Minutes of 2nd meeting of National Expert Committee on Diagnosis and Management of Tuberculosis under Revised National Tuberculosis Control Programme

Venue: Committee Room, 249 A, Nirman Bhawan, New Delhi

Date: 2nd -3rd December 2014

The 2nd meeting of the National Expert Committee on Diagnosis and Management of Tuberculosis under Revised National Tuberculosis Control Programme (RNTCP) was held on the 2nd& 3rd December 2014 at Committee Room "249 A", Nirman Bhawan, New Delhi.

The agenda and list of participants are annexed in Annexes 1 and 2 respective

The objectives of the meetings were:

- To update the progress made since the last national expert committee meeting
- To review various newer policy impacting evidences and proposed studies on newer diagnostics and treatment aspects of TB and take policy decisions

Day 1 (2nd December 2014)

Inaugural session:

Dr R S Gupta inaugurated the meeting by welcoming all the experts for the meeting followed by a brief round of introduction. He also briefed about the objectives of committee meeting to all members. DDG then invited Dr Ira Ray, Chairperson of the committee to address the members.

Dr Ira Ray welcomed all members and stressed that the committee should meet more frequently to take stock of progress. The co-chair Dr Sharma welcomed all the committee members.

Agenda 1

Dr KS Sachdeva, presented the "Actions taken on key recommendations of the 1st Meeting of National Expert Committee on Diagnosis and Management of Tuberculosis under RNTCP, 3rd-4th January 2013" that was followed by discussion by

the committee members to firm up the decisions and recommendations. The key action taken on recommendations are as below

Recommendations	Actions
Workshop for all identified eight laboratories from the states at NTI Bangalore with facilitators from all NRLs for training in Second Line Drug Susceptibility Testing (SLDST) certification	Workshop conducted at NTI Bangalore to formulate uniform guidance and training agenda for SLD. The same was circulated to all selected IRLs and State
Designation of additional two NRLs and inform about their role and responsibilities as NRLs.	Two labs (BMHRC Bhopal & RMRC Bhubaneswar) designated NRLs and informed about role and responsibilities
CTD to communicate the decision of the committee to DG-ICMR	DG-ICMR informed about decision for designation of NRLs by CTD
CTD to re-distribute the states amongst the NRLs and allot states to these two additional NRLs based on geographical proximity.	States distributed among the NRLs in NRL CC meeting and same was communicated to state
NTI to extend mentorship to both the additional NRLs for the next 2 years to develop their capacity to undertake all functions of NRLs.	NTI and NRLs are mentoring the labs for OSE, provided training for all new NRL staff
Constitute a sub-committee with representative from NRLs and selected IRLs for further strengthen the effective implementation of external quality assurance (EQA) for sputum smear microscopy	NTI Bangalore conducting situation analysis for EQA and based upon the report sub-committee will be formed. The draft document submitted by NTI Bangalore is being circulated to all NRLs for comments. Two workshops with NRLs are planned in month of February 2015.
Follow up cultures can be safely undertaken on 1 sample in DR TB	All NRLs, IRLs and States informed about the decision and implemented.

cases	
Centre of Excellence for the diagnosis of difficult cases like pediatric TB, Genital TB, Extra-Pulmonary TB and Bone TB, need to be developed	COE for EP-TB established at AIIMS, New Delhi.
Re-confirmation of Rifampicin (Rif) Resistance detected during CB-NAAT testing in new TB cases	CB-NAAT guidance document incorporated the same and issued to all state
CTD to verify and take necessary steps to ensure the correctness of all data from the study sites.	NRL and CTD developed checklist for CB-NAAT sites supervision. NRL approved the checklist. CTD staff visited representative sites for data verification

Following key decisions were made based on presentation and discussions that followed

- Re-organizing work NRLs:
  - As two new NRLs at BMHRC Bhopal and RMRC Bhubaneswar are now functional, mentoring NRLs were requested to review the progress of these NRLs to identify areas for additional support and completely transition the activities to newly established NRLs by mid 2015.
  - Andhra Pradesh and Telangana as separate states to be allotted to NRLs post bifurcation of Andhra Pradesh.
- Alignment of RNTCP guidelines as per Standards for TB Care in India (STCI):
  - Fast track revision of the RNTCP technical and operational guidelines to align with STCI and all the standards shall be incorporated in service delivery
- Extra pulmonary TB guidelines which are at advanced stage of preparation shall be shared with committee in next meeting
- Programme should have repository of work in TB being done by various bodies and organizations across the country.

