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research, education, development

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Mission Report

July 11 to July 18. 2018

Expert Dr. Harald Hoffmann

Supranational Reference Laboratory Munich-Gauting

Abbreviations

ATT	Anti-tuberculosis therapy
BSC	Biosafety Cabinet
DR-TB	Drug resistant TB
DST	Drug susceptibility testing
GENETUP	German Nepal Tuberculosis Project
GFATM	Global Fund
IQC	Internal quality control
KTW	KuratoriumTuberkulose in der Welt e.V. (non-profit NGO supporting the Nepalese NRL since >30 years
MGIT	Mycobacteria growth indicator tube (Becton Dickinson, USA)
MIC	Minimal Inhibitory Concentration
NSP	National Strategic Plan
NTC	National TB Center
NTP	National TB Program
SCI	Save the Children, Principle Recipient of Global Fund Grants in Nepal
SRL	Supranational Reference Laboratory
SRLN	Supranational Reference Laboratory Network
TA	Technical assistance
TB	tuberculosis
WHO	World Health Organisation

Background

Lack of diagnostic capacity is a crucial barrier preventing an effective response to the challenges of tuberculosis (TB) and drug-resistant TB (DR-TB), with only slightly more than 20% of the estimated burden of MDR/RR-TB patients currently being detected. This is particularly true in Nepal. Efficient response to diagnostic challenges of TB and DR-TB requires urgent and massive scale-up of laboratory services requiring a paradigm shift in providing laboratory policy guidance, technical assistance, and knowledge transfer. Lack of laboratory capacity is the main bottleneck also for surveillance of resistance to anti- TB drugs (DRS) which is a cornerstone of any effective TB control program. Establishing, equipping, financing, and ensuring sustainability of appropriate laboratory networks are challenging, complex and expensive. The establishment of well-maintained TB laboratories with appropriate bio-safety measures and equipment for quality assured testing presents the greatest challenges for both initial financing and sustainability. Strengthening TB laboratories requires not only the introduction of the modern diagnostics at various levels of the network, but also ensuring the quality of every step in the diagnostic process, including sample collection, receipt and registration of samples at the laboratory, testing of samples and recording and reporting of the results. TB Supranational Reference Laboratory Network (SRLN) is supporting the World Health Organization (WHO) Global Project on anti-TB drug resistance surveillance and with the objectives to estimate the magnitude of drug resistance globally and provide data to inform WHO policy decisions.

Since 1994 the SRLN continues to be a key technical resource in support to the strengthening of the laboratory capacity in countries. The SRL Munich-Gauting, one of the founders of the SRLN, is partner of the Nepalese National Reference Laboratory and National TB program since long before the

establishment of the SRLN and is linked to the NTP in Nepal by a formal Memorandum of Understanding with the Ministry of Health. In this MoU, the SRL Munich-Gauting is determined as a long-term provider of highly specialized technical assistance for the scale up of laboratory services in Nepal and as the preferred technical partner to develop national laboratory capacity for TB and to strengthen drug-resistant TB surveillance and diagnosis. The long-term history of interaction and assistance of the Nepalese TB program and the SRL Munich-Gauting is a strongly facilitating factor.The SRL Munich-Gauting is assisting Nepal with the development and implementation of a National Strategic Plan, expansion of routine diagnostic services, technology transfer and implementation of novel, rapid TB diagnostics, external laboratory quality assurance, and training. Additionally, it is providing extended and highly specialised technical assistance that no other technical partners or partner organizations can make available.

Specific areas of technical assistance required to build laboratory capacity in Nepal include the following:

- Developing and/or strengthening national TB laboratory strategic plans;
- Strengthening laboratory capacity at central, regional and peripheral levels for TB detection, determination of drug resistances, and treatment monitoring, including culture, drug susceptibility testing (DST) and rapid molecular methods;
- In-country hands-on training with the monitoring of performance with implementation of these new tools through quality assurance mechanisms and follow-up technical assistance visits;
- Strengthen implementation of laboratory diagnostics by guiding improvements in specimen transport mechanisms, logistics and commodity management and recording and reporting systems
- Mentoring junior/support consultants to provide technical assistance missions; and
- Assisting reference laboratories implement a quality management system towards accreditation.

