Report on Conclusions and Recommendations

Line probe assay test procedure

Endorsed by WHO, 2008

•DNA
Extraction
From NALC/NaOH
Processed sputum

2) Amplification
by PCR



3) Hybridization

Reverse hybridization of amplified nucleic acids to specific DNA probes bound on strips



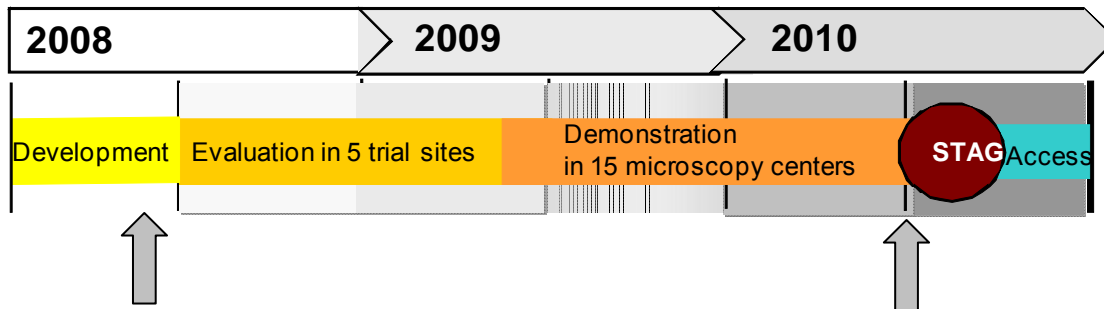
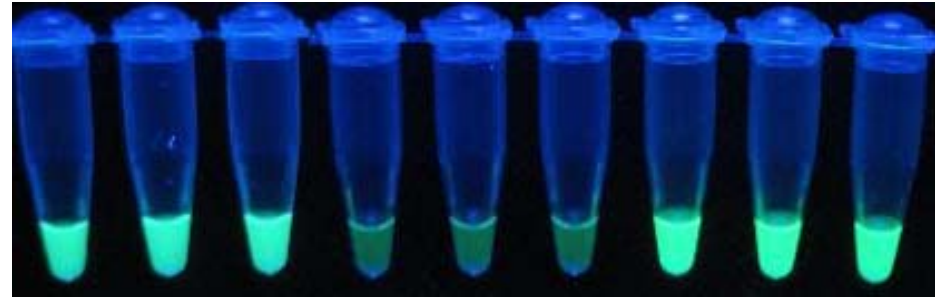
4) Evaluation

• Detection of MDR-TB reduced from 4-6 weeks to 48 hours

Molecular meets microscopy: TB LAMP (in Development/Evaluation)



LAMP demonstration at microscopy center in Mumbai, India



Challenges upstream:
Reaching required sensitivity &
simplicity

Challenges downstream:
Implementation of disruptive
technology
Laboratory preparedness

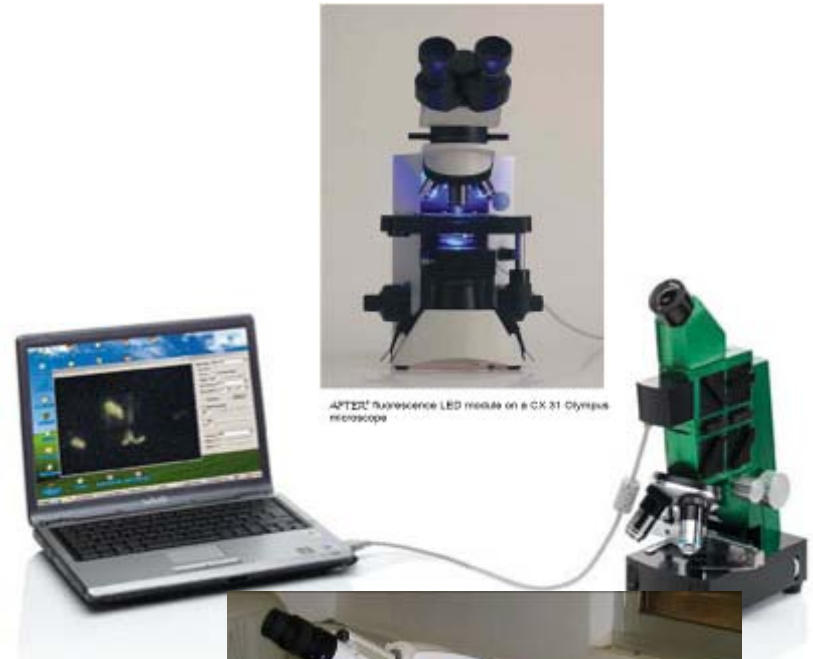
A technology platform:

- TB
- Malaria
- HAT
- Potential for ...

