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

Harmonization of tools towards accreditation

Background

Accredited laboratories are recognized as meeting certain quality standards and having the necessary technical processes in place, as well as administrative systems needed to ensure quality results. A strong laboratory quality management system is critical to ensuring the quality of testing, and weak laboratory systems have direct impact on patient care. Many activities are involved in controlling and ensuring quality. An organizational structure known as the quality system is necessary to ensure that:

- These activities are always carried out at the right time and by the right person;
- The number of appropriately trained staff is available;
- The necessary equipment and consumables are available;
- Manuals, guidelines, forms and SOPs are in place so that processes are always carried out correctly.

Quality management encompasses all of the planning, leadership and management activities necessary to ensure that an organization functions correctly – that is, to ensure that the quality system functions properly. These activities are at the top level of the quality-management system.

Currently, four main sources of information and guidance exist and can be used to assist TB laboratories in developing and maintaining a QMS:

- The International Organization for Standardization (ISO) standard 15189:2012;
- The GLI stepwise process towards TB laboratory accreditation: quality management;
- The framework known as the WHO guide for the stepwise laboratory improvement process towards accreditation in the African Region (SLIPTA);
- The framework known as the Strengthening laboratory management towards accreditation (SLMTA).

ISO standard 15189:2012

The most recent edition of this standard (15189:2012 Medical laboratories – requirements for quality and competence) contains a description of the components necessary for a QMS to be effective in a medical laboratory.1 These components have been further organized into 12 groups of quality-system essentials by the Clinical and Laboratory Standards Institute.2

GLI stepwise process towards TB laboratory accreditation: quality management

The GLI stepwise process towards TB laboratory accreditation is an online tool available at: http://gliquality.org. This computer-based interactive tool can help national TB reference laboratories implement in a gradual manner all of the requirements of ISO 15189:2012, which will lead to the development of a properly functioning QMS. The use of this tool may require the involvement of a consultant or group of individuals to act as the driving force to encourage a laboratory to work through the tool systematically, as well as to provide technical support to the implementing laboratory. Embarking on this process will require additional dedicated human resources capacity, which must be considered.

WHO guide for the stepwise laboratory improvement process towards accreditation in the African Region

SLIPTA was originally developed by WHO’s Regional Office for Africa. This checklist is based on the ISO 15189:2007 standard and the Clinical and Laboratory Standards Institute’s guideline GP26-A4:2011. The checklist was developed to monitor progress in improvement of a laboratory’s QMS. It is based on the 12 quality-system essentials, and it is applicable to all laboratory settings and disciplines.3 This tool has been modified by FIND to address specific elements for TB laboratories and is referred to as TB-SLIPTA.

Strengthening laboratory management towards accreditation

This is a task-based mentoring programme developed by the United States Centers for Disease Control and Prevention, to enable laboratories to implement the different components of a QMS, with the ultimate goal of achieving accreditation as a practicing laboratory.4 The Foundation for Innovative New Diagnostics (FIND) has developed the TB stepwise laboratory management towards accreditation training programme. This is a modified version of the SLIPTA programme, called TB-SLMTA, that includes TB-specific modules and guidance (in areas such as safety, sputum collection and specimen transport) and TB-specific activities, examples and tools.5

Why accreditation?

Accreditation is a means of recognizing a laboratory’s quality and competence. Accreditation is achieved when a laboratory has a QMS in place that complies with the requirements of ISO standard 15189:2012. An independent accreditation body assesses the laboratory to determine whether the QMS functions as it should and whether it complies with the ISO standard. This accreditation body must operate according to ISO standard 17021:2011 (Conformity assessment – requirements for bodies providing audit and certification of management systems) and must be an affiliate or member of the International Laboratory Accreditation Cooperation.6 National laboratories are encouraged to meet all of the requirements of ISO standard 15189:2012. At a minimum, lower-level laboratories are required to implement internal and external quality-improvement mechanisms. All diagnostic techniques used in a laboratory should be quality assured. It is important that supervision and technical support are routinely provided from the upper level of the laboratory network to the lower level to ensure that the network operates effectively.

At this stage, the task force is working towards the goal of harmonizing all of the schemes together and identify similarities, differences and complementarities to better support the end-user implementing a quality management system. Specific technical assistance to countries implementing a quality management system is being coordinated through the WHO Global TB Programme and requests for assistance can be sent via email to gli_secretariat@who.int

References:


Dr Christopher Gilpin
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World Health Organization
New drugs, new regimens and new Drug Susceptibility Testing

Recent advancements in the development of new drugs and regimens for TB call for the need for the development of standardized drug susceptibility testing methodology.