Achievements of the collaboration of the SRL Munich-Gauting with the Nepalese NTP, Nepal

For yet three decades, the SRL Gauting is providing major financial support as well as intermittent technical assistance to the GENETUP department of the NRL which is currently the only operating DST unit in Nepal due to an ongoing refurbishment of the NTC laboratory. Upon demand of its partners in the country and with funding from WHO / USAID, the SRL is intensifying its technical assistance to the country since three years and expanding its activities also to the NTC by

- providing assessments and recommendations for the refurbishment of the NTC laboratory (NRL department) which is currently ongoing, and the regional culture laboratory in Pokhara which is planned for near future;
- assisting with the implementation of a common quality management system in both NRL departments;
- training staff in diagnostic techniques and internal quality control;

- planning new premises for the GENETUP department of the NRL and helping NATA with fund-raising for its construction;
- helping the NTP with the development of a National Strategic Plan by drafting a chapter of TB laboratory diagnostics, proposing an Xpert MTB/RIF roll-out strategy, reviewing the draft versions, checking forecast calculations and presumptions, and providing budget estimates for the laboratory sector.

In the three most recent missions, experts of the SRL-Munich-Gauting have concretely

- provided TA with the development of the National Strategic Plan for the years until 2021 as well as with the planning of NSP implementation,
- helped with the planning of the refurbishment of the NTC laboratory premises,
- developed together with the local partners an improved and more modern QMS structure with a complete set of technical SOPs and recording documents and helped set-up identical QMS structures in both NRLs,
- harmonized the QM systems of GENETUP and NTC,
- improved the system of internal quality control of DST and trained specialists of both NRL departments in this technology in the SRL's institute in Gauting, Germany,
- helped with the planning of an optimal GeneXpert laboratory network.

Aims and terms reference

During the briefing in the NTC department of the NRL changes of the beforehand drafted ToR were requested by the heads of the NRL department. The final aims of the mission were:

1. **Monitoring of achievements in NSP implementation**
   In 2016 the NSP was developed in collaboration of NTP, WHO and SRL. In the 2017's mission, Dr Hoffmann together with his local partners in the NTC have developed a strategy how to implement the NSP in the laboratory sector. During the actual mission, the achievements in NSP implementation were assessed.
2. **Review of refurbishment and re-organization of NTC laboratory**
   The NTC laboratory has meanwhile been refurbished partly following the recommendations from previous missions. During is actual mission, Dr Hoffmann assessed the refurbishment and provided recommendations for improvement and commissioning of diagnostic services in the new environment.
3. **TA with the implementation of an equipment registry in the NTC laboratory**
   In two previous missions, the SRL partner has provided TA with the implementation of a Quality Management System. The registry of lab equipment is the next step with highest priority for further QM implementation.

4. **Implementation of training contents conveyed in the SRL Gauting, Germany**

   Two weeks before the expert's mission, laboratory specialists from both NRL departments (NTC & GENETUP) were trained at the SRL Gauting, Germany, to perform extensive and quantitative quality controls of DST drug solutions. Those training contents were planned to be implemented in the Nepalese NRL during a practical on-site training.

5. **Review of QM activities since the most recent on-site training in March**

   In three on-site and one international training, QM commissioners from both NRL departments were trained in the implementation of identical quality management systems with the ultimate aim to have the same structure of the system and equal documents in both NRL departments. In a recent mission, a QM expert of the SRL partner provided advanced QM trainings in both NRL departments. In the current mission the SRL expert planned to review progress and challenges since the last training in further QM development.

6. **TA with further optimization of the diagnostic TB laboratory network**

   Building up an efficient, hierarchically organized, and better integrated TB laboratory network is one of the top ranked projects in the NSP. During this mission, the SRL expert planned to discuss and review progress and next steps in the network development with the NRL team.

1. Monitoring of achievements in NSP implementation

Background: As confirmed by the NTP director during the briefing meeting on July 13th, 2018, the implementation of the NSP endorsed in 2017 is one top priority of the National TB program in Nepal. In 2017, the SRL partner has assisted with the development of an NSP implementation plan. A road map was drafted considering all major topics of the NSP ranked by their priorities and shared with the NRL, NTP, national and international stakeholders.

