

Issue 3 - October 2014

In this issue

From the Vice-Chair
Promoting laboratory
integration

Cover story
Bridging the diagnostic
and treatment gap for
MDR-TB

Stories from the field
SRL Network

GLI Resources
Xpert MTB/RIF
Training Package

Target product profiles

Xpert MTB/RIF Update

News from GLI Partners
International
Organization for
Migration (IOM)

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





Dr. Rumina Hasan

Aga Khan University Hospital, Karachi, Pakistan
Vice-Chair of the Global Laboratory Initiative

**Proposed
GLI priorities 2014-2015**

- Assist countries in the development of the TB laboratory component of National Strategic Plans
- Develop an implementation plan for already developed GLI tools available on the GLI website
- Promote the integrated use of the GLI stepwise process towards accreditation with other tools and checklists for implementation of Quality Management Systems
- Develop guidance on engineering requirement for different risk level TB laboratories
- Develop a strategy to improve human resources for laboratory management
- Finalize the development of new GLI tools

FROM THE VICE-CHAIR

Promoting laboratory integration

There has been encouraging progress globally in the joint response to tuberculosis (TB) and HIV over the last decade. However, TB is still the leading cause of mortality among people living with HIV and efforts need to be urgently stepped up if HIV-related TB deaths are to be eliminated. Integration of TB and HIV activities is documented to improve patient outcomes and also to provide enhanced and cost-effective health care^{1,2}. To support such integration, the Global Laboratory Initiative (GLI) places great priority on advancing uptake and use of integrated laboratory tools. Towards this goal, the GLI has promoted integration of TB diagnostics, in particular Xpert MTB/RIF, into HIV services.

Some of the progress by GLI partners in this area include:

- A session on the use of Xpert MTB/RIF for people living with HIV at the GLI Partners' Meeting and Global Forum on Xpert MTB/RIF, held on 30th April -2nd May 2014³.
- A 12-module training package on the use of Xpert MTB/RIF, which includes guidance for the use of the assay among persons living with HIV, as well as a module on quality assurance and performance indicators⁴.
- The Xpert MTB/RIF implementation manual "Technical and operational 'how-to': Practical considerations"⁵.
- Participation of GLI partners in the development of target product profiles for rapid diagnostics which could be used at the point-of-care to improve the diagnosis of TB among persons living with HIV⁶.
- Active liaison with the WHO HIV Department by the GLI Core Group. The liaison person regularly participates in the GLI teleconferences to help identify collaborative activities for TB/HIV, including integrated laboratory services.

The World Health Organization (WHO) annually collects data for the Global Tuberculosis Report on the number of countries that have incorporated WHO policy for the use of Xpert MTB/RIF among persons living with HIV into national policies. More efforts are needed to ensure that Xpert MTB/RIF testing is fully integrated into HIV settings and the assay is being used according to WHO recommendations (i.e. as the initial diagnostic test among adults and children with HIV suspected of having TB), and that TB patients identified are effectively referred for treatment. Improvements in recording and reporting systems are also needed to ensure that the results from laboratory tests allow patients to be promptly initiated on appropriate therapy. WHO has published a Definitions and Reporting Framework for Tuberculosis in 2013⁷ that can be used by countries to revise and update their laboratory request forms and registers, which can facilitate improved monitoring and evaluation of the utility of Xpert MTB/RIF among persons living with HIV.

In this issue, the International Organization for Migration (IOM) serves as a good example of a GLI partner that has established several integrated laboratories for the diagnosis of multiple diseases, including TB and HIV (see page 7).

