global laboratory initiative
advancing TB diagnostics

momentum

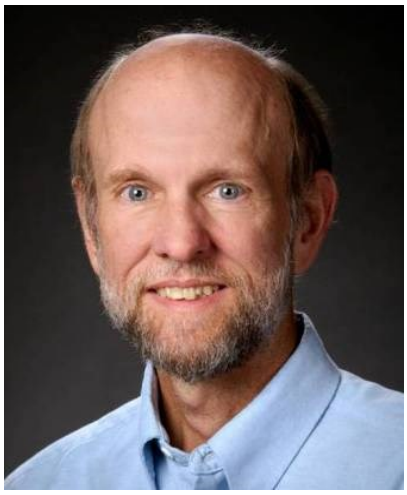
Newsletter of the Global Laboratory Initiative

Issue 1 - October 2013

In this issue

Stop TB Partnership

The GLI is a Working Group of the Stop TB Partnership with a Secretariat provided by WHO Global TB Programme



Dr. Thomas Shinnick
Centers for Disease Control and Prevention, Atlanta, USA
Chair of the Global Laboratory Initiative

GLI priorities 2013-2014

- Assist countries to develop national TB laboratory strategic plans
- Expand the SRLN to provide technical assistance and EQA
- Conduct a comprehensive review of existing GLI tools and guidance
- Develop the following new tools:
  - guidance for the accreditation of National TB Laboratories and TB Laboratory Networks
  - consensus guidance on EQA and validation of Xpert MTB/RIF
  - training materials for Xpert MTB/RIF and other molecular tests
  - laboratory consultant manual and consultant training strategy

FROM THE CHAIR

Accelerating access to quality TB diagnostic services

Established in 2008, the Global Laboratory Initiative (GLI) has since been playing a central role in setting strategic direction for strengthening laboratory capacity for TB diagnosis. Its multi-faceted and integrated approach has been paramount for successfully guiding the huge effort required for responding to the critical lack of quality assured laboratory services.

Serving as a coordination platform in global laboratory strengthening for a network of over 100 international partners

We are proud to represent a unique network of stakeholders dedicated to global- and country-level efforts to accelerate access to quality TB diagnostic services. Guided by the goals of the *Global Plan to Stop TB,* the GLI serves as a coordination and communication platform in the areas of global TB laboratory policy guidance, capacity development, quality assessment, and coordination of technical assistance. Overarching goals defined by the GLI Core Group for 2013-2014 include increasing access to quality-assured AFB microscopy and external quality assessment (EQA), as well as to rapid laboratory diagnosis of drug-resistant TB.

The GLI provides essential tools and guidance to assist TB endemic countries in the implementation of quality-assured laboratory diagnosis

Assisting countries to develop national TB laboratory strategic plans and strengthening the TB Supranational Reference Laboratory Network (SRLN) are at the top of the GLI agenda. Other priority activities are listed in the box alongside. If time and resources permit, the GLI considers additional activities to be pursued, such as defining strategies to guide human resource development for laboratory management and the implementation of new drug susceptibility tests.

We welcome the participation of any new and current GLI member in any of our priority activities.

> *“The GLI is achieving what was once considered an impossible dream.”*

Dr. Mario Raviglione
Director
WHO Global TB Programme

> *“The work and concrete results delivered by the GLI are a successful example of the collaboration of multiple partners.”*

Dr. Lucica Ditiu
Executive Secretary
Stop TB Partnership

TB Laboratory Accreditation remains a priority activity of the GLI

The unique GLI tools help countries implement high quality standards for laboratory services.

GLI Stepwise Process towards TB Laboratory Accreditation

Link to website

COVER STORY

5th Global Laboratory Initiative Partners' Meeting

Sharing experiences and advancing expanded laboratory capacity for TB diagnosis

Approximately 150 participants from 40 countries, including representatives from 17 of the 22 high TB-burden countries, attended the 5th Annual GLI Partners' Meeting on 15-18 April 2013. The meeting has become a key event on the calendar of the multiple partners dedicated to advancing quality TB laboratory services. The venue at the Fondation Mérieux conference centre Les Pensières in Veyrier-du-Lac, France, provided the ideal setting for productive plenary sessions and informal networking. The overall goal of the GLI Partners meeting was to bring together the stakeholders working in partnership to address the challenges of increasing access to diagnostics within quality laboratory services for better TB control. All the information from the meeting can be downloaded from the GLI website at http://www.stoptb.org/wg/gli/meetings.asp.