Key findings: Several key topics of the NSP have already been endorsed by the NTP. Among others, those included:

- A national TB prevalence survey has been launched and 21 out of 99 planned clusters had already been completed. Results are expected by fall 2018.
- With financial support from the Global Fund and technical support from FIND, Dr Praveen has joined as temporary consultant the team of the NRL assisting Ghimire Ghorkarna. He is helping the NTC with planning and realization of the refurbishment of the NTC laboratory and the implementation of DST in MGIT.

Challenges identified:

- The prevalence survey risks to stagnate due to the lack of culturing capacities. GENETUP has to interrupt culturing until Biosafety cabinets are maintained.

- Maintenance plans for the key equipment have not yet been established. Maintenance and filter exchange of the bio-safety cabinets (BSC) of the GENETUP laboratory were due in the first quarter of 2018. Shortly before the mission, one BSC signaled "100% filter blockage" and had to be removed from operation. Shortly after, the second BSC also signaled filter blockage.
- Of the ten TOP priorities defined in the NSP implementation roadmap developed in the 2017 mission, seven are not yet attacked.

Key Activities:

- Together with the head of the GENETUP laboratory, we checked the BSCs with the simple tools which were available on-site. It was found that one of the two BSCs was still providing sufficient safety for the staffbut not for the material.

Key Recommendations:

- Review and revise the NSP implementation roadmap of 2017 and re-adjust its prioritization and the time-plan. Plan for the implementation of those items of the NSP which have not yet addressed. The ten top-priorities defined in the implementation roadmap were:
    - Assignment of a TB laboratory network manager,
    - Strengthening the logistics / courier system,
    - Optimization of Xpert MTB/RIF diagnostics,
    - Service optimization of National Reference Laboratories,
    - Lab network and service optimization of culture and microscopy laboratories,
    - Bio- / work-safety, infection control, waste management,
    - Quality management & assurance,
    - Human Resource Capacity Building,
    - Data management,
    - M&E (= monitoring and evaluation).
- Decommission the defect BSC in the GENETUP laboratory and adjust procedures with relevant infection hazard for the staff, i.e. culturing and DST, to the reduced capacities of a single BSC until both BSCs are maintained ad certified according to relevant standards.
- Make sure that the call for tender offers for BSC maintenance is sufficiently specific to get a certification of adequate quality in order to protect the lab staff from unnecessary risk of infection. Ask the SRL partner to provide TA with the tender preparation. Since the use of the tender documents for BSC maintenance tenders, the Central Asian NRLs have tremendously improved the quality of the certification process and thereby strengthened laboratory safety.
- Immediately resume culturing of specimens for the prevalence survey in the NTC in order to assure appropriate continuation of the prevalence survey. Specimens which were previously sent to GENETUP for culturing should be redirected to the NTC.

Ad 2. Review of refurbishment and re-organization of NTC laboratory

Background: The NTC laboratory has been refurbished following recommendations of the SRL partner. The SRL-partner assessed the new premises and provided recommendations how to further improve infrastructure and how to implement diagnostics in the rooms in a most efficient way.

Key findings:

- Refurbishment works were close to finalization at the time of visit.
- Major recommendations of previous reports were realized. Noteworthy, the pre-amplification area has been separated from (post-) amplification areas of which ceilings have been closed which is minimizing the risk of DNA cross-contaminations.
- BSCs of decontamination have been connected to the ventilation system.
- The liquid culture and DST laboratory room has been equipped with ventilation, new BSCs, and MGIT machines. Soon, an autoclave shall be added. Then, the NRL is going to commission culture and DST in MGIT.
- The work-flow will most likely be substantially more efficient with the new arrangement of rooms and processes.

Challenges identified:

- BSCs are incorrectly connected to the room ventilation system.
- In one BSC, instead of a thimble above the canopy, pressure interruption has been realized by simple opening in the exhaust air duct. This leads to awhistle effect of laminal air hitting a sharp edge and creating turbulences. Those are even aggravated by air flowing in the duct through the same opening. The resulting effects is sketched in figure 1.