References

1. Rifat Atun, Diana E C Weil, Mao Tan Eang, David Mwakyusa. Health system strengthening and tuberculosis control. *Lancet* 2010; 375: 2169–78
2. Parsons LM, Somoskovi A, Lee E, et al. Global health: Integrating national laboratory health systems and services in resource-limited settings. *Afr J Lab Med*. 2012;1(1), Art. #11, 5 pages. <http://dx.doi.org/10.4102/ajlm.v1i1.11>
3. Meeting Report 2014: Xpert MTB/RIF Implementers Global Forum <http://www.stoptb.org/wa/gli/assets/documents/Xpert%20Implementers%20Global%20Forum%20meeting%20report.pdf>
4. Global Laboratory Initiative 2014. Training package on Xpert MTB/RIF http://www.stoptb.org/wa/gli/TrainingPackage_XPERT_MTB_RIF.asp
5. Xpert MTB/RIF implementation manual: technical and operational 'how-to': practical considerations. Geneva, World Health Organization, 2014 (available from http://apps.who.int/iris/bitstream/10665/112469/1/9789241506700_eng.pdf)
6. High priority target product profiles for new tuberculosis diagnostics: report of a consensus meeting. 2013 (WHO/HTM/TB/2014.18) (available from http://apps.who.int/iris/bitstream/10665/135617/1/WHO_HTM_TB_2014.18_eng.pdf?ua=1)
7. Definitions and reporting framework for tuberculosis – 2013 revision. Geneva, World Health Organization, 2013 (WHO/HTM/TB/2013.2) (available from http://apps.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf).



Outcomes for MDR-TB patients remain poor: globally, only 48% of the MDR-TB patients in the 2011 cohort were successfully treated.

Photo: Vanessa Vick

COVER STORY

Bridging the growing gap between diagnosis and treatment in MDR-TB

An unprecedented scale-up in test development and laboratory strengthening has been seen since 2009, when the World Health Assembly called for universal access to tuberculosis (TB) drug susceptibility testing (DST) and treatment of all patients with drug-resistant disease. Six DST technologies were subsequently approved by the World Health Organization (WHO) and the uptake of new, rapid diagnostics was catalyzed by synergistic investments from national governments, donors and implementing partners. As a result, in-country laboratory capacity to detect multidrug-resistant TB (MDR-TB) has significantly improved, as outlined in the 2014 WHO Global Report.

Drug resistance surveillance data indicate that in 2013, approximately 480 000 people developed MDR-TB worldwide. If all notified TB patients (6.1 million, new and previously treated) had received a DST in 2013, an estimated 300 000 cases of MDR-TB would have been detected. Of these, 136 000 were actually diagnosed and reported to WHO in 2013, which represents a tripling in MDR-TB detection compared with 2009 (but nevertheless shows a continuing gap in diagnosis).

In 2013, 97 000 patients eligible for MDR-TB treatment were started on second-line regimens, a three-fold increase compared with 2009. Unfortunately, even with improved diagnosis and enrollment on treatment, outcomes for MDR-TB patients remain poor: globally, only 48% of the MDR-TB patients in the 2011 cohort were successfully treated. 16% died, 24% did not have their treatment outcome documented or interrupted treatment, and 12% were not cured despite receiving treatment.

Moreover, health service capacity to treat patients has not kept up with the pace of diagnosis, creating growing "waiting lists" for MDR-TB treatment in several countries. Worrying, 39 000 patients eligible for MDR-TB treatment (plus an unknown number detected in previous years) did not start treatment in 2013, presenting an increasing ethical dilemma. In addition, lack of adequate patient follow-up remains a major health service constraint.

