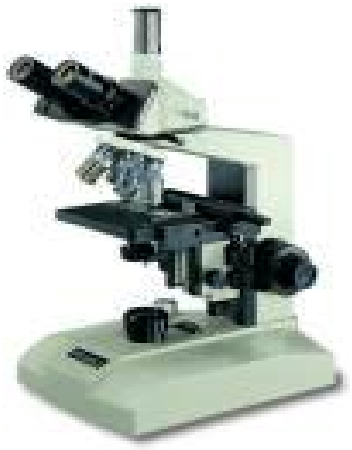
Importance of the laboratory in TB control



Introduction

Substantial progress has been made in recent years towards achieving the targets for global tuberculosis (TB) control. The current targets for the end of 2005, set by the World Health Assembly,[1,2] are to detect 70% of new sputum smear-positive TB cases and to cure 85% of them. The latest data show that the rate of treatment success (82% in 2003) is within reach of the critical targets. However, despite an increase in the rate of case detection (53% in 2004), it is evident that efforts must be intensified to detect more TB cases and reach the 70% case detection target in all countries.

Laboratory network performance remains poor, despite the fact that TB diagnosis and monitoring of treatment progress relies heavily on bacteriological examination of clinical specimens. However, by responding quickly and providing high-quality services at the laboratory level, improvements in the early diagnosis of TB cases will be achieved, thus decreasing the risks of further disease transmission, unfavourable outcomes and, in the worst cases, death.

No reliable laboratories = No detection of TB patients = No DOTS = No TB control

Situation analysis

Suboptimal performance of TB laboratories hinders the availability and accessibility of high-quality services to all people presenting with symptoms of TB disease. Laboratory staff suffer from feeling undervalued and overwhelmed. As a result, low motivation and dedication cause obstacles that are often reflected in weak or poor partnerships with the national TB control programme (NTP). In many cases, this results in insufficient allocation of financial resources towards laboratory operations and expansion activities. Laboratory technicians can feel isolated and disconnected from the important TB control planning processes. This has a cost – in terms of deepening the human resource crisis that nearly all low- and middle-income countries now face in TB control.

TB control, especially that of multidrug-resistant TB (MDR-TB), requires sound implementation of DOTS to prevent the onset of new MDR cases, and a careful introduction of second-line anti-tuberculosis drugs with adequate laboratory support to stop the creation and circulation of resistant strains. However, currently in 4 of the 22 highest TB burden countries (HBCs), there is no functional laboratory network, and 7 of these HBCs do not have a fully functional national reference laboratory

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1 Resolution WHA44.8. Tuberculosis control programme. In: *Handbook of resolutions and decisions of the World Health Assembly and the Executive Board*. Volume III, 3rd ed. (1985–1992). Geneva, World Health Organization, 1993 (WHA44/1991/REC/1).

2 *Stop Tuberculosis Initiative. Report by the Director-General*. Fifty-third World Health Assembly. Geneva, 15–20 May 2000 (A53/5, 5 May 2000); available at: www.who.int/gb/ebwha/pdf_files/WHA53/ea5.pdf).

(NRL). Implementation of quality-assurance programmes for smear microscopy is unsatisfactory, i.e. 4 out of 22 of HBCs do not have an external quality assurance (EQA) scheme, while other countries have reported its limited implementation. In addition, laboratory infrastructure and technical capacity to perform diagnostic tests, particularly culture and drug susceptibility testing (DST), are suboptimal.

Laboratory subgroup

To address these and other laboratory issues, the Subgroup on Laboratory Capacity Strengthening (SLCS) was established in August 2002 to assist countries in extending the provision of reliable, high-quality diagnostic services. The subgroup consists of members of the supranational TB reference laboratory network, other laboratory experts, and representatives from international and national organizations involved in strengthening and maintaining proficient TB laboratory diagnosis. The Subgroup secretariat is based in WHO, and SLCS members meet annually to discuss important strategic and technical issues.

