2nd Annual GLI Meeting
Annecy, 15 - 16 October 2009

A roadmap for TB laboratory strengthening within WHO policy frameworks and national laboratory strategies

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On behalf of the GLI Core Group

World Health Organization

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Stop TB Partnership

Outline

- Addressing diagnostic and laboratory gaps
- Rationale for a Roadmap
- Process, purpose, scope
- Core elements
- TB diagnostic algorithm (what/where/when)

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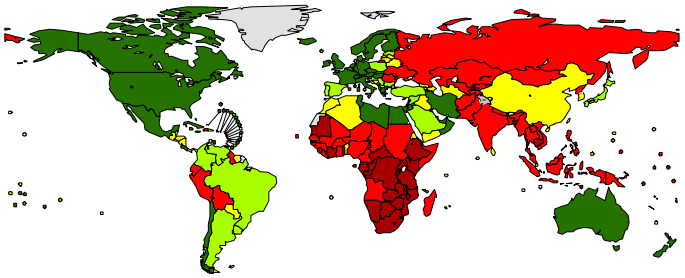
Global TB estimates - 2007

(Updated February 2009)

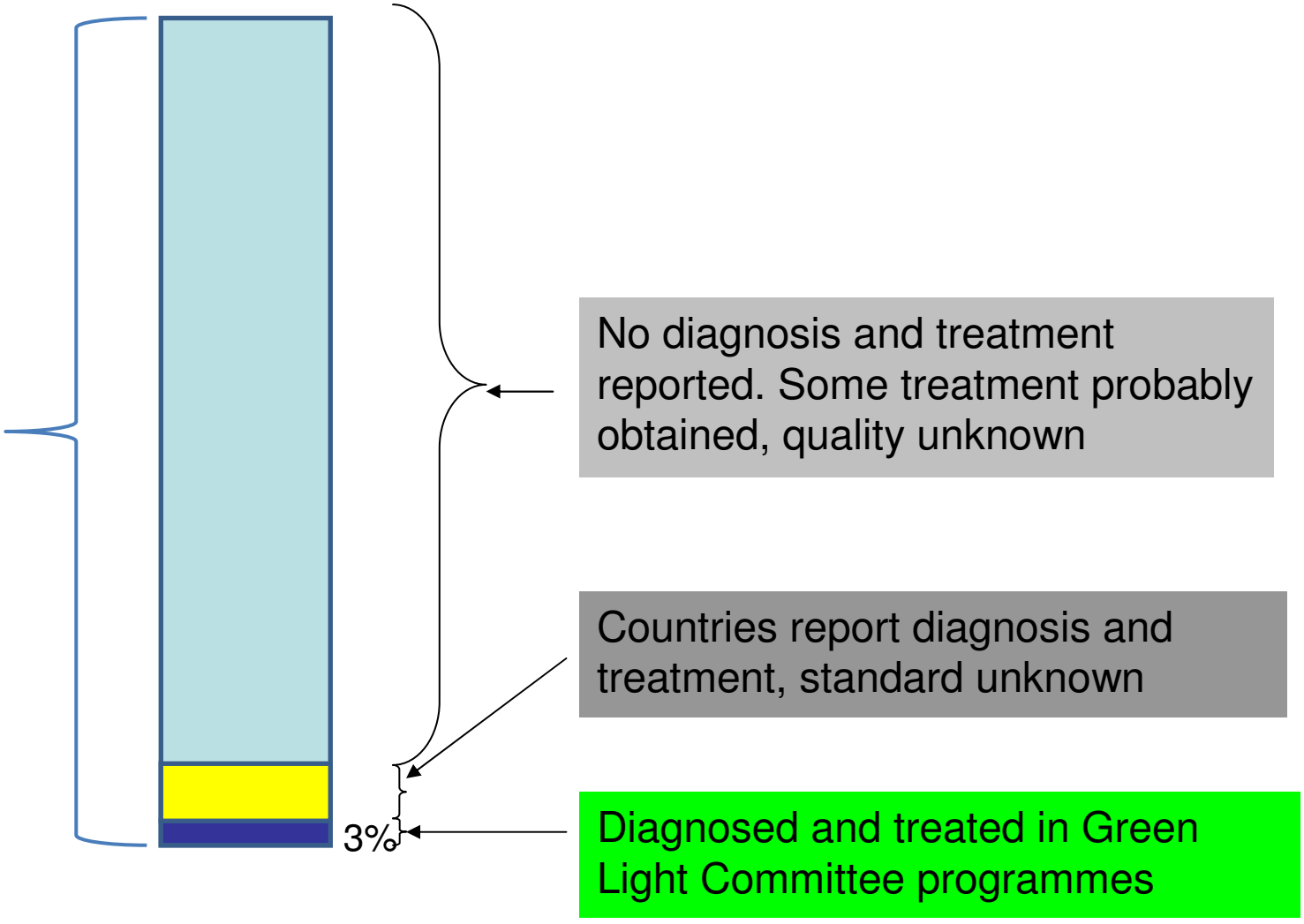
WHO THE STOP TB DEPARTMENT



	Estimated number of cases	Estimated number of deaths
All forms of TB **Greatest number of cases in Asia; greatest rates per capita in Africa**	**9.27 million** **(139 per 100,000)**	**1.77 million** **(27 per 100,000)**
Multidrug-resistant TB (MDR-TB)	**511,000**	**150,000**
Extensively drug-resistant TB (XDR-TB)	**50,000**	**30,000**
HIV-associated TB	**1.4 million**	**456,000**

Overall problem:

MDR-TB diagnostic and treatment levels far too low



Laboratory scale-up

Driven by

- Case detection moving towards universal access
- HIV- associated and drug resistant TB

Challenged by

- Weak health systems
- Inadequate human resources
- Insufficient programmatic and managerial capacity
- Inadequate infrastructure (biosafety)
- Problems of availability and access
- Slow technology transfer
- Lack of recognition of laboratory importance in TB control, weak communication between NTPs and laboratory services

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Acceleration

Recent developments:

- At least 20 new technologies in various stages of development and evaluation
- Distinct target areas for drug-resistant TB being addressed
- WHO policy formulation
  - Liquid culture, rapid speciation and line probe assays endorsed by WHO 2007-2008;*
  - LED microscopy and selected non-commercial culture and drug susceptibility testing methods expected in 2009
- Expanded access to new diagnostics and laboratory strengthening

*Available at: http://www.who.int/tb/dots/laboratory/policy/en

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Why a Roadmap?

Process

- May 08: GLI CG meeting
  - GLI strategic objectives defined
- May 08: 1st annual GLI meeting