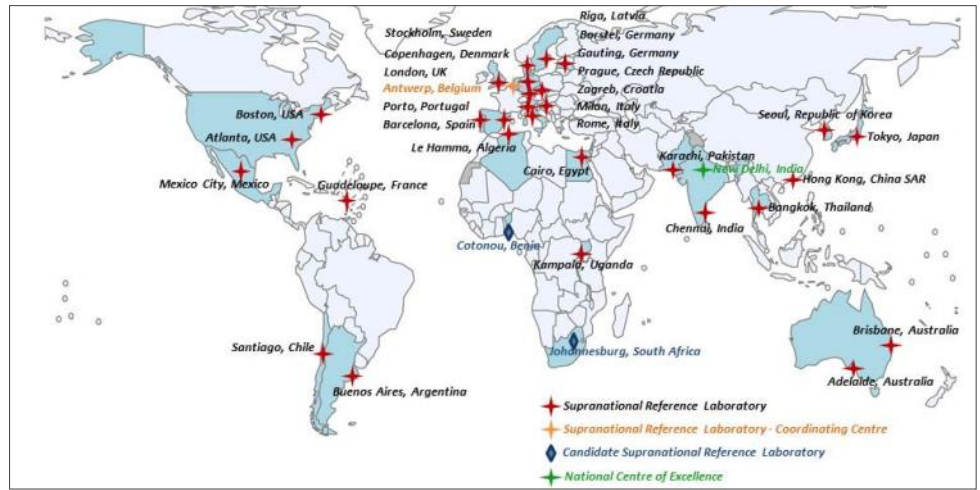
As the scale-up of rapid diagnostics continues, increasingly more patients will be detected with MDR-TB. A major challenge will be to ensure that all persons diagnosed with MDR-TB are started on treatment. Reducing and eliminating the growing gap between diagnosis and treatment need concerted effort by all partners in TB control. Addressing poor treatment outcomes for patients due to inadequate drug regimens, non-completion of therapy, and health system weaknesses are overlapping priorities for the Global Laboratory Initiative (GLI) and the Global Drug Resistance Initiative (GDI).

Potential collaboration and synergy between the GLI and GDI include activities that would remove systemic inefficiencies and reduce diagnostic and treatment delays, e.g. through refined and simplified diagnostic and treatment algorithms, improved specimen and patient referral networks, improved recording and reporting systems, decentralised testing and treatment initiation, as well as community-based MDR-TB care. One joint, practical approach by the GLI and GDI could be to ensure that all health care workers (nurses, clinicians and laboratory staff) are adequately informed and trained on WHO policies for MDR-TB case finding, diagnostic policies, treatment initiation and treatment monitoring following a patient centred approach. Other areas to be addressed together include the use and interpretation of rapid DST results, seamless communication between laboratories and health services responsible for treatment, and increased advocacy strategies to enforce the message of test-to-treat-to-cure: 'no treatment without diagnosis, and no diagnosis without treatment'.

A combined session of the GLI and GDI Core Group meetings is being convened in Barcelona on the 27th October 2014 to develop a joint work plan on joint activities to bridge the MDR-TB diagnostic and treatment gap. We look forward to the outcomes and next steps.

Dr. Karin Weyer
*Coordinator: Laboratories, Diagnostics and Drug Resistance,
Global TB Programme, WHO*

Comprehensive information about the SRL Network is available at:
<http://www.stoptb.org/wg/gli/srln.asp>



SRLN report repository

Online repository of technical reports from the SRLs to improve laboratory capacity

47 missions from 40 countries are available at:

<http://www.stoptb.org/wg/gli/assets/documents/map/3/atlas.html>

National Centres of Excellence

Three laboratories in the Russian Federation have been nominated for evaluation as National Centres of Excellence. WHO will undertake a laboratory assessment to determine their preparedness for joining the network.

STORIES FROM THE FIELD

TB Supranational Reference Laboratory New report repository established

The Supranational Reference Laboratory Network (SRLN) is a subgroup of the Global Laboratory Initiative (GLI). The SRLN is a key technical resource supporting the Global Project on Anti-tuberculosis Drug Resistance Surveillance and also works to strengthen laboratory capacity in countries with a high burden of TB. The SRLN, with the support of the GLI, has expanded to 33 laboratories including 2 candidate reference laboratories and one national Centre of Excellence, in order to respond to the urgent need to scale-up laboratory services to meet the diagnostic challenges of co-infection with TB and HIV, as well as drug-resistant TB.

The new report repository will be key in sharing recommendations from the SRLs for improving laboratory capacity

Improving the coordination of technical assistance provided by the SRLN and other partners remains a priority for the network. To this aim, an online repository of technical reports has been established as a key mechanism to share findings and recommendations from the SRLs for improving laboratory capacity (<http://www.stoptb.org/wg/gli/assets/documents/map/3/atlas.html>).

The network has also adopted a standardized format for describing the activities and findings from different missions. As of October 2014, 47 laboratory mission reports from 40 countries were made available (among them, 28 USAID priority countries funded for laboratory strengthening in 2013-2014 were assisted by the SRLs). More individual laboratory mission reports are being uploaded on the SRL website as they become available. Other GLI partners are encouraged to contribute and submit any technical assistance reports to the GLI Secretariat for the report repository.