Currently, there is only one WHO-recommended first-line regimen for treating drug-susceptible TB, which includes isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA) and ethambutol (EMB): (HRZE). An alternative regimen, PaMZ – Pa824 (a nitroimidazole), moxifloxacin, and pyrazinamide – is being evaluated in phase III clinical studies among adult patients with newly diagnosed drug-susceptible pulmonary TB or smear-positive pulmonary MDR-TB. If the planned Phase III studies show benefit it is likely that the regimen will be introduced and implemented. Optimally, a next generation test would allow for the diagnosis of TB disease and detection of drug resistance upfront to inform decision-making concerning the choice of first-line therapy, presence of additional second-line drug resistance and need for further testing.

Progress has been made recently with the development of new drugs for TB, and WHO has issued interim policy guidance for the use of both bedaquiline and delamanid for use as part of an appropriate combination regimen for pulmonary MDR-TB in adult patients. Besides individual compounds, new combinations of drugs are being tested in various Phase II trials, including earlier available anti-TB drugs which are currently being re-purposed (i.e. clofazimine, linezolid).

For the effective use of these new and re-purposed anti-TB drugs the development of reliable drug susceptibility testing (DST) methods are critical. Several members of the WHO TB Supranational Reference Laboratory Network have signed confidentiality and material transfer agreements with manufacturers of these drugs to allow for the development of standardized DST protocols and determine critical breakpoint concentrations. The preliminary results are encouraging and sufficient evidence is expected to become available toward the end of 2015 thus enabling WHO to recommend standardized DST methodology for these agents.

WHO strongly recommends for countries to establish a culture collection of strains isolated from patients on treatment with the new and repurposed anti-TB agents. This will generate a valuable resource that could potentially be used for the development of next-generation rapid molecular based DST methods. Furthermore, the collection of individual patient treatment outcome data as well as analyzing programmatic data would present an additional value allowing the interpretation DST data with treatment outcomes.
National Centres of Excellence for the SRL Network in the Russian Federation

During the meeting 6th Global Laboratory Initiative (GLI) Partners’ meeting convened by the Global TB Programme, World Health Organization, Geneva, Switzerland in 2014 a new category of membership of the WHO TB Supranational Reference Laboratory (SRL) Network was announced and the first National Centre of Excellence for the SRL network was designated.

A National Centre of Excellence for the TB Supranational TB Reference Laboratory Network (SRLN-CE) is a new category of laboratory specifically designed to recognize well performing laboratories in large middle-income countries (BRICS). A designated SRLN-CE has an equivalent status as a SRL within the network but primarily works to build-in-country laboratory capacity. Countries with laboratories currently eligible to apply for designation as an SRL-CE include Brazil, Russian Federation, India, China and South Africa. To be eligible for this designation, laboratories need to be nominated by their Ministry of Health to the WHO country office, establish a collaboration agreement with an existing SRL, undergo a laboratory assessment by WHO, and actively implement a quality management system towards accreditation.

Three laboratories were subsequently nominated by the Ministry of Health, Russian Federation to undergo an evaluation to assess their suitability for designation as a SRL-CE. The three nominated laboratories were as follows:

- Central Tuberculosis Research Institute (CTRI), Moscow
- Novosibirsk Tuberculosis Research Institute (NTRI), Novosibirsk
- Ural Research Institute for Phtysiopulmonology (UrRIPP), Yekaterinburg

Prior to the visit a questionnaire was distributed to each laboratory to collect information regarding staffing levels, workload and methods used as well as quality assurance mechanism and equipment in use. A standardised checklist was used to assess each laboratory. Each assessment was conducted with the participation of a laboratory expert nominated by the Ministry of Health.

The assessment mission looked at the technical performance of different laboratories and examined mechanisms to allow a standardized reporting system of epidemiological data in relation to incidence, sensitivity and specificity. The ability to monitor laboratory performance and allow inter-laboratory comparisons is dependent on ensuring laboratory quality through external quality assessment and through recording of quality performance indicators.

All three of the evaluated TB laboratories in Federal Institutes were recognized as being well performing facilities with a high quality infrastructure and high caliber of suitably qualified technical staff and are suitable for designation as National Centres of Excellence for the SRLN. Formal recognition of the new member laboratories will be announced during the Joint Partners Forum for strengthening and aligning TB diagnosis and treatment.
ISO 15189 Accreditation- Lessons to Share

From 2010-2014 TB CARE I, partners utilized the GLI Accreditation Tool to implement Quality Management Systems (QMS) in three National TB Reference Laboratories (NTRLs): Botswana, Benin, and Uganda. At the end of TBCARE I a guidance document was devised after a thorough review of the 5 year experience. A mixed-method approach was used to evaluate project implementation which included a desk review, a literature review, the collection of quantitative data on laboratory performance and the collection of qualitative data to identify factors that either drove the QMS implementation forward or, alternatively, hindered the process. This guidance document is designed to provide public TB laboratories with best practices when considering embarking on the challenging journey to ISO 15189 accreditation.