  - Consultant findings on stakeholder interviews and country fact finding visits
  - Break-out group discussions to identify gaps and next steps
- Oct 08: Dedicated TBCAP funding
- Oct 08 - Jun 09:
  - Conceptual framework defined
  - Country case studies pursued and common themes identified
  - Stakeholder interviews continued
  - WHO policy recommendations incorporated
- Jun 09 – Aug 09
  - Intensive revision by Writing Committee, GLI CG and external laboratory experts

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Purpose and scope

- Structured framework for TB laboratory strengthening based on WHO-GLI norms and standards, documented best-practices at country level, growing lessons from the field ('learning by doing')
- Generic document encompassing managerial, operational and technical aspects of TB laboratory strengthening within the context of national laboratory strategic plans
- Broad user base including NTP and NRL managers, technical agencies, donor agencies, implementing partners, programme budgeting and planning officers
- Living document, responsive to changes in TB diagnostic landscape and WHO policy frameworks

- Supported by resource list for tools and technical procedures

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Core elements

- Laboratory infrastructure and maintenance
- Equipment validation and maintenance
- Specimen referral and transport mechanisms
- Policy framework for implementing new TB diagnostics
- Laboratory commodity and supply chain management
- Laboratory information and data management systems
- Laboratory quality management systems
- Laboratory human resource development

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Stepwise approach (1)

Policy change at country level, based on

- Local epidemiology (TB, HIV, MDR-TB)
- NTP priorities for case detection (risk groups)
- Laboratory networks and capacity
- Laboratory staff resources and skills base
- Treatment policies for drug-resistant TB
- Financial resources

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Stepwise approach (2)

Expansion of laboratory services based on

- Tiered system (peripheral, intermediate, central)
- Available technologies
- Ancillary laboratory needs related to specialised treatment (eg. ART, second-line anti-tuberculosis drugs)
  - General microbiology, biochemistry, haematology, etc.
- Integrated approach

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Stepwise approach (3)