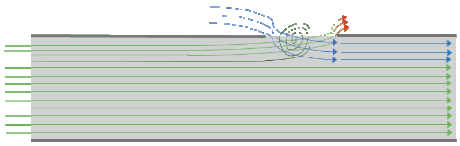

Fig 1: Turbulences and escaping air at sharp edged openings in air ducts with laminal flow.

- The other BSC is connected with a *duct in duct* connection (sketched in figure 2). A damper is positioned right above the exhaust filter of the BSC. This construction bares several risks:
    - The opening around the inner duct might be too small leading to uncontrolled under-pressure in the exhaust air duct which would then suck air from the BSC. This would reduce the content in the pressure chamber and thus the downward air flow with the effect of reduced material safety.

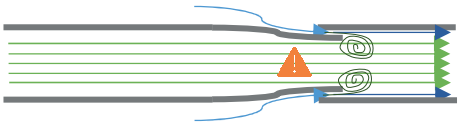

Fig 2: Duct in duct connectionwith the risk of increase resistance in the exhaust airways due to turbulences or narrowed airways.

    - Resistances from the damper or created by turbulences in the duct connection might be too strong leading to reduced outflow of air which would directly affect staff safety.
- In-flow air is not dust-filtered. Particularly during the hot season, air in Kathmandu can be strongly polluted by particulates and dust. This rapidly congests the relatively expensive HEPA filters of the BSCs which require replacement by highly specialized bio-engineers. Dust filters e.g. integrated in the entrance door where obviously the vast majority of air flows in would tremendously reduce pollution in the culture laboratory with the positive effects of

  - Life extension of HEPA filters, BSCs, centrifuges and other sensitive equipment,
  - Reduction of culture contaminations.
- Several racks, tools and materials are made from wood which cannot be effectively disinfected.

Activities: The correct design of BSC connections to room ventilation systems has been explained to the head of the NTC laboratory and his temporary assistant.

Recommendations:

- Revise the ventilation system and insist on a correct installation of the exhaust air ducting fulfilling WHO recommendations (see figure 3).
- Plan the installation of an inflow-air pollution filter (level of filtration M6 or F7).
- Immediately start using the fluid culture / MGIT room(particularly for the prevalence survey)independent from availability of the waste autoclave. Develop a waste disposal concept which reduces the need of this autoclave and allows to store waste until its arrival.
- Only sputum tubes / primary specimen containers and positive culture tubes require autoclaving. Positive cultures shallbe stored for at least six months for potential retrospective demands such as DST, molecular resistance testing, genotyping. Thus, for the first six months only used sputum containers need to be autoclaved before disposal.
- Only use disinfectable racks and tools in your medium and high risk TB laboratories. Replace all woken racks and tools by metal material and regularly disinfect it.

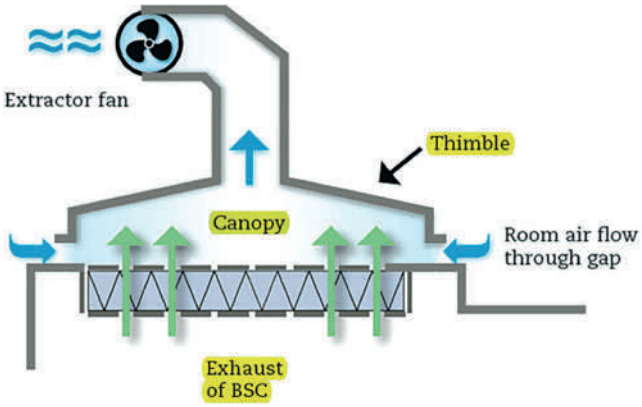

Fig 3: Design of exhaust air connection to the room ventilation system as recommended by WHO (TB laboratory biosafety manual, WHO/HTM/TB/2012.11)

Ad 3. TA with the implementation of an equipment registry in the NTC laboratory

Background: A comprehensive inventory of all laboratory equipment is one of the mainstays of laboratory management. Planning of maintenance, budgeting, future investment, service expansion and the laboratory internal quality management system all require a complete and up-to-date list of equipment. This should be available not only for the two departments of the NRL but also for the complete TB laboratory network.

Key findings: The GENETUP department of the NRL maintains an inventory of its equipment since several years. It has implemented SOPs for all major equipment in use. In both departments, manuals and documents are available for most of newer equipment. The NTC department has drafted several equipment SOPs.