Figure 1 shows how to get to the report repository via <http://www.stoptb.org/wg/gli/assets/documents/map/3/atlas.html> and by clicking on a selected country name in the table (e.g. Kyrgyzstan).

Figure 2 shows the location of laboratory reports, the laboratory country profile, the lead SRL and other partners supporting laboratory strengthening in the country.

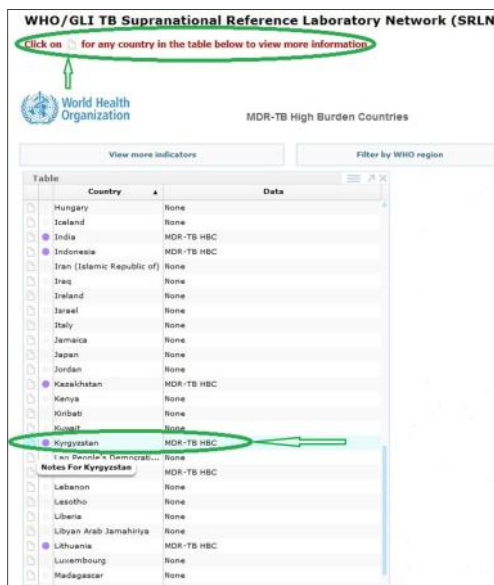


Figure 1

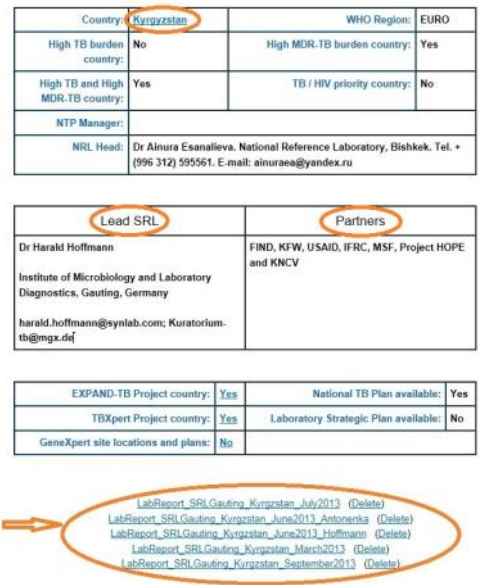
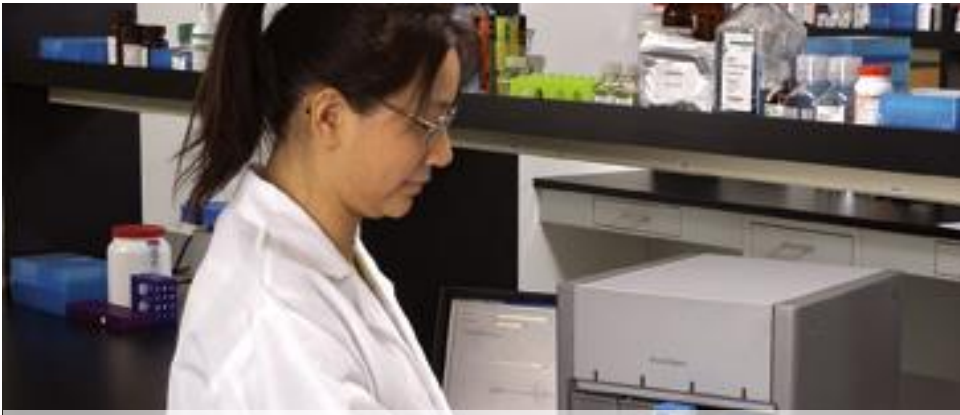


Figure 2



The GLI training package on Xpert MTB/RIF provides module-based PowerPoint files that can be customized according to country specifics and trainer preferences. Photo: Cepheid

GLI RESOURCES

GLI training package on Xpert MTB/RIF

The Xpert MTB/RIF assay was endorsed by WHO in 2010 and has been rolled out in more than 110 countries, with over 8.8 million cartridges having been procured. Despite enormous potential in improving diagnosis of TB and patient outcomes, a number of operational challenges are being faced in many countries which may limit the impact of the test. A need was identified for a comprehensive and standardized training that would address many of these gaps.