Meeting highlights

GLI progress in reaching the targets of the Global Plan to Stop TB

Dr. Thomas Shinnick, from the US CDC and Chair of the GLI, reviewed important progress made by the GLI in the implementation of new tools and initiatives to address TB laboratory strengthening priorities. He highlighted how the GLI is making progress in addressing the critical lack of quality laboratory services for TB diagnosis, which has been a major barrier in reaching global targets.

Significant progress in the EXPAND-TB project: 81 laboratories established in 25 countries and nearly 54,000 MDR-TB cases detected since 2011

The EXPAND-TB project is an example of successful collaboration of multiple partners, including FIND, WHO, GLI and the Stop TB Partnership Global Drug Facility, that is funded by UNITAID and other donors. Aiming to enhance TB laboratory capacity for the diagnosis of MDR-TB in 27 countries, this project has made significant progress towards achieving the target of detecting 115,000 MDR-TB by the end of 2014.

Xpert MTB/RIF: The fastest growing innovation in TB control is already showing impact

Implementing countries and technical partners highlighted the impact in piloting or wide-scale roll-out of Xpert MTB/RIF and reported a significant increase in detection of bacteriologically positive TB cases and rifampicin-resistant cases, as well as a significant reduction in time to diagnosis. Implementers agreed on the need for strong monitoring and evaluation to demonstrate impact and discussed possible measures.

SRL Network Consultation: a coordination platform providing key technical assistance to 36 TB and MDR-TB high-burden countries

Members of the WHO/GLI TB Supranational Reference Laboratory Network (SRLN) are providing an immense amount of technical assistance and guidance. Participants discussed new priorities for improving the functioning of the network and for sustaining and expanding support from the SRLN.
For more information, please visit http://www.stoptb.org/wg/gli/srln.asp.

The nomination of the NTRL Uganda as WHO/GLI TB Supranational Reference Laboratory. From left to right, Drs. C. Gilpin and K. Weyer, WHO GTB, M. Joloba, NTRL Uganda, and D.K.W. Lwamafa, MoH Uganda.

STORIES FROM THE FIELD

The World Health Organization welcomes a new member to the TB Supranational Reference Laboratory Network

"The SRL Network remains a key technical resource, ensuring the introduction of new WHO-endorsed tools into laboratories with appropriate infrastructure and biosafety measures."

Dr. Christopher Gilpin
GLI Secretariat
WHO Global TB Programme

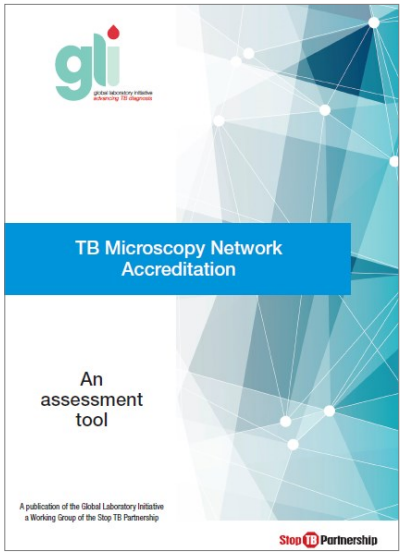
Since 1994, The WHO/GLI TB Supranational Reference Laboratory (SRL) Network has been working with National TB Reference Laboratories (NRLs) and National TB Programmes (NTPs) to build laboratory capacity for improved diagnosis of TB. Over the years, the network has slowly grown and currently comprises 33 specialist member and candidate SRLs that provide technical assistance to the 36 TB and MDR-TB high-burden countries. The newest member to the network – the National TB Reference Laboratory in Kampala, Uganda is now formally designated as a full member of the SRL network.