LED Microscopy

Under development

- Low cost of ultra-bright LEDs
- Affordable price \leq existing light microscopes
- Wider routine use in DEDCs
- Long lifespan (\sim 15-20,000 hours)
- Low power consumption
- Provision for operation with batteries
- Enhanced robustness
- No need for air conditioning facility
- No need for a dark room
- Diagnostic performance \geq standard FM
- Decreased technician workload



High tech in low tech settings (in Development/Evaluation)



**Automated Sample Prep,
Amplification and Detection**

<120 minutes

Major advantages in workflow

- fully automated with 1-step external sample prep.
- time-to-result 1 1/2 h (walk away test)
- throughput: up to 16 tests / module / run
- no bio-safety cabinet
- closed system (no contamination risk)

A technology platform that can work across diseases:

- TB & Rif Resistance
- Potential for HIV viral load
- Potential for ...

AG rapid detection

(Extensive program in Ag/Ab development)



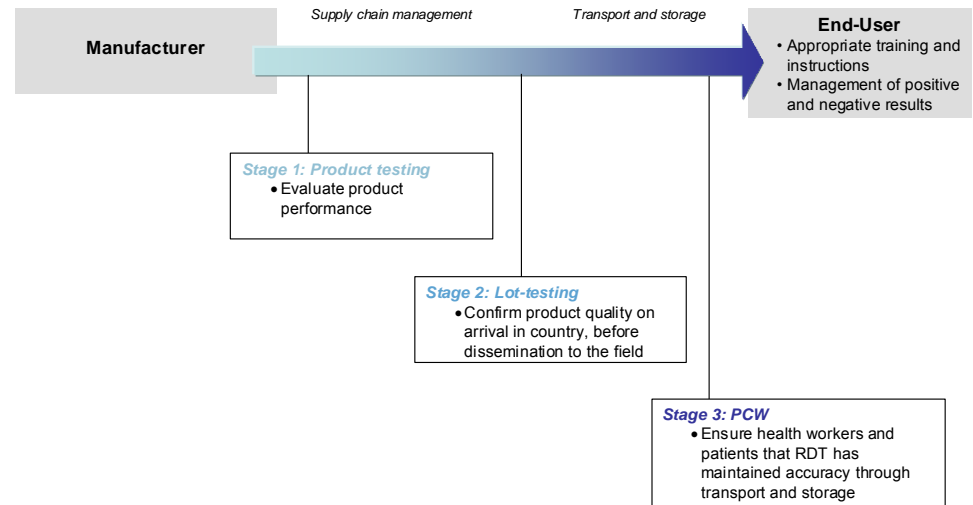
- Moving diagnosis as close as possible to the patient



Early & intensive case detection

Quality Assurance for Malaria RDTs

- 60+ brands known to WHO
- 30 million tests procured in 2005
- Est. ~70 million procured in 2007
- Most endemic countries have no, or weak, regulatory framework
- A range of types of malaria RDTs, i.e. card / cassette / dipstick are on the market
- Key technical issues with RDTs include:
 - ✓ Sensitivity
 - ✓ Stability
 - ✓ User accuracy and safety



Quality Assurance activities for malaria RDTs has to be built in throughout the supply chain

- At the level of the manufacturer
- In-country delivery
- At the end-user level

Addressing issues in the in-country supply chain

Manual for transport and storage of malaria Rapid

Diagnostic Tests at central storage facilities

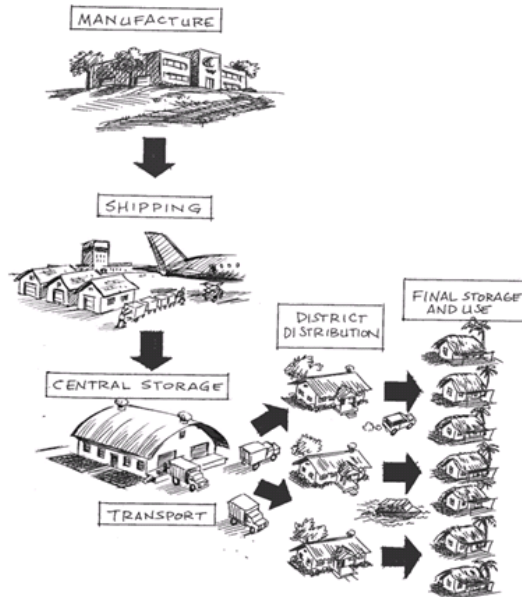
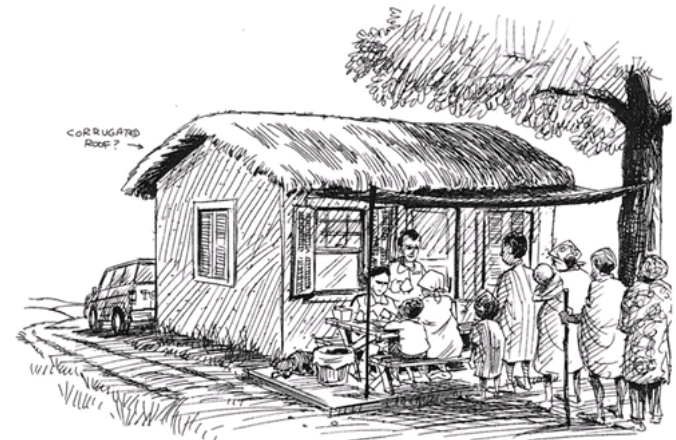