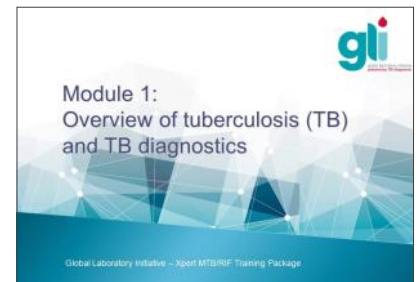
The Global Laboratory Initiative (GLI) convened a consortium of its partners, including FIND, KNCV, US CDC, USAID and WHO, to develop a modular Xpert MTB/RIF training package with funding from USAID (TB CARE I). The modules are based on materials originally developed by FIND, KNCV and Cepheid. Guidance for country customization is given in the slides for ease of adaptation and use. Depending on the audience, modules may be selected according to need (e.g. basic users, supervisors, clinicians).

Topics covered include: Overview, biosafety, specimen collection, procurement, installation, Xpert MTB/RIF technology, results, reporting, troubleshooting, maintenance and a clinical guide to Xpert MTB/RIF.

A quality assurance module has been developed, is undergoing expert review, and will be posted shortly. The training package is available in English, Russian, French and Portuguese.

Dr. Heidi Albert
FIND

Dr. Heather Alexander
Centers for Disease Control and Prevention

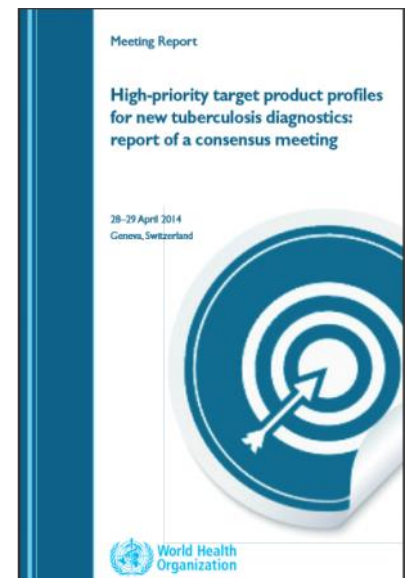


The Training Package is available at:
http://www.stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF.asp

High-priority target product profiles for TB diagnostics

Diagnostic manufacturers are increasingly expressing the need to be informed about the type of TB diagnostics they should invest in, as well as the potential market size for these products. The development of target product profiles (TPPs) is therefore an important step to align the needs of end-users with the specifications and targets that product developers should meet in terms of the performance and operational characteristics of such tests.

In April 2014, the WHO Global TB Programme convened a meeting on behalf of the Global Laboratory Initiative (GLI) and the New Diagnostics Working Group (NDWG) of the Stop TB Partnership to develop consensus on the minimal and optimal specifications of four different types of TB diagnostic tests that were identified by multiple stakeholders to be high priority. Extensive work by McGill University, FIND, Médecins Sans Frontières (MSF), the NDWG and the GLI informed this process.



The meeting report is available at:
http://apps.who.int/iris/bitstream/10665/135617/1/WHO_HTM_TB_2014.18_eng.pdf?ua=1



Photo MSF

Key data and tools

Global procurement statistics
as of 30 September 2014 (cumulative)

Instruments: 3,553
Modules: 17,029
Cartridges: 8,807,910
Countries: 110

Note: data reflect commodities procured under concessional pricing

Countries with largest numbers of GeneXpert modules deployed:

South Africa: 4,260
China: 3,812
Brazil: 729
India: 640
Nigeria: 620
Philippines: 492
Bangladesh: 376
Kenya: 370
Ethiopia: 340
Zimbabwe: 320