- **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

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Analytical process

- Quantify or estimate TB, TB-HIV and MDR-TB burden
- Identify and target patient risk groups, eg.
  - Treatment failures
  - Non-converting patients
  - HIV+ individuals
- Quantify or estimate diagnostic need to identify cases
  - Number of suspects to be screened
  - Number and type of laboratories at each service level
- Estimate budget for comprehensive laboratory services
  - All core components
  - Capacity for diagnosis and monitoring
  - Ancillary laboratory tests

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Laboratory algorithm

Starts with

- Screening policy for suspects
- Microscopy services as entry point

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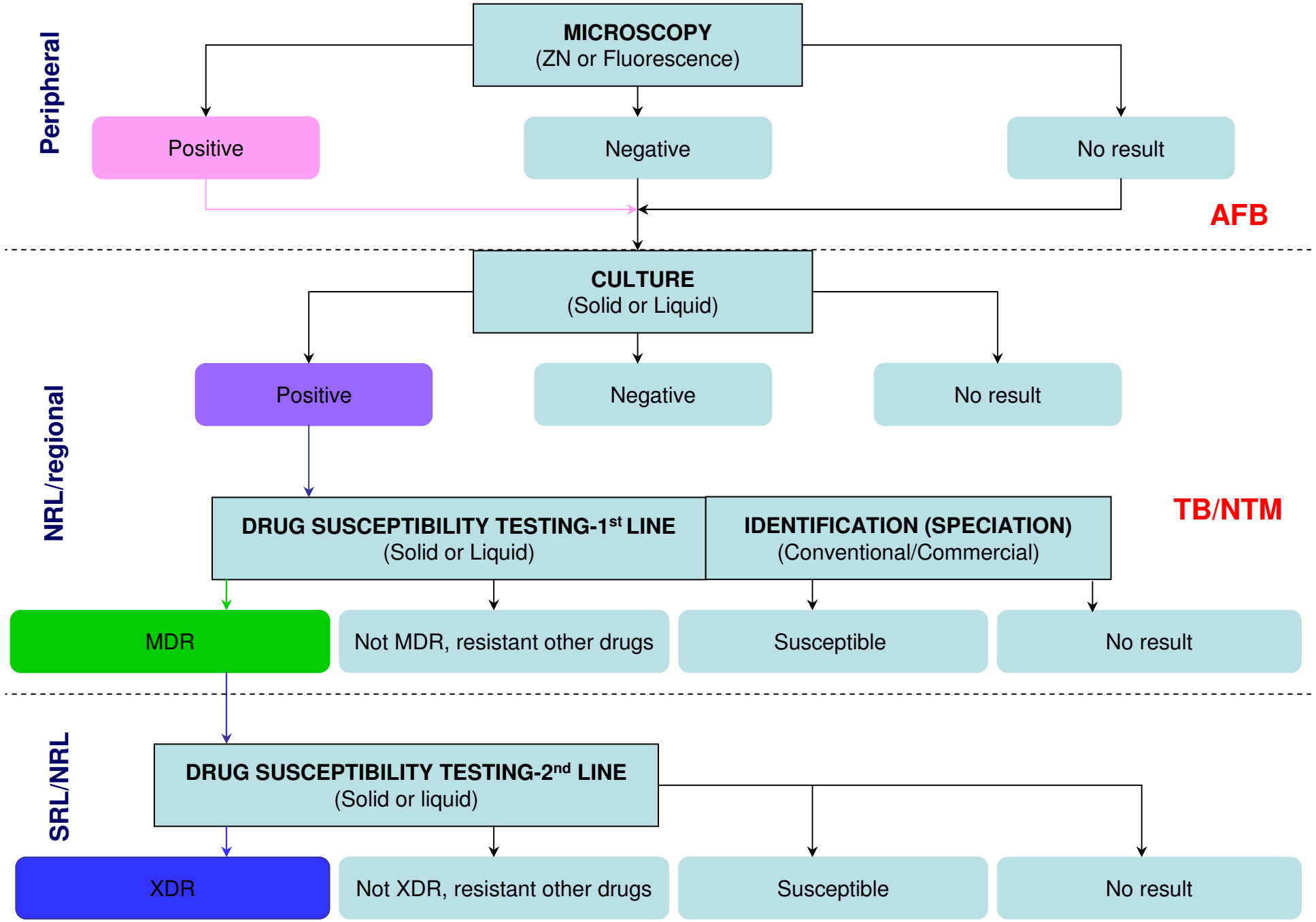
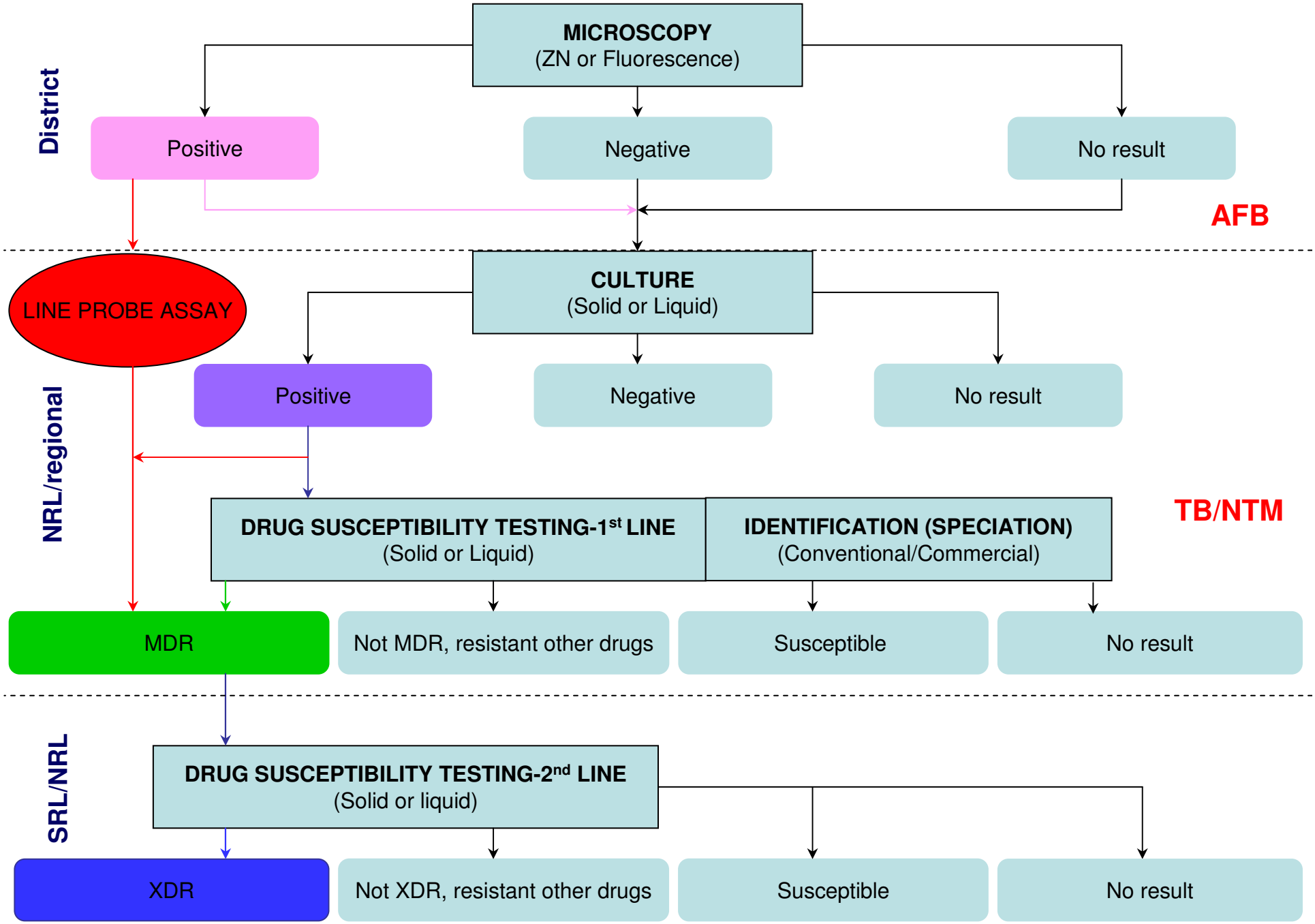

Peripheral
MICROSCOPY
(ZN or Fluorescence)
Positive
Negative
No result
AFB
CULTURE
(Solid or Liquid)
NRL/regional
Positive
Negative
No result
TB/NTM
DRUG SUSCEPTIBILITY TESTING-1st LINE
(Solid or Liquid)
IDENTIFICATION (SPECIATION)
(Conventional/Commercial)
MDR
Not MDR, resistant other drugs
Susceptible
No result
SRL/NRL
DRUG SUSCEPTIBILITY TESTING-2nd LINE
(Solid or liquid)
XDR
Not XDR, resistant other drugs
Susceptible
No result