Agenda 2

Dr R S Gupta presented the programme updates. He covered basic TB epidemiology, trends, progress made on implementation of National Strategic Plan 2012-17, notification of TB, Programmatic Management of Drug Resistant TB (PMDT), TBHIV & TB DM collaborative activities, Pediatric TB, Initiative for Promoting Affordable & Quality Tests (IPAQT), Engagement of community pharmacists, update on financing through WB and GFATM projects, STCI, National Drug Resistance Survey, Accelerating access to quality TB diagnosis for pediatric cases in 4 major cities in India, Innovative intensified TB Case finding and appropriate treatment at high burden ART centres in India, Universal access to free quality assured anti-TB drugs Patna, Mehsana & Mumbai, e-NIKSHAY, Collaborative activities between RNTCP and Pharmaco-vigilance Programme of India for pharmaco-vigilance and ADR monitoring, Bedaquilline- Conditional Access Programme (BDQ-CAP), DRTB counselling project, DST guided treatment pilots, baseline 2nd line DST, Validation of 2nd line LPA, Implementation of New Diagnostic algorithm and implementation pilot on use of daily anti-TB treatment regimen under RNTCP in selected 200 districts

Dr Ira Ray suggested a small study to support evidence from the program regarding one FU sample for the Drug Resistant TB Patients. It was informed that evidence from the program data regarding advantages in use of one FU sample for the drug resistance TB patients without any impact on clinical decision and patient monitoring has already been undertaken by the programme and published in 2012. The policy decision was taken in the last meeting based on the results of this study shared then.

Dr Rohit Sarin raised concerns over the footnote that GoI has yet to accept the WHO estimates for TB burden in India expressed in Global TB Report that makes it difficult to explain at various international platforms. To this Dr RS Gupta responded saying now the country programme accepts WHO estimates for TB burden in the country.

Dr Usha Gupta raised a query regarding TB notification from private sector to which Dr R S Gupta responded that although the progress made is promising but needs to be accelerated and CTD in collaboration with IMA is working on improving TB notification from private sector as well as quality diagnostics, prescription practices and adherence support.

Dr Varinder Singh expressed issues faced by private sector in referring DR TB suspects and or pediatric TB suspects for C&DST and Xpert MTB/ Rif and suggested linking major private hospitals with RNTCP certified laboratories officially. The committee accepted the suggestion.

Dr R Solanki recommended that the medical college laboratories should be prioritized under lab scale up plan. Dr K S Sachdeva responded that most of the government medical colleges have been included in the proposed list of C&DST laboratories in the revised national lab scale up plan (2014-19), however, the laboratories with existing capacities or requiring minimum up-gradation will be prioritized. Also private medical colleges and private sector laboratories will be considered for certification and outsourcing lab services under the revised partnership schemes based on the needs of the state.

Dr Ameeta Joshi informed the committee regarding minimal lab requirements by MCI for recognition and urged the programme to take up the issue with MCI to facilitate lab upgradation in medical colleges. Dr Sarin reiterated the need of advocacy with central government institutes and regulatory bodies to modify the norm for laboratory requirements to facilitate TB laboratory up gradation.

Dr Urvashi Singh raised the issue of delay in RNTCP certification of Microbiology laboratory at AIIMS. Dr Sachdeva requested Dr Rohit Sarin to coordinate with Dr Urvashi to complete the certification process.

Dr Urvashi also emphasized on the need of long term follow up in TB patients. Dr Sachdeva responded that the 100 district pilot of daily regimen has the component of long term follow up among registered TB patients as per STCI.

Dr Malik Parmar suggested alignment of all the proposed pilots and feasibility studies under consideration /approval with Standards for TB care in India

Dr S K Sharma expressed concerns over gaps in coordination of RNTCP with ART centres and ART initiation rates in among TB HIV cases in Delhi. Dr Shikha shared the UNION study in Karnataka citing reasons of non-testing of HIV due to shortage of HIV testing kits, stigma and refusal to test by the elderly. Dr Sreenivas, emphasized the importance of newly initiated regional TB-HIV review meetings and urged the

programme to utilize the platform for improving the collaboration, joint monitoring and problem solving approach for enhanced access to care for both diseases.

Dr Anil Purty drew attention to poor understanding of TB notification along with NIKSHAY and necessity of well-defined roles and responsibilities of medical college facilities in TB notification

Dr Rajendra Prasad suggested wide dissemination of IPAQT lab initiatives and subsidies being provided under various tests to maximize benefits to the patients in private sector

Following Key decisions were taken based on presentation and discussions

- GoI to convey acceptance of WHO estimates on TB burden for the country to Global TB Programme, WHO HQ, Geneva through a formal email.
- Widely disseminate the increased DR TB case finding efforts as achievement for TB control to alleviate a common misunderstanding that the DR TB is on rise and the efforts for TB control have dismally failed in the country though the TB case notification under RNTCP is declining
- A formal communication to all ICMR institutes to take up TB activities to support the programme in scaling up research, diagnostics and treatment.
- Major private hospitals to be linked with RNTCP certified laboratories to streamline offer of quality assured C&DST services
- Advocacy with Medical Council of India to modify the norm for lab requirements for MCI recognition to suit TB laboratory up gradation
- Streamlining of death audits for DR TB patients registered under PMDT
- NIKSHAY development process to be periodically and closely monitored by the programme to expedite its completion within the planned timelines. Measures to be taken to improve timeliness of NIKSHAY entries and utilization of NIKSHAY data for treatment adherence monitoring.
- While strengthening TB HIV collaborative activities, address other co-morbidities like TB Diabetes and TB Tobacco. Collaborative framework and activities to be systematically scaled up based on lessons learnt from early pilot studies on TB DM and TB Tobacco in close collaboration with the National Programme for Prevention and Control of Cardiovascular diseases, Cancers, Diabetes and Stroke (NPCDCS) and National Tobacco Control Programme (NTCP).