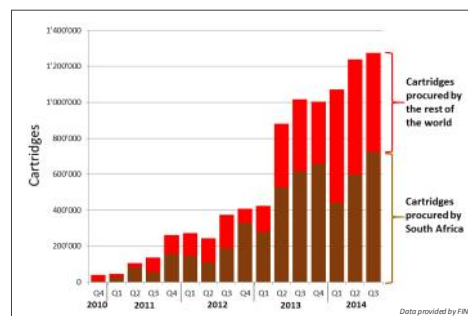
XPert MTB/RIF UPDATE

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

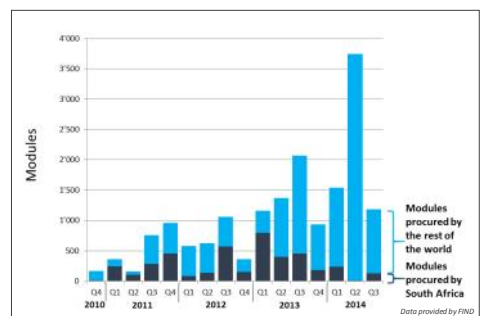
Global trends in procurement

Over a million Xpert MTB/RIF cartridges have been procured each quarter under concessional prices over the past year; 1.3 million cartridges were procured in Q3 2014. South Africa remains the largest user of Xpert MTB/RIF, having procured 56% of all cartridges globally since 2010. Other countries have greatly increased their testing capacity in recent quarters, and 75% of GeneXpert modules globally are now located outside of South Africa. Most notably, China and Brazil have procured significant numbers of GeneXpert in 2014 and together with India are expected to significantly scale-up Xpert MTB/RIF use in the coming year.

Quarterly number of Xpert MTB/RIF cartridges procured under concessional pricing



Quarterly number of GeneXpert modules procured under concessional pricing



WHO Implementation Manual on Xpert MTB/RIF

Following the release of updated recommendations on the use of Xpert MTB/RIF in October 2013, WHO published an accompanying Implementation Manual. The manual describes the evidence base for the Policy update; recommended positioning of the technology; testing and managing patients, including the selection of individuals to be tested and how to interpret results; case definitions and patient registration; practical considerations, including key prerequisites and actions, testing capacity, operation and storage conditions, biosafety, calibration and maintenance, quality assurance, and budgeting guidance; monitoring and evaluation; SOPs for processing extrapulmonary specimens.

Xpert MTB/RIF Implementers Global Forum

This year's Xpert MTB/RIF Implementers Global Forum was organized by the WHO Global TB Programme as part of the 6th GLI Partners Meeting. The Global Forum brought together representatives from high TB, TB/HIV and MDR-TB burden countries, non-governmental organizations, international institutions and initiatives, research institutes from developed and developing countries, industry and funding agencies. The Forum provided an opportunity to share lessons learned and challenges for wide-scale implementation of Xpert MTB/RIF in different epidemiological and resource settings, with a focus on evidence of impact and linking scaled-up diagnosis with scaled-up access to treatment.

The meeting report, with links to all presentations, can be accessed online at: <http://www.stoptb.org/wq/gli/assets/documents/Xpert%20Implementers%20Global%20Forum%20meeting%20report.pdf>

The Implementation Manual, together with the WHO policy update on Xpert MTB/RIF, can be accessed online at: http://www.who.int/tb/laboratory/xpert_launchupdate/en/



IOM provides laboratory services to migration health assessment programmes, mainly for refugees and migrants traveling abroad for resettlement or long term stay. Photo: IOM (R. Arpornsilp)

NEWS FROM GLI PARTNERS

IOM experience of operating integrated laboratory services

When referring to integrated laboratory services, in the context of GLI, we envisage a laboratory that performs tuberculosis diagnosis examinations together with HIV and other clinical assays. Such laboratories are not rare; most of the private sector laboratories provide integrated services following demand of their client base. The International Organization for Migrations (IOM), an intergovernmental organization, is not a private entity though it has been operating integrated laboratories for over a decade.