Challenges identified:

- The NTC department of the NRL has not yet compiled a list of its equipment. SOPs are partly drafted though not yet fully implementedfor the available equipment.
- In both departments, manuals are lacking for the majority of equipment which is older than three years.

Activities: During the mission, the SRL partner trained and assisted together with the heads of both NRL departments, the QM commissioner and the laboratory team of the NTC department to register, number, labell all equipment. The inventory was designed in a structure identical to the one of GENETUP. It is provided in **ANNEX 2** together with photographies as examples how the system is set up.

Recommendations:

- Continuouslymaintain and update the equipment inventories of the NRL.
- Starting from both NRL departments, equipment inventories should be elaborated for all TB laboratories of the network and centralized in the NTC.
- Search the internet or contact the manufacturers for comprehensive manuals for all equipment that also requires SOPs (see next bullet point).
- Develop SOPs for each equipment that is used for heating (e.g. incubator), cooling (e.g. refrigerators, freezers), measuring (e.g. balances), analytic processes (e.g. cyclers, Bactec™ MGIT™ 960), fluid transfer (e.g. pipettes), bio- and work-safety (e.g. BSCs), sterilization (e.g. autoclaves), and complex electronic devices (e.g. anemometer, dish washer). SOPs are not necessarily required for minor equipment such as vortexes, sputum shakers, printers etc. Equipment SOPs shall include information regarding daily, weekly, monthly and yearly maintenance requirements, cleaning and disinfection. A trouble shooting section should provide (links to) information regarding the handling or errors or alarms.
- Based on the centralized equipment inventories of all TB laboratories of the country,
    - annual maintenance plans should be developed for the NRL, all culture and GeneXpert laboratories;
    - annual investment plans and budget needs should be determined for maintenance, replacement and new lab equipment.

Ad 4. Implementation of training contents conveyed in in the SRL Gauting, Germany

Background: The drug susceptibility testing in MGIT checks for growth of TB bacteria in the presence of an anti-tuberculotic drug in its critical concentration. The drug concentration is adjusted by diluting (1:84 v/v) a concentrated “utility solution” in the MGIT medium. For second-line drugs, the utility solution is home-brewed in each laboratory by dissolving the required amount of drug powder in distilled water. During this process, several errors or deficiencies can occur which later-on severely impact DST results. For example, the drug powder can be spoiled (e.g. too old or wettened) and have lost activity or it can have been weighed out in a too little amounts (e.g. 10x less than required). In all those cases, the activity of the drug would be lower and the MIC consequently higher than expected. Bacteria could falsely pass the threshold of resistance (resulting in false resistant results). In cases of

increased drug activity in the medium (e.g. too much powder weighed, errors in the factor calculation) resistant bacteria with MICs slightly higher than the threshold would not grow and falsely declared susceptible by MGIT. Both types of false results have tremendous impact on patient management and treatment outcome.

The currently used internal quality control are not suitable to prevent such events. It only consists in the exposure of the fully susceptible *M. tuberculosis* reference strain H37Rv to the drug containing test medium. When the strain does not grow, IQC is considered passed. This does not allow to identify too high drug activities in the test tube and thus not prevent false susceptible results. Since the MICs of H37Rv mostly arevery low, deviations towards too low drug activities would also not be determined. In a training at the Institute of Microbiology and Laboratory Medicine (IML) in Munich-Gauting, Germany, specialists of both Nepalese NRL departments were trained to perform a quantitative quality control of each drug solution. Aim of this mission was to implement this improved internal quality control in both NRL departments.

Key findings: The specialists already had all knowledge and skills to implement the IQC. All required equipment was available. The H37Rv had been provided by the SRL partner with previous external quality controls and was still available and vital.

Challenges identified:

- The local conditions were quite different to the conditions in the IML Munich-Gauting. Therefore, some work-steps had to be adjusted.
- Filters and suringes for sterilization of small fluids are missing.
- Some small equipment (spatula etc.) are missing. GENETUP will order those item over the NTC.