District
MICROSCOPY
(ZN or Fluorescence)
Positive
Negative
No result
AFB
LINE PROBE ASSAY
CULTURE
(Solid or Liquid)
NRL/regional
Positive
Negative
No result
TB/NTM
DRUG SUSCEPTIBILITY TESTING-1st LINE
(Solid or Liquid)
IDENTIFICATION (SPECIATION)
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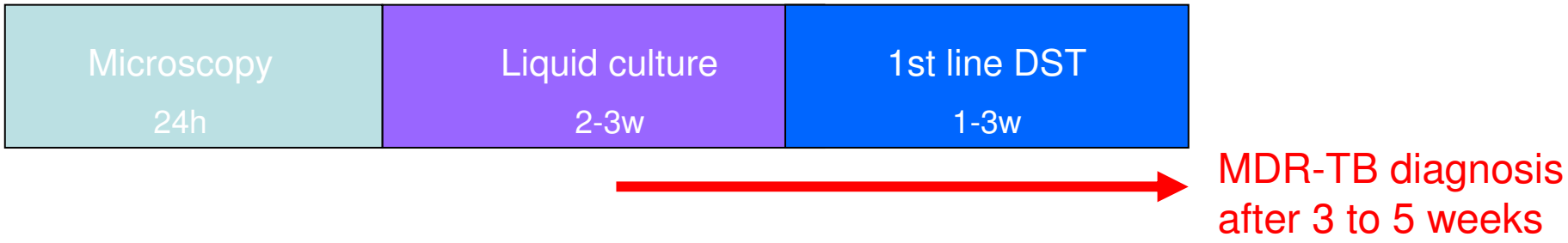
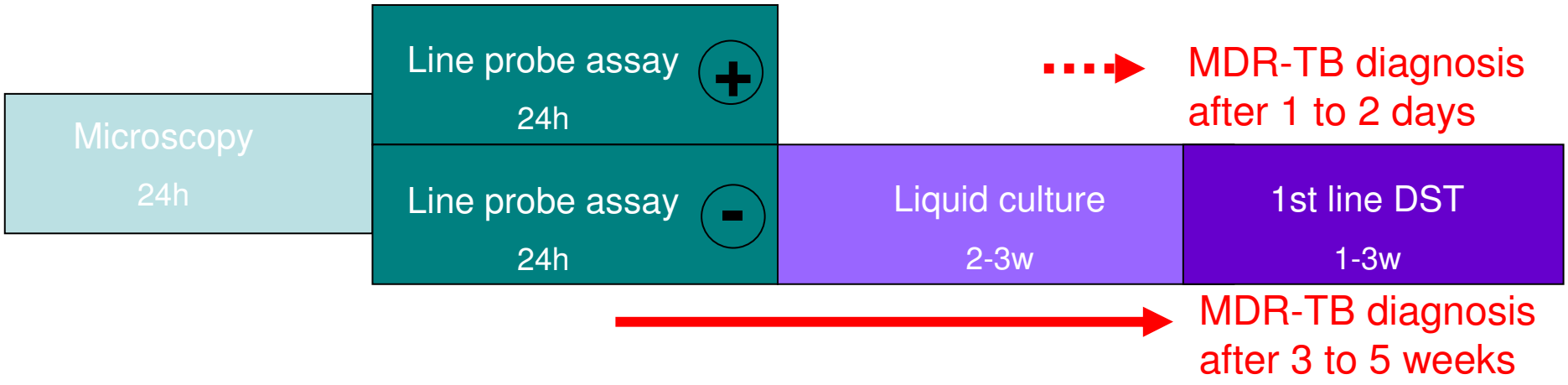
MDR
Not MDR, resistant other drugs
Susceptible
No result
SRL/NRL
DRUG SUSCEPTIBILITY TESTING-2nd LINE
(Solid or liquid)
XDR
Not XDR, resistant other drugs
Susceptible
No result