- Systematic dissemination and capacity building in STCI emphasizing on TB notification along with NIKSHAY to be expedited by the programme for doctors in medical colleges and private sector through task force mechanisms and doctors association like IMA, API etc.
- Wide dissemination of IPAQT lab initiatives to maximize benefits of WHO and STCI endorsed diagnostics to the patients in private sector while urgently linking these labs for notification of all diagnosed TB and DR TB cases under NIKSHAY.

Agenda 3

Dr K S Sachdeva made a presentation on "Findings of RNTCP WHO FIND 18-TU study on operational feasibility of CB-NAAT in India".

The study was set up in 18 TB units across the country in diverse settings catering a population of ~8.8 million. Baseline data was collected from 14 sites during the initial preparatory phase of 2-3 months. Preparatory activities i.e., training, referral linkages with all public health facilities and provision of air conditioners, power back up, security, etc, were taken up. The interventions i.e., same day sputum specimen transportation, all presumptive pulmonary TB & DR TB cases offered single CBNAAT test, treatment for TB based on CBNAAT result and RIF-resistant TB (RR-TB) patients referred for 2nd line treatment; specimen sent to reference lab for confirmatory DST were made.

The Study demonstrated that it is feasible to rapidly roll out Xpert MTB/RIF assay, utilizing the existing infrastructure under programmatic settings in India. Under routine programmatic conditions Xpert MTB/RIF assay provided 99.1% valid results. Compared to smear microscopy (14.5%) as the initial diagnostic test, with Xpert MTB/RIF (20.2%) positivity for bacteriological confirmed TB in routine settings. Higher proportions of TB cases were diagnosed based on Xpert MTB/RIF among HIV positive (27.6%) and in pediatric age group (10.4%), as compared to smear microscopy, 12.8% and 4.8% respectively under routine operational conditions across the study sites in India. With upfront testing of all presumptive TB cases with Xpert MTB/RIF, more than 5-fold increase in detection of RR-TB cases was also observed.

Dr Sarin inquired about the treatment offered to the RR-TB cases among newly diagnosed TB patients in this study. Dr Imran responded that as per the approved protocol, all such patients were subjected to LPA/LC (subject to availability) for reconfirmation of RR-TB meanwhile initiated on standardized regimen for MDR-TB. The treatment was continued or modified subsequently based on the LPA/LC results and DR-TB Centre Committee decision.

Dr Rahul Thakur responded to queries related to infrastructure requirement and issue related to decentralization of CB-NAAT laboratories that it was demonstrated that dust was a major reason rather than temperature for module breakdowns and failures. With the experience learnt from 18 TU sites study, Cepheid has modified the hardware. Dr Anand commented that under RNTCP WHO UNITAID TB-Xpert project with 43 CB-NAAT machines the module failures are very low. Dr KS Sachdeva emphasized the importance of temperature control for cartridge storage.

Following Key decisions were taken based on presentation and discussions

- Update in policy for use of Xpert MTB/Rif assay based on the latest WHO guidance:
    - Xpert MTB/Rif result reported as RR-TB among new TB patients shall be confirmed with a second Xpert MTB/Rif test on another sample. Result of second test shall be considered for treatment. However a fresh sample shall be tested on LPA/LC in the order of priority for reconfirmation. The concordance analysis shall be presented to the committee for review and informed policy decision on RR results among new TB cases on CBNAAT

    - In situations of conflict between the two technologies for DST, preference to be given to genotypic tests over phenotypic tests and the final answer is genetic pyro sequencing

Agenda 4

Dr S Anand presented "Update on RNTCP WHO UNITAID TB-Xpert Project".Under this project, 43 Xpert MTB/Rif machines and cartridges are provided to the country to scale-up rapid molecular diagnosis of TB and RR-TB and to innovate to engage private sector through public-private mix (PPM) initiatives to improve access to rapid

testing of patients who attend both public and private sector. Till June 2014, 28853 Xpert MTB/RIF tests were performed, 19174 among tested were diagnosed as M-TB and 3857 were RR-TB among diagnosed TB cases with only 7% tests reported as invalid or errors.

Dr Urvashi inquired about the indeterminate test and the protocol followed to which Dr Mayank responded that there is clear guideline for resolving discordant results among microscopy and CB-NAAT that fresh samples must be sent to LPA/LC labs.

Dr Sarin raised his concern about smear positive and X-pert MTB negative(27%) and requested case by case analysis to figure out if they are positive or negative microscopically to which Dr Mayank responded that these sites are fully managed by the programme with the existing human resource and infrastructure and the discretion of utilization is with the states. The analysis and monitoring of quality of smear microscopy has been clearly laid upon the IRL in co- ordination with NRLs.Dr Ira Ray emphasized that there should not be any stock outs of cartridges.