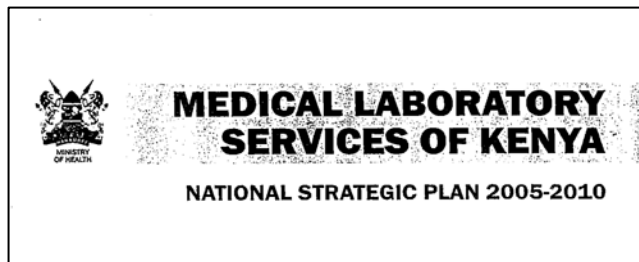
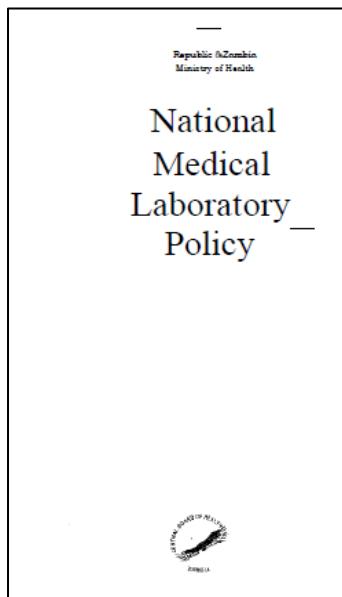
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Manual for the management of malaria rapid diagnostic tests at peripheral health care facilities



National Lab Policies and Implementation Plans may have to be developed or revised



Guidance document to assist countries
in the development of National
Laboratory Strategic Plans

World Health Organization – Regional
Office for Africa and United States
Centers for Disease Control (CDC),
Atlanta

Draft



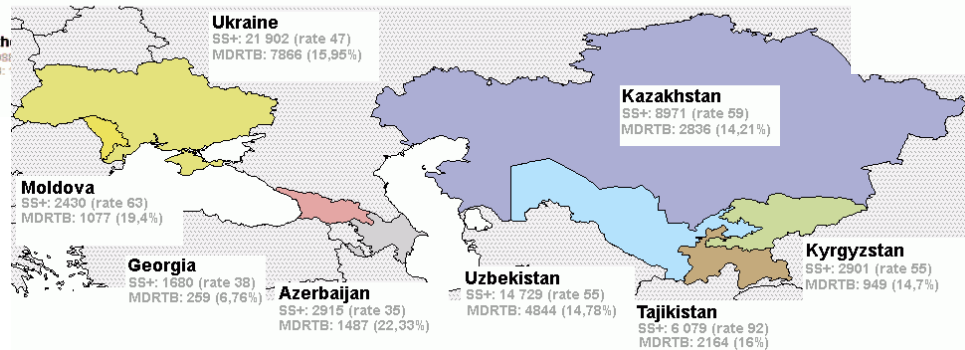
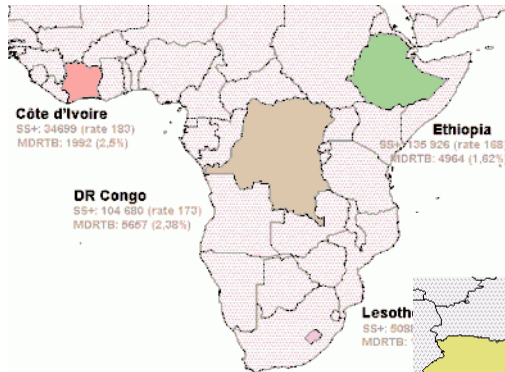
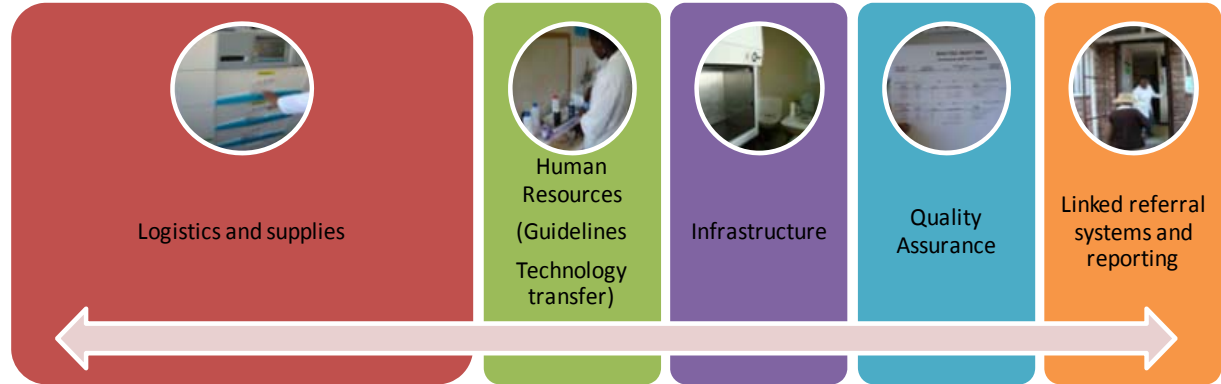
The Maputo Declaration on Strengthening of Laboratory Systems