**IN SUMMARY:** The analyses identified 19 “best practices” which are necessary for efficient and successful implementation of QMS for ISO15189 accreditation. These 19 practices aligned with 2 primary areas: 1) laboratory organization (including management) and 2) laboratory resources. Resources form the basis of QMS and primary laboratory process in general. Sub-optimal resources will lead to low quality of services. The “catch 22” remains that quality resources often are dependent on external factors. Thus, an early assessment on the quality and availability of resources with the anticipation of potential challenges is essential before embarking on the ISO journey. Implementing QMS is a great endeavor that affects all aspects of the laboratory from basic processes to areas of management and leadership. Organizational skills are needed to facilitate and coordinate this process such that the change is achieved efficiently and effectively without total disruption of routine laboratory services to support national TB control.

Policy Framework for implementing tuberculosis diagnostics

WHO’s global strategy for TB prevention, care and control for 2015–2035 (known as the End TB Strategy) prioritizes the early diagnosis of TB, which should include the universal availability of DST, and systematic screening of contacts and high-risk groups. Therefore, all national TB control programmes should prioritize the development of a robust network of TB laboratories that have adequate biosafety standards, use modern methods of diagnosis, use standard operating procedures (SOPs) and appropriate quality assurance processes, and that have qualified and sufficient human resources; these priorities should be comprehensively addressed in national strategic plans.

On 27th April 2015, the Global TB Programme, World Health Organization launched its Policy Framework for implementing tuberculosis diagnostics which presents a structured framework for introducing WHO’s recommended diagnostic techniques for TB. It is expected that countries will adapt this generic policy framework within the contexts of their own epidemiological situation and resources. No single policy framework can address all issues in detail due to the diversity of resources and needs in different countries, and geographical variation in the epidemiology of TB, HIV-associated TB and drug-resistant TB. Therefore, this document aims at providing a generic framework or template for implementing TB diagnostics; it encompasses the managerial, technical and operational processes required for developing and implementing a national strategy for TB laboratories to ensure the early diagnosis of TB and universal access to DST, as well as to ensure there is systematic screening of contacts of people with TB and high-risk groups.
Global trends in procurement

Over ten million Xpert MTB/RIF cartridges have been procured since 2010, and 1.2 million cartridges were procured in the final quarter of 2014. South Africa remains the largest user of Xpert MTB/RIF, having procured 57% of all cartridges globally since 2010. Other countries have greatly increased their testing capacity in recent quarters, and 76% of GeneXpert modules globally are now located outside of South Africa.

GLI training module on Xpert MTB/RIF quality assurance

A consortium of GLI partners including FIND, KNCV, US CDC, USAID and WHO have developed 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, and are in PowerPoint format for country customization. Depending on the audience, modules may be selected and adapted according to need (e.g. basic users, supervisors, clinicians). Topics covered include: Overview of TB and diagnostics, biosafety, specimen collection, procurement, installation, Xpert MTB/RIF technology, results interpretation, reporting, troubleshooting, maintenance, and a clinical guide. Recently developed is a module on quality assurance, which describes the key components of a quality assurance programme including training and competence assessment, instrument verification, method validation, quality control and lot testing, quality indicator monitoring and external quality assurance/assessment (EQA). All modules are available in English, French, Portuguese and Russian, and may be downloaded at: http://stoptb.org/wg/gli/TrainingPackage_XPERT_MTB_RIF.asp

Key data and tools

Global procurement statistics as of 31 December 2014 (cumulative)

- Instruments: 3,763
- Modules: 17,883
- Cartridges: 10,013,600
- Countries: 116

Note: data reflect commodities procured under concessional pricing

Countries with largest numbers of GeneXpert modules deployed:

- South Africa: 4,260
- China: 3,876
- India: 750
- Brazil: 720
- Nigeria: 624
- Philippines: 492
- Uganda: 412
- Ethiopia: 388
- Zimbabwe: 388
- Bangladesh: 376
- Kenya: 374
- Pakistan: 336
FIND supports TB laboratory strengthening to accelerate access to diagnostics

As an international non-profit organization that supports the development, evaluation and implementation of urgently needed diagnostics for poverty-related diseases, FIND is concerned with all aspects of increasing access to new and emerging diagnostic technologies. In 2014, FIND was designated a World Health Organization Collaborating Centre in Tuberculosis Laboratory Strengthening and TB Diagnostic Technology Evaluation. The four-year appointment acknowledges the role FIND plays in evaluating and introducing new TB diagnostic solutions and building the laboratory capacity needed to effectively control TB.