Dr Usha Gupta voices the concern that on one hand we are presenting 18 TU sites study to validate the X-pert data and on the other hand expanding CB-NAAT sites where there is an implementation. To this, Dr Malik clarified her doubts that the expansion of CB-NAAT sites has followed in sequence after the validation study and the programme is now at the stage of expanding this technology to 300 more sites as per the national strategic plan 2012-17.

Following Key decisions were taken based on presentation and discussions:

- NRLs may proactively take up the capacity building of IRLs concerned in strengthening EQA for smear microscopy as well as streamlining the coordination, data management, reporting, trouble-shooting and monitoring the performance of all CB-NAAT labs in every state.
- CTD should strengthen the system for close periodic monitoring of module failures, cartridge stockout / expiries to promptly address the problem to minimize lab turn down with active involvement of IRLs and NRLs.

Agenda 5

Dr Bharati Kalottee presented "Update on RNTCP USAID FIND Pediatric TB Xpert Project". The project is being implemented in 4 major cities i.e. Delhi, Kolkata, Hyderabad and Chennai. Key hospitals and private clinics catering to pediatric populations were identified and referral network was established for sample collection and transport. The SOP for sample collection from children and EP TB cases was used for capacity building of the technicians of the identified sample collection sites. More than 45 sensitization and advocacy meetings were organised across the country. In a period of six months, the presumptive pediatric TB cases tested in these cities have increased by more than 20 times from 352 to 7314. Large number of non-sputaspecimen were tested and >3 fold increase was observed in comparison to smear microscopy. Additional gain of 10 times in BAL, 8 times in CSF and and 6 times in induced specimen. Among the four cities RR-TB reported among pediatric patients is highest in Delhi (13.8%) followed closely by Kolkata (13.5%).

Dr Sarin expressed his concern about high M-TB positivity rate in Delhi. He requested the programme to collect the current practices which are done by the sites and can be documented in this project. Dr K S Sachdeva responded that these are implementation pilot and good practices shall be incorporated in SOPs under programme.

Following Key decisions were taken based on presentation and discussions

- The good practices and processes from the Pediatric TB Xpert project to be incorporated in programme guidelines
- Prioritize use of CB-NAAT assay for diagnosis of TB in Pediatric and EP TB cases under the programme. Update the CB-NAAT guidance document accordingly.
- CTD to communicate to the states to systematically identify key sites in every district for training in sample collection from children and EP TB sites based on the SOP recently shared by CTD and link them up with the CB-NAAT sites wherever available.

Agenda 6

Dr Mayank Ghedia presented "Revised Laboratory scale-up Plan (2015-19)".As on September 2014, 59 RNTCP certified laboratories are functional with 11 labs proficient for second line DST (SL-DST). 41 laboratories out of 43 plannedin the lab

scale up plan (2009-14) have been upgraded and certified for various technologies. The salient features of the revised lab scale up plan (2015-19) include at least one laboratory at each state, establishment of two additional NRLs, involvement of Medical colleges, establishment of Genetic sequence laboratory at NRLs, upgrading laboratory toward NABL certification, CB-NAAT laboratory at all districts and medical colleges and LED-FM deployment in high work-load settings.

Dr Varinder Singh voiced the concern of difficulty in accessing government laboratory services for C&DST. He elaborated the challenges faced in routing the presumptive DR TB cases through DTOs. Dr Sachdeva responded that samples and request for C-DST forms from all presumptive DR TB cases can be sent directly by the collection center to the linked laboratory with a copy of the request form sent to the DTO.

Dr Urvashi Singh, requested the programme to utilize the expertise of Department of Microbiology, AIIMS-New Delhi in the field of molecular diagnostics in study of DST patterns

Following Key decisions were taken based on presentation and discussions

- List of 48 medical colleges under up-gradation can be shared by the programme with FIND India to explore possibility of setting up labs in these places on a fast-track mode. These can be set up on priority basis with the help from DGHS office in next 2 to 3 months
- AIIMS to submit the proposal for molecular epidemiology
- CTD to get the list of 120 medical colleges where the PMSY provided fund and advocate for establishment of DR-TB center and lab at all places.
- To simultaneously build and balance the treatment capacity
    - Decentralised DR TB centres (4-6 bedded AIC complaint wards wherever possible) at district level with nationally trained specialist doctors must be established to cover all district to manage non-seriously ill ambulatory MDR/RR-TB cases over the period of expansion.
    - Ensure adequate second line drugs forecasting, timely procurement and efficient supply chain management to balance the increased access to rapid diagnostic with SL-DST and averting a situation of a wait-list of diagnosed DR-TB cases for want of drugs.

