

MEETING REPORT

GLOBAL CONSULTATION OF THE WHO-GLI TB SUPRANATIONAL REFERENCE LABORATORY NETWORK

Meeting Date: 14 - 15 April 2010
Meeting Venue: Salle A, World Health Organization, Geneva, Switzerland

Background

The TB Supranational Reference Laboratory Network (SRLN) was created in 1994 in order to support the WHO-IUATLD Global Project on TB drug resistance surveillance. The objectives of the Global Project are to estimate the magnitude of drug resistance globally, determine trends and provide data to inform WHO policy decisions. Core principles of the Global Project are to ensure accurate and representative sampling of the populations under study, allow for the differentiation of new and previously treated cases and ensure that laboratory results are quality assured. Originally, fourteen laboratories volunteered to form the SRL Network based on institutional capacity and own resources to support the Global Project. This resulted in a concentration of the SRLs in Europe.

The original terms of reference required that each of the SRLs had a permanent functional TB laboratory providing quality culture and drug susceptibility testing (DST), with a commitment to support at least two countries with DST proficiency testing (PT), to provide external quality assurance during drug resistance surveys, and to provide training on culture and DST in relevant countries as needed.

To ensure proficiency in the SRLN, it was agreed that all SRLs would participate in annual DST PT using standardised strain panels. These are distributed by one of the SRLs designated as Coordinating Centre. The SRL in Ottawa, Canada volunteered to provide this service for PT Rounds 1-5 and subsequent rounds 6-16 have continued via Antwerp, Belgium as the Coordinating Centre.

Between 1994 and 2009, the SRLN was expanded to 29 laboratories, largely driven by regional initiatives and institutional interest in joining the network.

The SRLN and the Global Laboratory Initiative

Consensus evolved in 2007 among key stakeholders that a Global Laboratory Initiative (GLI) was needed to guide and coordinate the massive scale-up in tuberculosis (TB) laboratory capacity to address the diagnostic challenges of drug-resistant and HIV-associated TB. This required a major shift in providing laboratory policy guidance, setting norms and standards, coordinating technical assistance, and accelerating knowledge transfer, within integrated laboratory networks. The concept of GLI was therefore presented to and endorsed by the Coordinating Board of the Stop TB Partnership (STP) in October 2007, effectively integrating the previous Stop TB Partnership Subgroup on Laboratory Capacity Strengthening and the SRLN. The role of WHO within GLI was subsequently endorsed by the WHO Strategic and Technical Advisory Group for TB (STAG-TB) in June 2008. In October 2008, recognising the scope and challenges of scaling up TB laboratory services, the STP Coordinating Board voted unanimously to upgrade the GLI to full STP Working Group status, with the GLI Secretariat hosted by the WHO Stop TB Department (STB). Following STB restructuring in late 2009 a new Unit focussed on TB diagnostics and laboratory strengthening (TBL) was established, *inter alia* coordinating the SRLN and providing the GLI Secretariat.

Challenges for the SRLN

The SRLN continues to be the backbone of the Global Drug Resistance Surveillance Project; however; given the pressing need for scaling up laboratory services an expanded focus for SRL activities is urgently needed. Despite being a great technical resource for laboratory scale-up and

capacity development, the SRLN is generally under-utilised, largely due to a crucial lack of funding and human resource capacity. While there is a skewed concentration of SRLs in Europe there are only three SRLs in Africa, where the need for laboratory strengthening is most pressing. In addition, very few SRLs are linked to francophone and lusophone-countries.

In-country support is not evenly shared across the SRLN. In some instances, there is overlap between SRLs supporting different countries. Several countries are not linked to an SRL and some SRLs support several countries while others do not support any country. In addition, the level of technical support provided to countries by each SRL differs widely and country needs on laboratory strengthening do not necessarily match available expertise within the SRLN.

Funding of the SRLN is currently the biggest single challenge. The vast majority of technical assistance provided by the SRLN has been as a result of individual and/or institutional commitment and many of the SRLs need to be commended for the work that they have achieved in supporting their partner laboratories with minimal or no funding. Urgently addressing the issue of sustained and adequate funding for the SRLN - given the demand and scope of laboratory strengthening services required - is therefore critical if targets for global scale-up of laboratory capacity are to be achieved.

Meeting Objectives

The overall meeting objective is to discuss options for strengthening the SRLN through collaboration with GLI partners, and starting the process for a new business model in order to support future SRLN activities. The meeting will aim to:

- Disseminate recent developments in WHO policy guidance on new TB methods/tools
- Develop revised TORs for the SRLs
- Develop criteria for the selection of new SRLs and to evaluate existing SRLs
- Review the process for the creation of formal links between SRLs and national reference laboratories (NRL)s
- Discuss requirements and funding mechanisms for SRLs to develop and implement work plans for sustained coordinated technical assistance to countries beyond quality assurance for DST.