Activities:

- Guidance and technical assistance was provided to assist both NRL departments with the on-site implementation of the IQC. The training has been performed with a single drug. The same procedure can then 1:1 be transferred to other drugs.
- The SRL expert has developed an excel-tool which automatically calculates all weights and concentrations for the preparation of the IQCand an SOP for the interpretation of the results (see extra Excel file in **ANNEX 3**).

Recommendations:

- Further implement the IQC for all other drugs.
- The SRL will prucure and provide the required filters for fluid sterilization.
- As a basic validation procedure, determine your MICs three times with H37Rv for all SLD that are tested in the Nepalese NRL.
- Share the IQCMIC values with the SRL partner who will in returnprovide the results from all other NRLs allowing all participants to better assess the outcome oftheir IQCs.

Ad 5. Review of QM activities since the most recent on-site training in March

Background: In March 2018, Mrs Elisabeth von Rudno, the QMS expert of the *KTW*, has performed a structured audit of the QMS in the Genetup department of the NRL. The audit report is attached in **ANNEX 4**. Following the audit, she has provided targeted training. During a separate training in the NTC department the expert assisted with the structuring of the QMS and the development of electronic QM documents. Aim of the current mission was to assess the progress in both departments since the last training.

Key findings:

- Many QMS documents are available in electronic form in both NRL departments and only wait for implementation.
- The QMS in GENETUP has well developed since recent visits and has almost reached the one star level on the SLMTA scale.

Challenges identified:

- In the NTC, QMS development has been interrupted since the last training mainly for two reasons, i.e.
    - due to the long lasting refurbishment of the NTC,the laboratory was closed for several months,
    - the QM commissioner of the NTC has a multitude of other quite challenging tasks and responsibilities including the GeneXpert laboratory network coordination and the implementation of new GeneXpert machines, the focal point for SCI and GFATM, and performing TB diagnostics in the NTC.
- In GENETUP, QMS development has slowed down for the major reason of too much diagnostic work due to the on-going prevalence survey.

Activities:

- The Expert followed up on achievements of theQM commissioner in GENETUP since the recent QM audit. Results are presented in the **ANNEX 4**.
- Together with the QM commissioner and the head of the NTC laboratory, the expert discussed causes and potential solutions for the delay of QM development in the NTC. The partners agreed that a major cause of the slow progress lies in the accumulation of a multitude of tasks at the position of the QM manager.

Recommendations:

- Give much higher priority to QM development. The integration and use of a comprehensive QMS in routine diagnostics significantly improves quality of services, attracts international donors and scientific partners, and tremendously helps the laboratory-, the TB laboratory network- and the NTP management to plan, budget and invest.
- In the NTC,

- adopt and implement all SOPs which are already available in electronic form. The implementation goes through the following steps:
  - Read, review and revise the available versions;
  - Rename, number, label and print the revised SOPs;
  - Let the head of the laboratory confirm the scientific content of the SOP by his signatures;
  - Let the QM commissioner confirm form and structure of the SOP by his signatures;
  - Provide a short staff training on the content of the SOP;
  - Ask every lab worker whose work might be affected by the SOP to read and sign the reading proof;
  - Supervise the work of the lab staff in routine diagnostics and confirm in a short protocol form that everybody is correctly following the SOP.
- Re-address tasks and responsivities in the laboratory team. QM management in addition to diagnostic work is a full-time job. Additional tasks endanger the progress of QMS development.

- In GENETUP,
  - short-term finalize and implement all SOPs which are already available as drafts;
  - follow-up on the deviations identified / reported and respond line by line to the recommendations provided by E. von Rudno in her audit report from March 2018.
  - Start with the development and implementation of management SOPs. Since procurement of materials and external services is a crucial factor for successful laboratory work, it is considered most useful to start with procurement SOPs.
    - Procurement SOP 1: Standard procedures and forms for ordering items and external services through (i) NTC, (ii) GFAMT, (iii) external partners, (iv) directly with institutional budget;
    - Procurement SOP 2: Standard procedures and forms for the receipt, control, documentation and recording of deliveries of material or external services;
    - Procurement SOP 3: Standard procedures and forms for the storage of material;
    - Procurement SOP 4: Control and trouble shooting of procurement procedures;
    - Procurement SOP5: Evaluation of suppliers.