IOM provides laboratory services to migration health assessment programmes (HAP), mainly for refugees and migrants traveling abroad for resettlement or long term stay. Health screening requirements are defined by the destination countries and often focus on infections of public health importance, such as tuberculosis, HIV, malaria, STIs etc. Based on the instructions given by the donors, the services may include only few (TB or STI), several or a wide range of laboratory examinations. The main facilitating factor for establishing integrated laboratory services in IOM operations is donor support: If donors support and provide funding, technical difficulties are relatively easy to solve.

Currently IOM operates six integrated laboratories, in five countries. All have TB culture facilities with HIV, syphilis, hepatitis and several other clinical laboratory assays, whilst one of them runs biochemistry laboratory as well. The technical side of establishing such laboratories is quite straightforward and no major challenges are encountered. Laboratories are normally headed by one manager, who assigns focal points responsible for different sections such as TB, serological testing, molecular biology, reagent preparations, etc. All personnel are usually trained to perform the entire range of examinations available in their respective facilities.

The challenges of establishing integrated laboratories may be related to the regulations of the country where laboratories operate. At certain times, different services require separate licenses, which have to be obtained from different entities not collaborating with each other.

These challenges may apply to the public sector laboratories in many countries. Tuberculosis and HIV services can be organized as separate segments of health services, often compelled by donors. Vertical programming of TB, HIV, malaria or other diseases, which is a recognized issue, may prevent integration of laboratory services.

The IOM experience shows that mainly the support of donors, their interest and recognition of cost-effectiveness of integrated laboratories allow establishing and running facilities that provide services for diagnosis of multiple diseases.

Levan Gagnidze
Regional Coordinator for Laboratory Services
IOM Regional Office Bangkok

momentum

more information

Upcoming Events

45th Union World Conference

28 October - 1 November 2014, Barcelona, Spain
Conference website: <http://barcelona.worldlunghealth.org/>

Important laboratory-related meetings at and around the Conference

Pre-meeting

GLI Core Group Meeting jointly with GDI Core Group (closed meeting)
Monday, 27 October 2014, 09:00-18:00
Hotel Diagonal Zero, Barcelona

Post-Graduate course

Update on clinical and programmatic management of MDR-TB and XDR-TB
Wednesday, 29 October 2014, 09:00-17:00
Barcelona Convention Centre Room 133/134

Workshops

Practical laboratory issues in low-resource settings
Wednesday, 29 October 2014, 09:00-17:00
Barcelona Convention Centre, Room 116

Complexities of molecular and phenotypic diagnostics in clinical management
Wednesday, 29 October 2014, 13:30-17:00
Barcelona Convention Centre, Room 114

Bacteriology & Immunology Sub-section Meeting

Friday, 31 October 2014, 10:15-11:15
Barcelona Convention Centre, Room 117

ASLM Conference 2014

30 November - 4 December 2014, Cape Town, South Africa
Conference website: www.aslm2014.org

1st Global Laboratory Initiative - Global Drug-resistant TB Initiative Partner's Meeting

27th April-1st May 2015

WHO Headquarters, Executive Board Room, Geneva, Switzerland

The programme will include:

- Global Forum of Xpert MTB/RIF Implementers
- TB Supranational Reference Laboratory Consultation

Selected Publications

WHO Global Tuberculosis report 2014 http://www.who.int/tb/publications/global_report/en/

UNITAID TB diagnostic landscape report, 3rd edition http://unitaid.org/images/marketdynamics/publications/UNITAID_TB_Diagnostics_Landscape_3rd-edition.pdf

UNITAID TB medicines landscape report, 2nd edition http://www.unitaid.eu/images/marketdynamics/publications/UNITAID-TB_Medicines_Landscape-2nd_edition.pdf

Treatment Action Group (TAG) 2014 report of tuberculosis research funding trends, 2005-2013, <http://www.treatmentactiongroup.org/tbrd2014>

© WHO 2014

Contributors: Heidi Albert, Heather Alexander, Levan Gagnidze, Chris Gilpin, Rumina Hasan, Jean Iragena, Thomas Shinnick, Wayne Van Gemert, Karin Weyer

Cover page photo: UNITAID / Gerhard Jörén and Riccardo Venturi

Contact: gli_secretariat@who.int

GLI website: <http://www.stoptb.org/wg/gli/default.asp>