Meeting outcomes

- Consensus on revised TORs for the SRLN
- Consensus on selection criteria and an agreed framework for evaluating existing SRLs;
- Consensus on the way forward for co-ordinating the SRLN laboratory strengthening efforts
- Framework for a business proposal for SRLN funding

Participants

The Global Consultation of the World Health Organization - Global Laboratory Initiative TB Supranational Reference Laboratory Network (WHO-GLI SRLN) was held at WHO, Geneva, Switzerland 14-15th April 2010. The heads of 22 of the 29 designated SRLs participated in the meeting along with the Core Group members of the Global Laboratory Initiative, the Regional TB adviser AMRO, and 4 TB laboratory focal points (AFRO, WPRO, SEARO, EMRO). Eight representatives from donor agencies and partners were present as observers.

Final Agenda

Chair: Christopher Gilpin, WHO
Rapporteur: Dick van Soelingen , SRL Netherlands

WEDNESDAY, 14 APRIL

09:00 – 09:15	Welcome	Karin Weyer, WHO
09:15 – 09:30	Meeting scope and objectives Review and adoption of meeting agenda	Chris Gilpin, WHO
<i>Objective 1: To disseminate recent developments in WHO policy guidance on new methods/tools</i>		
09:30 – 10:00	WHO policy guidance update.	Chris Gilpin, WHO
10:00 - 10:30	Current draft WHO-CDC biosafety recommendations for TB laboratories	Tom Shinnick, CDC
BREAK 10:30 – 11:00		
<i>Objective 2: To develop revised TORs for the SRLN and discuss eligibility criteria and a mechanism for accrediting SRLs</i>		
11:00 – 11:15	GLadMap - Global Laboratory database	May Chu, WHO
11:15 – 11:30	Overview of SRLN efforts to date	Armand van Deun, SRL Belgium
11:30- 12:30	Regional perspectives on SRLN requirements, structure and expansion	EMRO, SEARO, WPRO, AFRO, PAHO
12:30 – 13:00	Discussion	ALL
LUNCH 13:00 – 14:00		
14:00 – 14:20	The Global Laboratory Initiative Roadmap	Karin Weyer, WHO
14:20 – 14:40	Expansion of the SRL network in Africa	Armand van Deun, for TBCAP
14:40 - 15:00	Proposed TORs for the SRLN	Chris Gilpin
15:00 - 15:30	Discussion	ALL
BREAK 15:30 – 16:00		
<i>Objective 3: To discuss eligibility criteria and a mechanism for accrediting SRLs</i>		
16:00 - 16:30	Eligibility and inclusion criteria for the SRLN	Chris Gilpin
16:30 - 17:00	SRL accreditation -What is needed ?	John Ridderhof, GLI Chair
17:00 - 17:30	Discussion	All

Chair: John Ridderhof, Chair GLI
 Rapporteur: Ivan Bastian, SRL Australia

THURSDAY, 15 APRIL

Objective 4: To review the process for the creation of formal links between SRLs and NRLs		
09:00- 10:00	Summary of Day 1 and consensus to date	Chris Gilpin, WHO
10:00- 10:15	Creation of formal links between SRL and NRLs - What is needed?	Daniela Cirillo, SRL Italy
10:15- 11:00	What support do SRLs need to provide co-ordinated technical assistance to countries?	Discussion session
BREAK 11:00 – 11:30		
Objective 5: To discuss requirements and funding mechanisms for SRLs to develop and implement work plans for sustained coordinated technical assistance to countries beyond quality assurance for DST		
11:30 – 11:50	Expanding And Accelerating Access To Diagnostics For Patients At Risk Of Multi-Drug Resistant Tuberculosis (EXPAND-TB) project	C N Paramasivan, FIND
11:50 – 12:15	European Centre for Disease Prevention and Control- European Reference Laboratory Network ECDC-ERLN	Francis Drobniowski, SRL United Kingdom
12:15 - 13:00	Discussion	ALL
LUNCH 13:00 – 14:00		
14:00 – 14:20	SRL technical assistance for drug-resistance surveillance	Matteo Zignol, WHO
14:20 - 14:40	Donor perspectives on SRLN funding (Governmental)	Gavin Macgregor-Skinner, USAID
14:40-15:00	Donor perspectives on SRLN funding (Private sector)	Patrizia Carlevero, Eli Lilly
15:00-15:30	Discussion	ALL
BREAK 15:30 – 16:00		
16:00 - 16:30	Co-ordinated technical assistance -The way forward	Chris Gilpin, WHO
16:30 – 17:15	Discussion	ALL
17:15 - 17:30	Next steps	Chris Gilpin, WHO

Meeting outcomes and action steps

Objective 1: *To disseminate recent developments in WHO policy guidance on new methods/tools*

A presentation was made to clarify the relationship between the Global Laboratory Initiative (GLI) Working Group (WG) and the GLI secretariat provided by the TB Laboratory Strengthening and Diagnostics Unit (TBL) of the StopTB Department.