The GLI Secretariat at WHO Global TB Programme welcomes Dr. Moses Joloba and his team from Uganda to the SRL Network and congratulates them for their unwavering dedication to meet the eligibility and inclusion requirements for joining the network. The laboratory becomes only the second SRL in the African region and has already commenced supporting other African TB laboratories outside Uganda. This has transformed the way for TB laboratories to improve their capacity to rapidly and reliably diagnose persons presumed to have TB and drug-resistant forms. WHO endorsement of new diagnostic tools is, however, only the first step in a complex process for rolling out new tools in high TB burden settings. Many elements need to be considered when implementing new technologies. These include laboratory infrastructure, biosafety measures, human resource development, supply chain management, specimen referral processes and quality management systems (QMS).

Helping reach international laboratory standards in resource-constrained settings

Several TB diagnostic technologies have now been evaluated and endorsed by WHO. It is therefore not surprising that many TB laboratories, and in particular those in the African Region, require a lot of support and technical assistance to introduce new technologies at different levels of the laboratory network. TB Supranational Reference Laboratories play a key role in providing this support. Under GLI coordination, with support from the USAID TB CARE I project, and the SRL-Antwerp, the newly designated SRL-Uganda has adopted the GLI stepwise process towards accreditation scheme for implementing a QMS. The SRL Uganda was subsequently accredited in September this year for meeting the requirements of the international *ISO*15189 standard. Congratulations on this great achievement!

TB diagnosis mainly relies on AFB-smear microscopy in most high TB-burden countries. (Photo Lorna Chiu).



The new manual will be available soon on the GLI website at:
http://www.stoptb.org/wg/gli/documents.asp

GLI RESOURCES

New: An essential tool for AFB-microscopy network accreditation

With more than 37,000 microscopy laboratories in the 22 high TB-burden countries, the vast majority of TB cases are still diagnosed and monitored by AFB-smears. Thus, high-quality smear microscopy remains an essential diagnostic tool. A major barrier, however, is assuring quality in weak laboratory systems where there are few laboratory standards. Functional laboratory networks require countries to have documented policies, guidelines and procedures that should be uniform and in line with global recommendations. The new AFB-microscopy network accreditation manual provides guidance in these areas to ensure that the myriad of TB microscopy laboratories deliver quality results.

The GLI has just endorsed a new tool developed under the USAID sponsored TB CARE I project. Recognizing the importance of quality AFB-smear microscopy as a fundamental method for TB control across all settings, the concept was first proposed by former GLI Chair, Dr. John Ridderhof, from CDC Atlanta. Subsequently, The Union brought together laboratory experts from CDC, KNCV, MSH and WHO, as well as Dr. Sabira Tahseen, head of the Pakistan NTP, and Dr. Marijke Becx-Bleumink, independent consultant. This group developed the microscopy network accreditation tool to assist countries to adopt and implement sound TB microscopy policies.

A systematic approach to strengthening microscopy network management

As no relevant standards were available for the evaluation of TB microscopy networks,11 standards were developed as part of the assessment tool. These standards cover all microscopy aspects of networks, including the link to a referral system for more advanced tests. The assessment tool provides practical guidance to countries on how to meet the requirements for the 11 standards. A country network will be accredited only if all essential requirements are met. Four areas are distinguished: 1) policies, guidelines and support for the network; 2) implementation of policies and technical execution of tests by quality services; 3) external quality assurance procedures; and 4) guidelines on linkage to a referral system for more advanced tests. These areas represent four phases in the accreditation process, that do not need to be successive.

> *"Quality AFB-smear microscopy remains a fundamental method for TB diagnosis in high TB-burden countries."*
>
> Dr. John Ridderhof
> Centers for Disease Control and Prevention
> Former GLI Chair

Optimizing microscopy networks will contribute to strengthening country laboratory networks globally

The tool is intended to be used by National TB Programmes as a self-assessment tool, but can also be used by independent external assessors to evaluate the functioning of the TB microscopy network. For this purpose, it includes a comprehensive list of links to global policies, guidance and recommended practice. This should go a long way towards a critical appraisal and gradual improvement of microscopy networks, which remain essential for TB control. A pilot of this tool in Pakistan demonstrated that in recent years microscopy has received too little attention due to the rapid succession of new and more demanding tests that needed to be introduced. Even if accreditation may not be within immediate reach of most NTPs, an assessment of their network will highlight deficiencies and the often relatively small investments and corrections needed. At the moment, countries are not always aware of these deficiencies and the new tool will show them where and how to look, providing sound advice for optimization.