- All new six AIIMS to establish DR-TB center and LAB and provide services to the respective states.
- Complete geographical coverage for Criteria C to be achieved by March 2015
- Expedite the process of certification of 40 laboratories for Second line DST by December 2015
- Identify high DR-TB endemic hot-spots in India and advance them to Universal DST in 2015. Systematically plan in consultations with state for phased advancement to universal DST by districts with control implementation and close monitoring to aim for nation-wide scale up by 2017.
- A subcommittee to be formed to develop evidence based normative guidelines on diagnosis and management of NTM under the programme

Agenda 7

Dr Paramsivan, presented a study proposal **"Validation of LPA for detecting resistance to Fluoroquinolones, Aminoglycosides (Kanamycin, Amikacin) and Cyclic Peptides (Capreomycin) using MTBDRsl® test and Evidence Collection to explore its potential usefulness for RNTCP-PMDT".** The study would be conducted with the aim of exploring the potential of available molecular diagnostic platform, Line Probe Assay (Genotype MTBDRsl®) in reliably diagnosing drug resistance to fluoroquinolones and second line injectable and collect evidence to assess its potential usefulness for RNTCP-PMDT. The objectives of the study include i) Validation of Genotype MTBDRsl® assay for determining the resistance to fluoroquinolones and second line injectable compared with proven existing phenotypic DST method; and ii) To collect in-country evidence for drawing inference about the utility of Genotype MTBDRsl® assay in diagnosing additional drug resistance for deciding course of treatment of DR-TB cases in programmatic setting.

DGHS raised concerns regarding delay in adaptation of LPA Second line DST under the programme. To this Dr Sachdeva responded that this validation study would be a short one but would guide the programme with the evidences generated for informed policy decision on future scale up.

Following Key decisions were taken based on presentation and discussions

- The LPA validation study shall be taken up at five laboratories across the country in states where baseline SL DST diagnosis and appropriate treatment modifications have been rolled out.
- The study to be presented to the National OR Committee under RNTCP for further inputs and endorsement.

Agenda 8

Dr Ranjani Ramchandran, presented "**Revised Diagnostic Algorithm for RNTCP**". As recommended by the expert committee during its first meeting in 2012, a sub-committee revisited the available evidences and revised the algorithm that was subsequently approved by the ministry. The revision of diagnostic algorithm for TB under programme is a necessity in the wake of declining smear negative TB diagnosis and various studies informing about the diminished sensitivity and efficiency along with availability of newer diagnostic modalities. The revised diagnostic algorithm is based on the principles of availability of diagnostic technology, sensitivity and specificity, appropriate positioning of the Xpert-MTB/Rif (CBNAAT) and X-ray in the algorithm to synergize for improving reliability and diagnostic yield of the algorithm, relevance with National Strategic Plan 2012-17, practical (user friendly) and promotes early diagnosis.

There was a discussion offer of CBNAAT in smear positive and X-ray negative cases. The group deliberated and decided that if these groups of patients are from high MDR prevalent areas (>5% MDR in new cases) then CBNAAT to be offered upfront.

Dr Rupak Singla raised the query that if X Ray is not there upfront then the program will bear or reimburse the cost. Also needs to be defined clearly in the Diagnostic algorithm as to what will be done if X Ray is not available. To this Dr Sachdeva responded that X ray availability within the general health system would continue to be the main source, however, cost reimbursement of X-Ray from private facilities would also be considered under the programme.

Following Key decisions were taken based on presentation and discussions

- Identification of 5 sites for implementation pilot to test the feasibility of implementation and gather evidence on scalability of initiative

- The Algorithm for Extra-pulmonary TB to be presented in the next committee meeting
- A subcommittee to be formed for diagnosis and management of Non Tubercular Mycobacteria. The constitution of the subcommittee is as follows

    - **Dr Anuj Bhatnagar,** Head, Respiratory Medicine, RBIPMT, New Delhi
    - **Dr Rohit Sarin,** Director, NITRD
    - **Dr Urvashi Singh,** Chief, Tuberculosis Section Department of Microbiology, All India Institute of Medical Sciences, New Delhi
    - **Dr Ameeta Joshi,** Prof Head Microbiology at Grant Medical College, JJ Hospital Mumbai
    - **Dr Ranijni Ramchandran,** Technical officer, laboratories, WHO-INDIA
    - **Dr Varinder Singh,** Professor Pediatrics ,Lady Hardinge Medical College, New Delhi
- An oversight committee to be set up for finalizing Pediatric Diagnostic algorithm. Dr Varinder Singh to be the chair with following members.

    - **Dr S.K Kabra,** Professor, Paediatric Pulmonology Division, AIIMS
    - **Dr Soumya Swaminathan,** Director, NIRT
    - **Dr Sangeeta Sharma,** Senior Specialist (Pediatrics), NITRD, New Delhi
    - **Dr GR Sethi,** Director Professor and Head Dept. of Pediatrics, Maulana Azad Medical College, Delhi
- The Pediatric TB module to be presented to the committee in the next committee meeting

Agenda 9

Dr Syed Imran Farooq presented the status of "**Baseline 2nd line DST at start of MDR-TB treatment".** CTD approved offer of Baseline Second line DST to all the Rif resistant/MDR TB patients in six states of Delhi, Gujarat, Maharashtra, Karnataka, Kerala and Tamil Nadu. Except Maharashtra, all the states have started implementing baseline SL-DST among Rif resistant/MDR TB patients. 6 laboratories certified for SL-DST and 13 DR TB centres across these five states in the country are providing services with baseline SL-DST. Till November '14, 42122 presumptive MDR TB cases were tested for FL-DST, 3355(8%) were found to be Rif

resistant/MDR TB in India out of which 818 (32%) were tested in these five states for baseline SL-DST. Additional Ofx resistance was found to be in 163(20%), additional Kana resistance in 11(1.3%) and XDR TB was diagnosed in 32(4%) cases tested for baseline SL-DST.