An overview of WHO policy guidance on liquid culture, rapid speciation, line probe assays, light emitting diode (LED) microscopy, second-line drug susceptibility testing (DST) and rapid DST using non-commercial methods was presented. It was agreed that TB Supranational Reference Laboratory Network work be informed via email of any updates to WHO policy guidance on the GLI website.

Action

Presentations from the consultation to be uploaded to the GLI website with the meeting report. <http://www.stoptb.org/wg/gli/>

An overview of the outcomes of two Expert Group meetings on TB laboratory biosafety requirements was presented. Consensus recommendations were made for minimum biosafety requirements for three different levels biorisk for TB testing including;

- Direct AFB-smear microscopy
- Processing specimens to concentrate bacilli for smear, culture, DST, molecular tests
- Manipulating cultures for smear, subculture, identification, DST, molecular tests

A risk based assessment for each TB diagnostic procedure was evaluated according to the risk of generating infectious aerosols and the concentration of bacilli. A draft WHO TB Biosafety manual is undergoing review by the Expert Group panel and will be distributed to the SRLN for comment before the end of May 2010

Action

Draft WHO TB Biosafety Manual to be circulated to the SRLN for comment following final feedback from expert working group members. Expected time line for distribution end of May 2010.

An overview of the Global Laboratory Directory (GLaD) was presented. GLaD is a support system designed for connecting and sustaining laboratory networks and their activities. Its function is to provide new and existing networks a portal for more visibility, peer-to-peer support, promote cross-lateral activities and provide access to successful solutions and templates.

Action

Coordinate the update of the SRLN on the GLaDMap global laboratory database. <http://www.gladmap.org>

Objective 2 *To develop revised terms of reference for the SRLN.*

Draft terms of reference (TORs) for SRLs active in Africa were developed at the meeting "Optimizing the functioning of the Supranational Reference Laboratory Network (SRLN) on the African continent" Cairo, Egypt 20-21 October 2009 which was jointly organized by The Union and PMU/TBCAP.

These draft TORs were used as a starting point for developing TOR for the SRLN globally. Following feedback from the WHO Regional Offices and input from the SRLN the TORs were revised and finalized to match laboratory strengthening services available from the SRLN with country needs.

Draft Terms of Reference for WHO-GLI TB Supranational TB Reference Laboratory Network

Programmatic

1. Liaise with Global Laboratory Initiative (GLI) technical partners, National TB Reference Laboratories (NRLs) and National TB Programmes (NTPs) to facilitate implementation of WHO policy guidance on TB diagnostics and laboratory norms and standards.
2. Support the integration of quality TB diagnostic services within national laboratory policies and strategic plans incorporating cross cutting laboratory issues including quality management systems, supply management, specimen transport and referral and human resource development.
3. Advocate for TB laboratory worker protection with use of current WHO TB bio-safety recommendations.
4. Support the implementation of an appropriate data management system.
5. Provide guidance on quality management systems for a process towards achieving laboratory accreditation to international standards.

Technical

Serve as the focal point for coordination of technical assistance to NRLs (or equivalent) to enable:

1. Monitoring of the proficiency of drug susceptibility testing of *M.tuberculosis*
 2. Implementation of quality assured AFB microscopy (including external quality assessment) in laboratory networks
 3. Development of capacity and proficiency in performing conventional and new WHO endorsed technologies including:
 - a. Microscopy methods
 - b. Culture and identification methods
 - c. Drug susceptibility testing (phenotypic and molecular methods)
 4. Development of laboratory components of drug resistance survey (DRS) protocols, data validation, and quality assurance as required
 5. Susceptibility testing against first and/or second-line drugs (for both patient management and surveillance) until NRLs establish capacity
 6. On-site technical training or in-house training of laboratory staff as needed
 7. Review of laboratory proposals in Global Fund applications
 8. Operational research, if relevant, on the introduction of new laboratory tools
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Objective 3: To discuss eligibility criteria and a mechanism for accrediting SRLs

The following set of minimum criteria were established for existing and new candidate SRLs

Draft eligibility and inclusion criteria for WHO-GLI TB Supranational TB Reference Laboratories

TB Supranational Reference Laboratories (SRLs) are expected to meet the following minimum criteria. New candidate SRLs are assigned a provisional SRL status and are mentored by their linked SRL for a period of at least one year prior to formal designation as a member of the SRL network.