Additionally, WHO has developed a four-year strategic plan (2006–2009) for the improvement of laboratory capacity, ensuring that laboratory networks will actively support the diagnostic procedures underlined in the new *Stop TB Strategy*[3] and *The Global Plan to Stop TB, 2006–2015*.[4] As laboratory services expand into additional areas such as TB/HIV and MDR-TB, universal access to quality-assured sputum smear microscopy should remain as the priority. However, capacity building for culturing *Mycobacterium tuberculosis* and for DST is equally key to progress in TB control. This will require the development of standardized operational procedures (SOPs) for culture and relevant training material to strengthen the technical capacity and performance of laboratories. In addition, proper monitoring and evaluation tools need to be developed. Strengthening of laboratory capacity to perform culture will require a substantial increase in human and financial resources and the development of closer, more effective collaboration between NTPs, laboratory experts and partner institutions.

Services for culture and DST should be introduced in a phased manner, at appropriate referral levels of the health system, to ensure accessibility of those services to eligible populations by 2015. All expansion efforts must be based on a laboratory network that maintains a high quality of service by regular training, supervision and support, and motivation of laboratory staff. This can only be achieved with technical support to countries from WHO, partners and international laboratory experts.

The laboratory strategic plan focuses on the following aspects:

Situation analysis via assessment of the laboratory network in global and regional HBCs
Country support in planning, training and identification of funds
Improvement of AFB smear microscopy
Standardization of laboratory materials, including training curricula
Developing/strengthening culture and DST capacity
Facilitating the transfer of existing modern technology to resource-limited settings
Monitoring and evaluation of laboratory improvement
Supporting the development of an operational research agenda and of new diagnostic tools

The strategy provides a framework and clear directions to address these urgencies at the international, regional and country levels. The document was endorsed by the SLCS during its annual meeting in October 2005 in Paris, France.

[3] Available at www.stoptb.org.
[4] *The Global Plan to Stop TB, 2006–2015*. Geneva, World Health Organization, 2006 (WHO/HTM/(WHO/HTM/STB/2006.35)

Strategy implementation status and constrains

The importance of the laboratory in TB control is now gaining prominence. More laboratory assessment missions are taking place, and technical assistance and guidance for improvements in TB laboratory performance are being provided. Standardized training packages on sputum smear microscopy, culture and DST are under development. Related training programmes are supporting these activities. Furthermore, a number of technical documents and guidelines for TB laboratories are in progress, e.g. SOPs, quality assurance for culture and DST, compendium of performance indicators.

In 2004, the DOTS Expansion Working Group declared laboratory strengthening its highest priority for TB control.[5] There is increasing recognition, for example in the *Stop TB Strategy*[3] and *The Global Plan to Stop TB, 2006–2015*,[4] that laboratory services are often the weakest link in DOTS implementation.

Unfortunately, current resources are insufficient to tackle the challenges and to properly support regions and countries in implementing their workplans for laboratory strengthening.

Unless urgent attention is focused on expanded laboratory efforts for quality-assured sputum smear microscopy, culture and DST, the targets set for global TB control and the TB-related Millennium Development Goal (Goal 6; Target 8)[6] will not be reached.

Sufficient financial and human resources must be available to continue providing leadership, coordination and guidance to accelerate expansion of laboratory capacity, including access to culture and DST. Since these activities will also serve improvements in the diagnosis and management of MDR cases and TB/HIV coinfected patients, as indicated in the *Stop TB Strategy*[3] and *The Global Plan to Stop TB, 2006–2015*,[4] strong financial support to the laboratory strengthening plan is essential.

Critical needs for 2006–2007

Development of standardized training materials and technical guidelines

There is an urgent need to develop uniform and comprehensive training packages and technical guidelines that promote the policy and recommendations of WHO and the International Union Against Tuberculosis and Lung Disease. In collaboration with partner organizations, the development of an AFB smear microscopy package has already been initiated. However, additional financial resources are necessary for the finalization of this project, including product design, reproduction and distribution.

In order to increase the quality of laboratory services, two additional training packages will be developed: EQA for smear microscopy and EQA for culture. In addition, TB laboratory guidelines will be revised according to the *Stop TB Strategy*[3] and *The Global Plan to Stop TB, 2006–2015*.[4]

Should funds be available, the AFB microscopy training package will be produced and distributed in the second quarter of 2006. It is anticipated that EQA training packages and TB laboratory guidelines will be finalized by the end of the second quarter of 2007.