The committee members appreciated this initiative and urged CTD to systematically scale this up as this has the potential to improve treatment outcomes in MDR TB pateints with appropriate treatment modifications early during their treatment.

Following Key decisions were taken based on presentation and discussions

- States to take ownership, enhance coordination, fast-track BSL III along with HRD and expedite the LC lab upgradation while CTD to monitor closely and support the states well in time.
- Take immediate measures to include Levofloxacin, Moxifloxacin (1,2), Kanamycin, Capreomycin and Amikacin in SL-DST panel along with FL-DST with INH (1,2), Pyrazinamide and Ethambutol.
- Simultaneously, plan to develop capacity of the SL-DST certified labs for expanded DST panel for PAS, Ethionamide, Linezolid and Clofazimine starting with the existing SL-DST certified labs.
- Undertake revision of PMDT recording and reporting formats- capture baseline SL-DST and DST guided regimen pilot and simultaneously update NIKSHAY PMDT input and output modules
- Revise second line drug forecasting to include baseline 2nd line DST
- Scale up offer of baseline SL-DST to all districts across the country in a planned and phased manner guided by the resources.
- Undertake re-planning of PMDT scale up in consultation with states to lay down a realistic roadmap for scaling up these policy advancements for alignment of treatment capacity especially second line drug procurement plans with the scale up of laboratory diagnostic capacity as per the revised national laboratory scale up plan 2014-19.

Dr Patki, Himalaya Herbal products presented "Proposal on prevention of hepatotoxicity with Liv.52 DS". He deliberated on the hepato protective role of Liv 52 against hepatitis induced by ATT. Dr Prahlad Kumar raised concern regarding the

safety of contents for use in human beings. Dr Rajendra Prasad suggested to generate evidence for use of Liv 52 along with anti TB drugs in TB patients. It was suggested to do a multicentric study and present the findings to the committee.

However the committee also opined that this should not have been an agenda point and the committee is not appropriate body to take the decision.
Following Key decisions were taken based on presentation and discussions

The proposal to be presented in National OR committee.

Day 2 (3rdDecember 2014)

Agenda 10

Dr Prahlad Kumar presented updates on "**First National Anti-Tuberculosis Drug Resistance Survey, India (2014-15)".** The survey has been launched in July 2014 with support of WHO India with the primary objective to determine the national prevalence of anti-tuberculosis drug resistance among both new and previously treated smear-positive pulmonary tuberculosis diagnosed in India. The secondary objectives of the survey are i) To determine the proportion of both MDR-TB (HR-resistance) and XDR-TB (HR+OK resistance) among both new and previously treated smear-positive pulmonary tuberculosis diagnosed in India and ii)To measure the level of HIV prevalence among the survey patients and its association with MDR and XDR.

The highlights of the survey is that it is the first survey in the world with a huge nationally representative sample size of ~5214 cases using population proportionate cluster sampling methodology, will be conducted with 13 first and second line anti-TB drugs in liquid culture and DST and genetic sequencing in a sample of the enrolled patients. A total of 120 TB Unit clusters across the country have been selected as a representative sample. As on date, 61 out of 120 TU clusters have initiated the patient enrollments. 7 have already completed the process off sample collection and transport. 59 TB Units are yet to start. The sample acceptance rates are as high as 98% and only 2/656 patients have been replaced due to sample rejection till date.

The committee members congratulated CTD, NTI and WHO for embarking on such an important survey that is expected to change the national and impact the global epidemiological situation of drug resistant TB with scientific evidence.

Following Key decisions were taken based on presentation and discussions

- All the TB Units to start sample collection and transport as per the enrolment plan
- Central TB Division to take up monitoring visits to lagging TB Units.
- NDRS Oversight committee meetings to be regularly conducted to closely monitor the progress and address challenges.

Agenda 11

Dr A Sreenivas presented **"Innovative Intensified TB HIV 3I's project (RNTCP-WHO-USAID)".** Death rates among registered TBHIV co-infected patients are as 13% compared to 4% in non HIV TB patients. India is implementing intensified TBHIV package since 2011 across the country. Although one of the 3 I's- Intensified Case Finding (ICF) has been implemented but the other two I's namely INH Preventive Therapy (IPT) and Infection control for TB has not yet been implemented under public sector. A RNTCP WHO USAID project for supporting ART centres for innovating intensified case finding and implementation of all 3 Is has been recently rolled out across 30 ART centres in 5 high HIV burden states of Andhra Pradesh, Telangana, Karnataka, Maharashtra and Tamil Nadu. The patient intake is expected to start from March 2015. The objectives of the project are to reduce TB mortality in PLHIV by early diagnosis and appropriate treatment and o prevent TB in PLHIV with IPT and IC