Maputo, Mozambique, January 2008

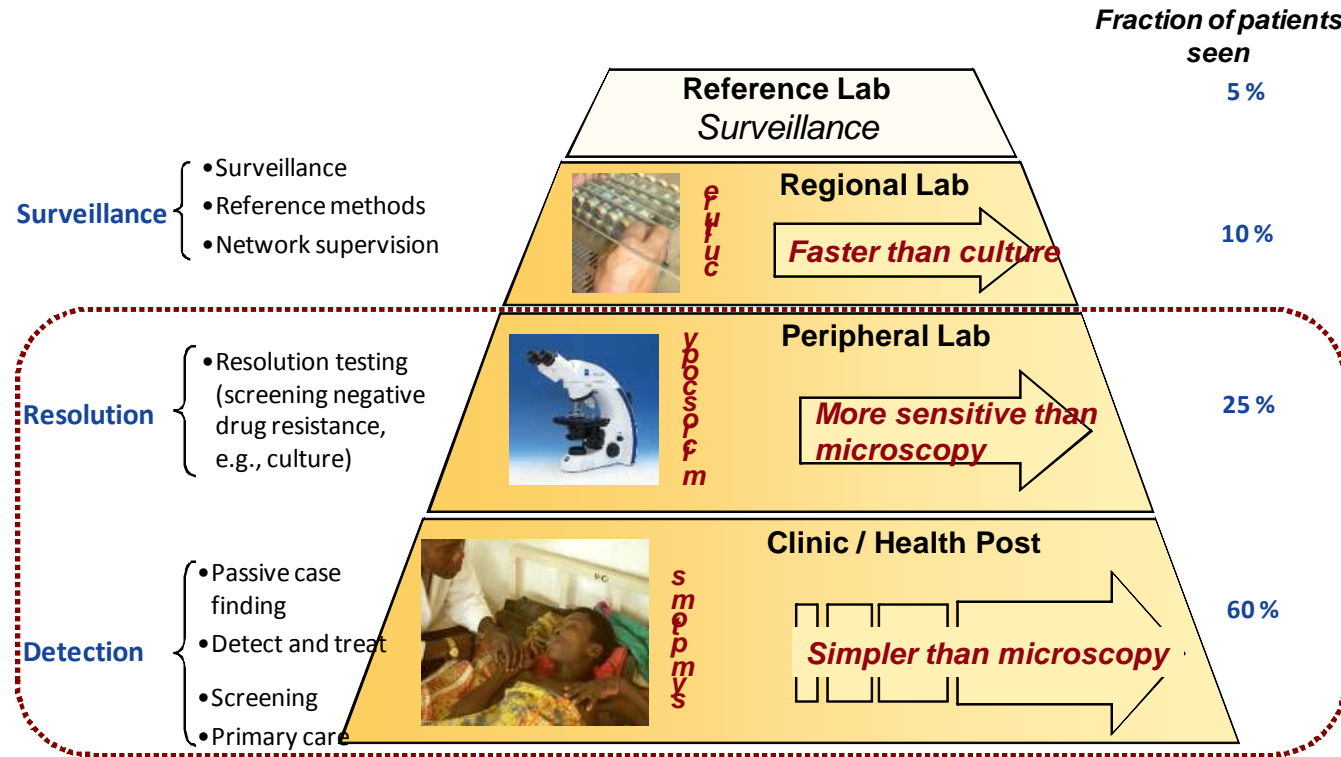
“Call on national governments to support laboratory systems as a priority by developing a national laboratory policy within the national health development plan that will guide the implementation of a national strategic laboratory plan. Governments should establish a department of laboratory systems within the Ministry of Health”

UNITAID: Narrowing the Gap

Partner collaboration to bring TB diagnostics to up to 16 countries – meeting procurement challenges in diverse settings



Standardization will drive an integrated laboratory network



Benefits include:

- Simplifying the supply chain (fewer suppliers if cross-disease platforms used)
- Lessened training requirements
- Improved chance of securing maintenance contracts to reach remote locations

Thank you!