Armand van Deun

With funding from USAID East African Regional Office, and a 6-year support through TB CAP and TB CARE I in partnership with CDC, the National Reference Laboratory in Kampala, Uganda, officially opened as the second Supra-national Laboratory in Sub-Saharan Africa on 10 July. (Photo Tristan Bayly).

NEWS FROM OUR PARTNERS

USAID FROM THE AMERICAN PEOPLE

TB CARE I

Providing global leadership and support to National TB control efforts

The USAID Bureau for Global Health has launched two mechanisms, TB CARE I and TB CARE II, for implementing its TB strategy. TB CARE I (2010-2015) was awarded to the Tuberculosis Coalition for Technical Assistance (TBCTA). With KNCV Tuberculosis Foundation (KNCV) as prime partner and housing the Program Management Unit (PMU), the Coalition consists of other six organizations working in TB control: the American Thoracic Society, FHI 360, the International Union Against Tuberculosis and Lung Disease, Japan Anti-Tuberculosis Association, Management Sciences for Health, and WHO. TB CARE I collaborates with other national and international initiatives in providing global leadership and support to National TB control efforts.

TB CARE I invests heavily in building laboratory capacity

In the last three years, TB CARE I allocated over US$ 15,7 million to strengthening laboratory services. Laboratory experts from the coalition, sometimes in collaboration with GLI colleagues from partner institutes, developed a variety of tools, such as guidelines, training materials and workshops to support intensified implementation of Xpert MTB/RIF; a handbook to develop national laboratory strategic plans; laboratory accreditation and assessment tools; a manual for TB laboratory consultants; and support to the development of the SRLs in Uganda and Benin.

Around 92% of TB CARE I available budget is directly spent at country level to assist NTPs in their efforts to move toward universal access. In the 22 TB CARE I supported countries, investments on laboratory strengthening exceeded US$ 12,7 million. Investments were targeted at technical interventions to enhance laboratory diagnostic services, including laboratory renovations, procurement of LED fluorescence microscopes, as well as technical support to EQA systems. Based on a decentralized approach for capacity building, TB CARE I promotes direct implementation of technical support through country offices. To this end, 24 full-time laboratory officers were recruited in 10 countries. They are in turn backed-up by laboratory experts from individual organizations and by one Laboratory Officer based at the PMU with KNCV.

Supporting Xpert MTB/RIF implementation and measuring impact: data shows reduced time to treatment initiation and increased detection of TB and MDR-TB cases

A special TB CARE I project aims to provide intensified support with the implementation of Xpert MTB/RIF in Nigeria, Indonesia and Kazakhstan. The objective of this project was to develop a systematic approach to Xpert implementation for all TB CARE I countries based on lessons learned, while measuring impact on case notification and treatment initiation. The experience in Indonesia provided impressive results and showed that the time to start MDR-TB patients on second-line treatment reduced on average by 66 days, from 81 to 15. Globally, Xpert MTB/RIF was introduced in 18 TB CARE I supported countries, with 81 TB CARE I funded machines in use and over 50,000 cartridges purchased. As of March 2013, data obtained from Cambodia, Indonesia, Kazakhstan, Kenya, Nigeria and Vietnam showed that out of the 4,776 successful tests performed on presumptive new cases, 985 (21%) were TB positive and 99 (10%) of these had a RIF-resistant result. Similarly, out of the 13,043 cases tested for presumptive MDR-TB, 6,912 (53%) were diagnosed as having TB, of which 2,208 (32%) had a RIF-resistant result.

TB CARE I fully supports GLI's mission and priorities and uses the GLI platform for coordination, communication and brainstorming about innovative ideas to improve laboratory capacity.

Maarten van Cleeff

> *"I take the opportunity of this first newsletter, to wish the GLI success in its pivotal role in supporting timely diagnosis of TB."*
>
> Dr. Maarten van Cleeff
> Director TB CARE I

Over 1 million TB cases diagnosed

With the initiatives and investments described above, in 2011, TB CARE I contributed to the diagnosis of over 1 million TB cases and 515,647 new confirmed cases across all TB CARE I countries. On average, this represents a 4.3% increase in new confirmed cases as compared to 2010.