MDR-TB diagnosis using conventional solid culture and DST

MDR-TB diagnosis using liquid culture and DST



MDR-TB diagnosis using line probe assay, liquid culture and DST

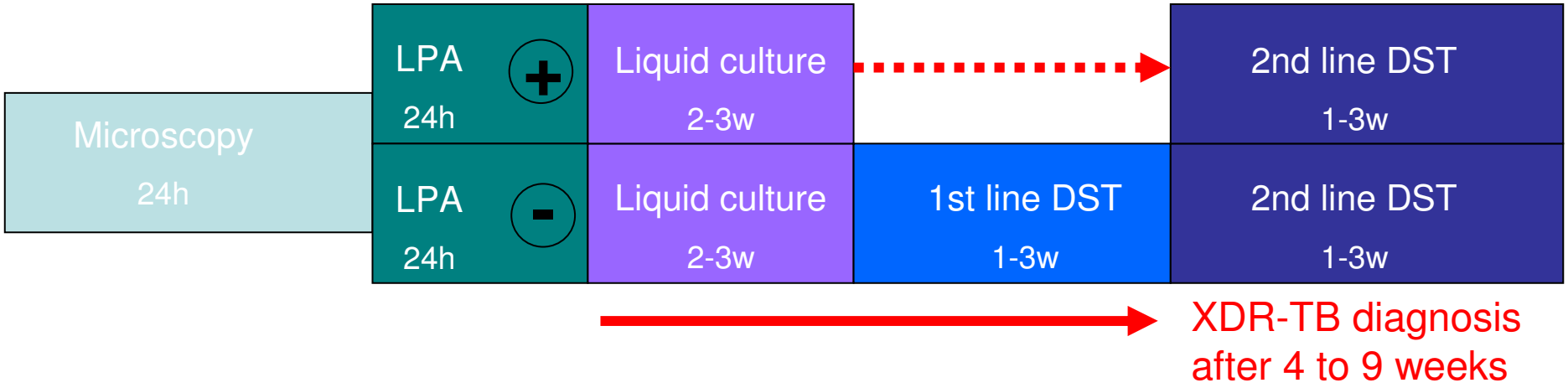


XDR-TB diagnosis using conventional solid culture and DST

* Methods not validated or standardised

XDR-TB diagnosis using liquid culture and DST

XDR-TB diagnosis using line probe assay, liquid culture and DST



Policy considerations

- Current technologies not mutually exclusive
  - Conventional culture capacity required for SM- specimens
  - Conventional DST capacity required to detect XDR-TB
- Liquid culture and line probe assay as gold standards, to be phased in without loss of existing culture and DST capacity
- LED microscopy as alternative for both fluorescence and conventional light microscopy (pending STAG endorsement)
- Selected non-commercial culture and DST methods not alternatives for gold standards, but may provide interim solution (pending STAG endorsement)

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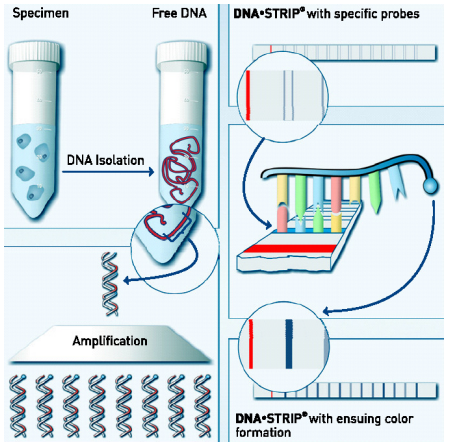
Strengthening TB laboratories

‘From unimaginable…to indispensable’



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Acknowledgements

- Consultants: Peer Ederer, Stephan Willms, Georgine Ganzer
- Country Ministries of Health, NTPs and NRLs: Ethiopia, Lesotho, Cote d'Ivoire
- Writing Committee: Chris Gilpin (lead), Jean Iragena, Gavin MacGregor-Skinner CN Paramasivan, John Ridderhof, Tom Shinnick, Armand van Deun, Karin Weyer
- GLI Core Group: John Ridderhof (chair), Lucia Barrera, Francis Drobniewski, Chris Gilpin, Vijay Gupta, Moses Joloba, Gavin MacGregor-Skinner, Kai Man Kam, Rick O'Brien, Tom Shinnick, Armand van Deun, Karin Weyer
- With additional input from: Catherine Mundy, Giorgio Roscigno, Akos Somoskovi, Veronique Vincent
- GLI partners interviewed: APHL, ASM, CDC, FIND, GTZ, KNCV, PATH, PEPFAR, PIH, TBCAP, Union, WHO

- And with apologies for any unintended oversight…

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