New diagnostic technologies can only be successfully implemented within a well-functioning laboratory system. To contribute to TB laboratory strengthening goals, FIND works with key agencies and international and regional partners such as GLI and the newly-formed GLI-Africa, the African Society for Laboratory Medicine (ASLM), WHO AFRO and the US Centers for Disease Control (CDC). Over the years, FIND has built considerable experience in implementing new TB diagnostics, building laboratory capacity in diverse resource-limited settings and implementing Strengthening Laboratory Management Towards Accreditation (SLMTA), a task-based training and mentoring programme developed by CDC and partners.

TB labs appear to be lagging behind general clinical labs in many countries in progressing towards laboratory accreditation. To change this trend, GLI and partners developed the GLI Steeewise Process Towards TB Laboratory Accreditation, an online tool for TB laboratories. Another tool, the WHO AFRO SLIPTA checklist, is used to measure progress towards laboratory accreditation and is implemented by ASLM in the African region. The SLIPTA checklist is also used to measure the impact of the SLMTA programme.

FIND has developed a unique approach to strengthening TB laboratory quality management systems by aligning components of existing laboratory strengthening tools to focus specifically on the needs of TB labs working towards accreditation. The TB-SLMTA training programme includes TB-specific modules and guidance (e.g. biosecurity, quality assurance, sputum collection and transport) with TB-specific activities, examples and tools – all following the successful SLMTA format and interactive, task-based teaching approach, and linking projects to ISO 15189 standard requirements.

FIND has also developed a TB-specific checklist to measure the progress of laboratories towards accreditation. The FIND TB Laboratory Quality Management Systems Towards Accreditation Harmonised Checklist is a modified version of the WHO-AFRO SLIPTA checklist used by general clinical labs that incorporates the requirements of the GLI tool. This TB-specific checklist allows SLIPTA scoring and comparison of progress with non-TB labs in any country, and builds on the local capacity for SLIPTA auditing that is already present in many countries.

Since 2013, FIND has trained 62 people from 19 countries in three regions and graduated 51 trainers. Country implementation of the TB-SLMTA programme is ongoing in six countries with a total of 31 TB laboratories participating.
Upcoming events

5th Advanced TB Diagnostic Research Course
July 13-17, 2015 McGill University, Montreal, Quebec, Canada
Apply online at [www.mcgill-idgh.ca](http://www.mcgill-idgh.ca)

46th Union World Conference
2-6 December 2015, Cape Town, South Africa
Conference website: [http://capetown.worldlunghealth.org/](http://capetown.worldlunghealth.org/)

African Center for Integrated Laboratory Training (ACILT) provides integrated hands-on training courses to expand laboratory capacity in Africa for the monitoring of major infectious diseases including HIV/AIDS and TB.

Courses provided by ACILT

- Early Infant Diagnosis (EID)/Viral load: 1-10 June, 17-26 Aug, 5-14 Oct, 23 Nov-2 Dec 2015
- TB Culture and Identification: 31 Aug – 11 Sep 2015

For more information, please contact Debbie Pretorius at debbiep@nicd.ac.za or +27 11 885 5305

JOINT PARTNERS FORUM

FOR STRENGTHENING AND ALIGNING TB DIAGNOSIS AND TREATMENT

GLI / GDI Partners Forum

Organized by the World Health Organization (WHO) Global TB Programme
WHO Executive Board Room, Geneva, 27-30 April 2015

Key WHO publications


New Structure of the GLI Core Group

Rick O’Brien, Rumina Hasan, Sabine Rüsch-Gerdes and Teshayneh Messele are gratefully acknowledged for their contributions to the achievements of GLI over the past several years. Their terms as members of the GLI Core Group ends on 1st May 2015 and they will be replaced by five new members.

The selection of new members was performed by the current Core Group members according to the GLI operating procedures ensuring that membership is balanced by gender, region, disease burden and GLI constituency. The elected candidates are as follows:

- Civil Society: Wena Moelich, South Africa
- MoH/NTP Manager from high-burden country:
  - Joseph Sitienei, Kenya
  - Alena Skrakhina, Belarus
- NRL/SRL: Sabira Tahseen, NRL Pakistan
- Partner: Martina Casenghi, MSF

Continuing members for 2015-2016:
Thomas Shinnick; Armand van Deun; Amy Piatak; Heather Alexander; Maarten van Cleeff; Maria Alice Telles; Alaine Umubeyi Nyaruhiira; Levon Gagnidze; Paul Klatser; Richard Lumb; Heidi Albert.

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