More significantly, the number of MDR cases put on treatment increased in two years by 42% from 8,262 patients in 2010 to 11,757 in 2012.

TB CARE I contributes to three USAID targets:

1. Sustain or exceed 84% case detection rate and 87% treatment success rate
2. Treat successfully 2.5 million new sputum-positive TB cases
3. Diagnose and treat 57,200 new cases of MDR-TB

It focuses on eight priority technical areas:

(i) Universal and Early Access, (ii) Laboratories; (iii) Infection Control; (iv) Programmatic Management of Drug Resistant TB; (v) TB/HIV; (vi) Health Systems Strengthening; (vii) Monitoring & Evaluation, Operations Research and Surveillance; (viii) Drug Supply and Management.

TB CARE I is results oriented

Activities are selected in such a way that they contribute to results, which are monitored annually in each of the countries enjoying TB CARE I support. The expected results for Laboratories are:

- Ensured capacity, availability and quality of laboratory testing to support the diagnosis and monitoring of TB patients
- Ensured availability and quality of technical assistance and services
- Ensured optimal use of new approaches for laboratory confirmation of TB and incorporation of these approaches in national strategic laboratory plans

Photo WHO

Key data and tools

Global procurement statistics
as of 30 June 2013 (cumulative)

Instruments:	1,402
Modules:	7,553
Cartridges:	3,196,920
Countries:	88

Resources

The WHO website provides extensive information and resources on the roll-out of Xpert MTB/RIF.

Link to website

Implementation documents

Rapid Implementation (link to PDF)

Checklist (link to PDF)

XPERT MTB/RIF UPDATE

Monitoring global roll-out of Xpert MTB/RIF and promoting coordination

Unprecedented growing demand creates new challenges: partners launch a unified forecasting initiative

As of 30 June 2013, a total of 1,402 GeneXpert instruments (comprising 7,553 modules) and 3,196,920 Xpert MTB/RIF cartridges had been procured in the public sector in 88 of the 145 countries eligible for concessional pricing. The number of cartridges procured in Q2 2013 was more than twice as many as procured in Q1 2013. By the end of Q2, Cepheid was able to overcome the challenges they had faced earlier in the year in keeping up with demand, which had resulted in a global shortage of cartridges. A unified forecasting initiative of major procurers and partners on planned orders, launched by the WHO Global TB Programme and Stop TB Partnership, is expected to reduce the risk of future disturbances to the global supply chain.

Outcomes and presentations from the Global Forum of Xpert MTB/RIF Implementers are available online

On 16-17 April 2013, implementers of Xpert MTB/RIF gathered with technical partners and donors in Annecy, France, to discuss experiences, challenges and evidence of impact in rolling-out Xpert MTB/RIF, as part of the 5th Global Laboratory Initiative (GLI) Partners meeting. Findings of the Global Forum can be found in the May 2013 edition of the WHO Update on implementation and roll-out of Xpert MTB/RIF, and presentations can be accessed via the meeting agenda on the GLI website.

2nd African Regional Training Workshop on Xpert MTB/RIF held in July in Botswana to support further development of national scale-up plans

The 2nd African Regional Training Workshop on Xpert MTB/RIF was held in Gaborone, Botswana, on 23-25 July 2013. The meeting, organized by TB CARE I and African Society for Laboratory Medicine with support from USAID and PEPFAR, brought together 90 participants from 11 countries and partners. The workshop aimed to provide support to countries with practical aspects of implementing Xpert MTB/RIF and to further develop national scale-up plans with special focus on diagnosis of TB in people living with HIV; to increase awareness of the latest global policy guidance on Xpert MTB/RIF and its implications for country implementation; and to share experiences with Xpert MTB/RIF implementation, discuss emerging best practices, and identify barriers and solutions to implementation challenges. A meeting report describing outcomes is under development.