Budgetary requirements: US$ 200 000

[5] *Final report of the 5th meeting of the DOTS Expansion Working Group, Paris, France, 27-28 October 2004*. Geneva, World Health Organization, 2005 (WHO/HTM/TB/2005.358; available at www.stoptb.org/wg/dots_expansion/meetings.asp).

[6] See www.who.int/mdg.

Organization of training courses for laboratory management, culture and DST

To improve the technical and managerial capacity of laboratory personnel in collaboration with partners, the following training courses will be organized:

- *TB laboratory management*. To increase the managerial capacity of NRL heads and senior personnel
- *Culture and DST*. Capacity building/strengthening of culturing of *M. tuberculosis* is necessary to detect more TB cases and ensure correct identification of resistance patterns for proper management of MDR cases.

Funds for development of these training materials have been identified, and the development process is already in progress. However, support is needed to organize 5 international training sessions: 2 on TB laboratory management and 3 on culture and DST (1 session in 2006; 2 sessions in 2007).

The training will be organized by WHO HQ in collaboration with partner organizations and laboratory experts. To facilitate the practical sessions, the courses need to be organized in a facility with access to the laboratory. The venue should therefore be the premises of either the NRL or the supranational TB reference laboratory.

Budgetary requirements: US$ 500 000

Increasing the pool of laboratory experts capable of assisting countries in improving their laboratory performance

WHO, in collaboration with partners, has secured resources to develop training materials and organize the first training course for laboratory consultants. However, to increase the pool of laboratory experts available to work closely with partners and national programmes on improvements in TB laboratory services, the laboratory consultant/newly developed training course should be organized on a regular basis. It has been estimated that to address urgent demands for technical assistance, 3 additional training courses should be organized, 1 in 2006 and 2 in 2007.

Budgetary requirements: US$ 300 000

Support to countries for capacity strengthening

The aim is to evaluate the structure and performance of the TB laboratory network and to assist countries with strengthening laboratory capacity, in order to extend the provision of reliable, high-quality laboratory services in conjunction with NTPs through:

- integrating laboratory network functions with the regular operations of an NTP;
- implementing systematic and efficient quality-assurance schemes;
- establishing good laboratory practices, including SOPs;
- establishing culture drug susceptibility testing capacity; and
- developing operational research ability in various diagnostic areas.

These activities will be performed in collaboration with technical partners and laboratory experts. The assistance will focus primarily on countries that fulfill the following criteria:

- global and regional HBCs
- political commitment
- availability of plans for laboratory improvements
- existence of plans for implementation of DRS and DOTS-Plus projects.

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It is anticipated that 20 assessment and monitoring missions will be organized in the forthcoming biennium. The support efforts will focus on the following countries that meet the aforementioned criteria: **AFR** (Ethiopia, Mozambique, Nigeria, Uganda, Zimbabwe); **AMR** (Brazil, Ecuador); **EMR** (Egypt, Pakistan); **EUR** (Kazakhstan, Kyrgyzstan, Russian Federation, Uzbekistan); **SEA** (India, Indonesia); **WPR (**Cambodia, China, Philippines, Thailand, Viet Nam).

Budgetary requirements: US$ 250 000

Coordination of activities and technical assistance

To ensure proper collaboration with partners, WHO regional/country offices and countries, it is essential that all activities on laboratory improvements are coordinated in a systematic manner. WHO HQ will compile and consolidate information on related projects/activities from laboratory experts, partners and WHO regional/country offices. Furthermore, NTPs will be contacted to identify their needs/areas for assistance and priorities. It is expected that these coordination activities will strengthen global collaboration, prevent duplication of effort, ensure efficient use of available human and financial resources, and ensure continuity of support provided to countries.

WHO will also assist countries in the development of their plans for laboratory improvements, and will monitor their implementation status. Technical assistance will be provided to countries on laboratory-related issues on an as-needed basis.

Furthermore, resources are required for the monitoring of the overall performance of laboratory networks, for the evaluation of their achievements and to identify needs for improvements.

Budgetary requirements: US$ 300 000