1. Officially recognized by the National Health Authority or Ministry of Health acting as National Level TB Reference Laboratory supporting a functional national or sub-national network of lower level laboratories. New candidate SRLs must have a formal link with an established TB Supranational Reference Laboratory.
2. Technical capacity to perform AFB microscopy, culture, identification and drug susceptibility testing (DST) of *M. tuberculosis* using phenotypic and molecular methods according to current WHO policy guidance.
3. Meet national laboratory regulations and conform to WHO and other international standards for performing TB testing
4. Proven DST accuracy (participated in at least 2 consecutive rounds of SRLN proficiency testing) with sufficient workload levels to maintain proficiency
5. Ability (including human resources, infrastructure and equipment) to support laboratories in other countries (as per SRL TOR)
6. Established or capacity to establish working relationships with the NRL in other countries through formal links
7. Commit to provide the minimum SRL service requirements which are to:
 - a. Establish formal links with at least two NRLs
 - b. Provide at least three technical assistance visits to countries every two years
 - c. Provide reports to WHO on SRL services provided to countries.
 - d. Report at least one activity per country per year

In reviewing the achievements of the SRLN it was recognized that some technical challenges remain unresolved and need to be addressed. The meeting proposed to establish a smaller technical working group with members of the SRLN led by the Co-ordinating SRL in Antwerp to develop TORs and a plan to address topics in the quality assurance of drug susceptibility testing including:

- Interpretative criteria for "difficult strains"
- Should DST and QA be limited to INH/RIF/quinolones/injectables?
- Compile data on non-SRLs proficiency
- Distribution of panel strains

<p>Action Establish a Technical Working Group on issues related to quality assurance of drug susceptibility testing</p>

Objective 4: To review the process for the creation of formal links between SRLs and NRLs

Following the Global Consultation a mapping exercise has been initiated to determine which SRLs are linked with countries and what type of technical assistance of laboratory strengthening activities have been undertaken in the last two years.

The Global Consultation of the WHO-GLI SRL network recommended the need to formalize designation of a TB laboratory as an SRL and its linkages with other national level reference laboratories for the provision of technical support

Actions for WHO, Geneva

- 1. Send letter to all heads of existing SRLs to formalize their designation.**
- 2. Send letter to all countries regarding the process for establishing formal links between countries and the WHO-GLI SRLN. A sample Memorandum of Understand will be provided as a template for linking SRL to countries.**
- 3. Formal letter of recognition from WHO to SRL Governments to advocate increased political commitment on the essential value of the SRLN activities in TB laboratory strengthening. Seek funding commitments.**

Objective 5: To discuss requirements and funding mechanisms for SRLs to develop and implement work plans for sustained coordinated technical assistance to countries beyond quality assurance for DST

As the skill set across the SRL network varies there may be a need to establish SRLs with Global or Regional functions such as preparation of QA material for DST, LPA or microscopy. Some SRLs may not have experience in strengthening microscopy network in developing countries or others may not have experience in the use of new tools such as LPA. Therefore, improved co-ordination of the SRLN is needed for it to function as a network and not as a group of individual laboratories providing ad hoc TA. Also, more than one SRL can support lab strengthening in different countries as needed providing the activities are complementary and co-ordinated through WHO-TBL.

As a way forward it was proposed to use existing funding for Technical Assistance which is available to WHO-TBL for laboratory scale-up under the umbrella of the EXPAND-TB project and for drug resistance surveillance. The meeting proposed to use EXPAND-TB as an entry point to link SRL support to GF recipient countries for the implementation of new rapid diagnostics for MDR-TB. SRLs with existing linkages with EXPAND-TB countries or SRLs with the capacity to provide technical assistance to these countries will be requested to assist with technical assistance missions to facilitate the required laboratory scale-up. The model being considered for funding technical assistance from the SRLN is to develop the concept of "technical assistance packages" which are estimated at USD 8,500 – 12,500 per one to two week technical assistance mission. It is anticipated that this approach can be used as a framework to develop a coherent business plan for funding TA for the network.

Action

Send out a call for SRLs with existing linkages with EXPAND-TB countries to assist with technical assistance missions to help scale-up implementation of rapid diagnostics for MDR-TB