Ad 6. TA with further optimization of diagnostic services in the TB laboratory network

Background: In the NSP it was planned to install a special TB laboratory network manager with the responsibility to increase the efficiency of services and collaboration of all TB laboratories of the country. Following this plan, SCI has hired an international specialist with TB laboratory experience as consultant assisting the head of the NTC department of the NRL. The QM commissioner of the NRL has taken the additional responsibility to also manage the GeneXpert laboratory network.

Key findings:

- A container laboratory has been installed in Pokhara.
- The ventilation system is under construction in Dharan.
- Equipment has been delivered to the regional laboratory of Surkhet. A container laboratory is planned.
- Refurbishment of the laboratory of Dangari is planned for 2019.
- The Xpert MTB/RIF laboratory network has been expanded to 58 machines in 56 laboratories (more details see **ANNEX 5**). Further 10 GeneXpert machines are expected to arrive in fall 2018. After 2019, 80 GeneXpert laboratories shall be functional.

Challenges identified:

- The logistical transportation system though identified as one of the key priorities of TB lab services has not yet been addressed in managerial planning;
- The smear microscopy laboratory network has remained unchanged;
- Culture diagnostics is not yet available for routine use for other laboratories than the NRL;
- MoH and NTP have so far not agreed upon a plan or standardized system for the
    - referral of orders and specimens from lower to higher level laboratories, e.g. from microscopy or GeneXpert laboratories to culture or DST centers;
    - logistical specimen transportation, communication and reporting system.
- Maintenance of laboratory equipment available in the network particularly in the NRL departments and the culture laboratory is not prospectively planned. In the GENETUP department of the NRL, delayed maintenance of BSCs has actually led to interruption of culture and DST diagnostics. This is particularly sensitive in the current phase of the ongoing prevalence survey.
- Bio-indicators for autoclaves and hot-air sterilizers are missing. The function of the devices is not controlled.
- The consultant has not yet started providing technical assistance with the development and management of the TB laboratory network.
- Burden of diagnostics, staff per analyzis and staff management are unequally distributed between the two NRL departments. The NRL departments are not meeting on a regular basis.

Recommendations:

- Give high priority to the TB laboratory network development. Do not only focus on GeneXpert machines but also expand culture diagnostics which is not only useful in primary diagnostics for several reasons but mandatory for follow-up diagnostics of MDR-TB cases under ATT.
- Revise the NSP and the NSP implementation roadmap and define new targets, time-lines and milestones for the TB laboratory network development.
- Prospectively plan and budget the yearly maintenance of key equipment for the whole TB laboratory network on the central level of the NTP. Particularly, calibration and certification of all BSCs is key for uninterrupted TB diagnostics.
- Order
    - bio-indicator systems for autoclaves and sterilizers,

  - temperature loggers for incubators, refrigerators, and freezers.
- Create a position for an (international) expert of TB laboratory network management with sufficient skills and management experience to guide the development of the laboratory network. Encourage him to collaborate with the SRL partner who has substantially contributed to the NTP over more than 30 years, to the NSP and the implementation roadmap. The SRL is quite well aware of the priorities of TB laboratory services in the country.
- Make sure that both NRL departments are much closer collaborating. Provide equal support to both NRL departments. Implement regular meetings of both NRL departments as agreed upon during previous missions and outlined in previous SRL reports.

In summary, the SRL expert has observed many good developments particularly in the two departments of the NRL, with the prevalence survey and with the expansion of the GeneXpert network in the country. He had fruitful and successful trainings with the staffs of both NRL departments and several helpful meetings with NTP managers, national and international stakeholders. He expresses his deep gratitude for the great hospitality that he experienced from the NTP director, the heads and teams of both NRL departments, of the NATA director and his team as well as the GENETUP team. Special thanks also go to the WHO country office and USAID who helped with the arrangements of the mission and showed high interest in its results.

Gauting, 17th September, 2018

Dr. Harald Hoffmann

Medical & Managing Director

ANNEX 1 **people met & itinerary**

ANNEX 2 **Inventory of NTC equipment**

ANNEX 3 **Internal Quality Control tool for DST**

ANNEX 4 **QM audit reports**

ANNEX 5 **GeneXpert Network (table & map)**