Published evidence is regularly updated

A list of published references about Xpert MTB/RIF continues to be regularly updated by WHO. Articles are categorized by topic: paediatric TB, extrapulmonary TB, cost-effectiveness, etc. This resource is available at: http://www.stoptb.org/wg/gli/assets/documents/map/XpertPublications.pdf

WHO policy update on the use of Xpert MTB/RIF

A WHO policy update on the use of Xpert MTB/RIF for the diagnosis of pulmonary and extrapulmonary TB in adults and children will be available before the end of 2013 from WHO website.

momentum more information

Upcoming Events

44th World Conference on Lung Health

October 30 - November 3, 2013,Paris, France

For information about the program and registration, visit the conference website at www.paris2013.worldlunghealth.org

Important laboratory-interest Union meetings

- **Working Group on Laboratory Accreditation**
  Friday, November 1, 10:15-11:15
- **Bacteriology and Immunology Sub-section**
  Saturday, November 2, 10:15-11:15

Some symposia on TB diagnostics and laboratory related topics:

Friday, November 1

- Critical issues and challenges for maximizing impact of Xpert MTB/RIF
- Improved TB diagnostics adding new dynamics to TB control

Saturday, November 2

- Rolling-out LED fluorescence microscopy: yield and challenges
- Can new diagnostic tools reduce time to treatment initiation?

Sunday, November 3

- Childhood TB diagnostics: we have made progress, but are we there yet?
- Innovative approaches to bringing new TB diagnostics to the private sector

MDR-TB Stakeholder Meeting: Old problems, new solutions

October 27-28, 2013, Paris, France
For more information, please email bhatiav@who.int

New Diagnostics Working Group Annual Meeting

Moving to point-of-care diagnosis - Symposium and panel discussion
Thursday, October 31, 2013, 9:00 - 12:30
Palais des Congrès, Paris, France, Room Havane

FIND and TB Alliance Symposium

Alignment of drug susceptibility testing and new TB drug regimens
Thursday, October 31, 2013, 13:30-17:15
Palais des Congrès, Paris, France, Room Havane

TAG Symposium - Cascades: Improving TB Care

Friday, November 1, 2013, 18h00 - 22h00
Hôtel Concorde La Fayette Batignolles/ Longchamp, Paris, Room 3
For more information: Lindsay.Mckenna@treatmentactiongroup.org

Selected Publications

Andrews JR, Lawn SD, Dowdy DW, Walensky RP. Challenges in evaluating the cost-effectiveness of new diagnostics for HIV-associated tuberculosis. Clin Infect Dis. 2013 Jul 17. [Epub ahead of print]. Abstract: http://www.ncbi.nlm.nih.gov/pubmed/23788239.

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Weyer K, Mirzayev F, Migliori GB, Van Gemert W, D'Ambrosio L, Zignol M, Floyd K, Centis R, Cirillo DM, Tortoli E, Gilpin C, de Dieu Iragena J, Falzon D, Raviglione M. Rapid molecular TB diagnosis: evidence, policy making and global implementation of Xpert MTB/RIF.. Eur Respir J.. 2013;42:252-71. Abstract: http://www.ncbi.nlm.nih.gov/pubmed/23180585

Denkinger CM, Nicolau I, Ramsay A, Chedore P, Pai M. Are peripheral microscopy centres ready for next generation molecular tuberculosis diagnostics? Eur Respir J. 2013;42:544-547. Abstract: NA.

Rigouts L, Gumusboga M, de Rijk WB, Nduwamahoro E, Uwizeye C, de Jong B, Van Deun A. Rifampicin resistance missed in automated liquid culture system for Mycobacterium tuberculosis with specific rpoB-mutations. J Clin Microbiol. 2013;51:2641-5. Abstract: http://www.ncbi.nlm.nih.gov/pubmed/23761146

Van Deun A, Maug AK, Bola V, Lebeke R, Hossain MA, de Rijk WB, Rigouts L, Gumusboga A, Torrea G, de Jong BC. Rifampicin drug resistance tests for tuberculosis: challenging the gold standard. J Clin Microbiol. 2013;51:2633-40. Abstract: http://www.ncbi.nlm.nih.gov/pubmed/23761144

Lu C, Liu Q, Sarma A, Fitzpatrick C, Falzon D, Mitnick CD. A systematic review of reported cost for smear and culture tests during multidrug-resistant tuberculosis treatment. PLoS One. 2013;8(2):e56074. Full text: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3574085

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