Under this project following strategies shall be implemented

- Intensified Case Finding in ART centres
    - Diagnostic algorithm
    - Use Xpert-MTB Rif
- Early initiation of TB treatment (Daily FDCs)+ART+CPT
- INH Preventive Therapy
- Infection Control
- Pharmacovigilance

The committee members congratulated CTD and WHO for taking up this project to improve survival of TB HIV co-infected patients as well as taking the opportunity of generating early experiences in implementation of upfront Xpert for early TB diagnosis in PLHIV and depending on the results treatment with daily FDCs or IPT and IC in HIV care settings in the high HIV burden states of India. This will guide the programme in future scale up these new initiatives.

Following Key decisions were taken based on presentation and discussions

- The data management protocols and early results of the project to be finalized and presented in the next committee meeting

Agenda 12

Dr Amar Shah presented **"Evidences on effectiveness of Family DOTS".** The study titled **DOT provided by a family member for children with tuberculosis: a non-inferiority, cluster-randomized trial in Gujarat, India** was presented along with other international evidences on effectiveness of family DOTS in all age groups. The study was conducted among children with newly diagnosed TB registered under RNTCP in June-Sept 2012, Gujarat. The study demonstrated that DOT by a family member is not inferior to that by a non-family member among new TB patients in children and can attain international targets for treatment success under programme conditions.

DGHS urged the programme to take up the family DOT and make DOT provision a flexible & patient friendly affair for better treatment outcomes and prevention of recurrences or resistance. Dr Sachdeva informed the house that the expert committee reviewing the regimen for TB under leadership of Dr Katoch had also requested that this decision be considered by the national expert committee for the entire country and not for the 100 districts identified for implementation pilot of daily regimen with FDCs to be discussed as the next agenda point.

Following Key decisions were taken based on presentation and discussions

- Considering the evidences presented, the committee took a policty decision to allow the option of having a family member provide DOT for patients with TB and revise the national guidelines with immediate effect.

- The necessary training, counselling and DOT provider honorarium under the programme can be extended to the identified family member also.

Agenda 13

Dr Jyoti Jaju presented to proposal on **"Implementation pilot of daily regimen".** Based on the recommendations of 1st National Expert committee, a high level of committee under chairman ship of Dr. V M Katoch, Secretary Health Research and DG-ICMR was constituted to examine the type of Drug regimen to be used for Drug sensitive TB under RNTCP by MoHFW. The Protocol for implementation pilot for daily regimen presented and endorsed by this committee. The implementation pilot shall be implemented with the primary objective of documenting treatment outcomes in the implementing (Daily regimen) and control (intermittent regimen) districts and with the secondary objectives i) to assess implementation feasibility of daily first line treatment in patients accessing care within the RNTCP for Drug susceptible Tuberculosis with respect to adherence to treatment in relation to DOT provision, ii) to document relapse rate among successfully treated TB patients and iii) identification and management of Adverse Drug Reaction

During discussions, Dr Sachdeva added that the program proposed that treatment adherence pilots using ICT tools and some innovative approaches can also be included in the implementation pilot of these 200 districts. However, Dr Katoch categorically mentioned that in these 200 districts only feasibility of daily ATT has to be seen, while simultaneous projects and studies to generate evidence on other effective modalities to monitor treatment adherence must be carried out outside of these 200 districts and such evidences must guide the policy decisions by the country experts. It was also decided that further scale up of daily FDC regimen can be considered based on early interim results on feasibility shown in this implementation pilot in 100 districts.

Following Key decisions were taken based on presentation and discussions

- The implementation pilot proposal was endorsed and the interim results to be presented to the committee by CTD in the next meeting.
- Following oversight committee to be formed

Post/Designation	**Name of the official currently holding the post**
DG (ICMR)	Dr. V M Katoch
Director NIRT	Dr. SoumyaSwaminathan
Director NTI	Dr. Prahlad Kumar
Director NITRD	Dr. Rohit Sarin
HOD, Dept. of Medicine, AIIMS	Dr. S K Sharma
HOD, Dept. of Pharmacology, MAMC	Dr. Uma Tekur
Chairperson, NTF	Dr. D Behera
DDG TB, CTD	Dr. R S Gupta
Director, Vallabh Bhai Patel chest Institute	Dr Rajendra Prasad
Former Director, AIIMS, New Delhi	Dr. L M Nath
ADDG TB (PMAC)	Dr. K S Sachdeva

Agenda 14

Dr S K Sharma presented "**Randomized controlled trial comparing the effectiveness and safety profile of daily versus thrice weekly intermittent drug regimen for smear positive pulmonary TB (Delhi state, chest clinics of Delhi)".** The objective of the study are to compare treatment outcomes (sputum conversion rate at 3 months, cure or successfully treated at end of treatment schedule), treatment failure rates, default rates, adverse effect(s) between the two arms. The following suggestions were given from the committee to be incorporated in the study are:

1. Study title says: Pulmonary smear positive patients, which actually should be pulmonary bacteriologically positive TB patients
2. Study exclusion criteria should be kept minimum to see whether in difficult patients such as HIV+ve, patient having difficulty in follow-up etc.. Should be included in the study.
3. Culture frequency may be reduced to once a month from once in fortnight during I12P phase

Agenda 15

Dr Anuj Bhatnagar presented the recommendations from national workshop on developing guidelines for DST guided treatment for all forms of drug resistant TB in India that was held at Mumbai in August 2014 where national experts from public and private sector developed evidence based consensus on the subject.He presented the recently analysed program data on evidence and levels of drug resistance with various DST patterns among MDR TB suspects tested under programme for last 6 years. This included the levels of mono/poly resistance to first line drugs other than R and poor treatment outcomes as well as amplification to MDR TB among such TB cases treated with standard RNTCP first line regimen under programmatic settings. The data presented was programmatic data from certified laboratories and DR TB Centres across the country till 2011. He also presented the significant reduction in treatment outcomes of MDR TB patients with baseline Ofloxacin resistance from the early cohorts who were treated with standardized MDR TB regimen (with Ofloxacin) under the programme. He then, presented the national consensus on the proposed diagnostic algorithm and the treatment algorithm for DST guided treatment to cover INH mono resistant, poly resistant TB cases to first line drugs as well as proposed modification in standardized regimen for MDR TB as the results for other first and second line drugs in liquid culture-DST are available by implementing the proposed diagnostic algorithm.

After the presentation, Dr Singla presented some more technical points for consideration of refinement in the algorithm and the treatment approaches based on the recent WHO Companion Handbook on PMDT release in August 2014. These were pertaining to use of a second CBNAAT to confirm RR TB in a newly diagnosed TB case using CB-NAAT, introducing use of two concentrations of INH with liquid C-DST or LPA results for INH (INH-A or KatG) to take the advantage of use of INH in regular or high doses in standard MDR TB regimen. The committee members deliberated and came to a consensus to include these additional points in the proposal.

Following Key decisions were taken based on presentation and discussions:

The following additions to be incorporated in the final national consensus developed at the Mumbai workshop:

Diagnostic algorithm-

- Modified diagnostic algorithm proposed will be followed. If R resistance has been detected by CBNAAT, in addition to other drugs, DST to H - both High & Low level will also be done by liquid culture and treatment modified accordingly.
- For samples reported by LPA- report must also mention- H resistance by Kat G or INH A mutation.
- For patients who do not fall under the definition of Presumptive MDR TB and diagnosed as tuberculosis by CBNAAT with resistant to Rifampicin – a second sample will be put up for CBNAAT and also for Liquid culture DST.

Treatment algorithm -

- Use of INH & Ethionamide-
  - If R resistance has been detected by CBNAAT, add INH in the standard doses to the treatment regimen till results of LPA or Liquid culture DST are known. If High levels of resistance are detected by Liquid culture- omit INH. If low levels of resistance are detected by Liquid culture- add high dose INH.
  - If LPA reports INH resistance by Kat G mutation- Omit INH
  - If LPA reports INH resistance by INH A mutation- Use High dose INH. Ethionamide in the treatment regimen will be replaced with PAS
- For patients who do not fall under the definition of Presumptive MDR TB and diagnosed as tuberculosis by CBNAAT and resistant to Rifampicin – the following will be the treatment:-
  - If second CBNAAT also shows R resistance- start regimen for MDR TB patients with INH till its results from Liquid culture are known. Perform DST to H & R as per WHO guidelines & SLDST on the liquid culture sent.
  - If second CBNAAT shows R sensitive- Start regimen for new TB patients and wait for report of Liquid culture DST. If Liquid culture shows R Sensitive- Continue regimen for new TB patients. If it shows R resistance- refer the patient to DR TB center committee for Clinical, Radiological & microbiological assessment and decision regarding starting regimen for MDR TB patients or continuing regimen for new TB patients depending upon the response to treatment given so far.
- Fluoroquinolone resistance

- In case of resistance to any Fluoroquinolone- start the Fluoroquinolone to which the patient tests sensitive but strength then the regimen by adding Clofazimine & PAS.
- In case the patient tests resistant to all Fluoroquinolone- omit Fluoroquinolone and add Linezolid, Clofazimine & PAS for the entire duration of treatment

Agenda 16

Dr Padma Priya presented the proposed guidelines for "Bedaquiline: conditional access programme in India[BDQ-CAP]".

The aim of BDQ-CAP is to provide access as well as assess the safety and effectiveness of Bedaquiline when given to patients with sputum smear-positive pulmonary pre-extensive drug resistant (pre-XDR) or extensive-drug resistant TB (XDR-TB). Along with providing access to BDQ to pre-XDR and XDR TB patients, this programme will also help us to find out the proportion of and time to sputum culture conversion when BDQ is given along with existing group 5 drugs, in pulmonary pre-XDR and XDR TB patients.

The meeting of Expert Committee on Regulation of Newer Anti-TB Drugs was held on 26thNovember 2014. The committee approved the BDQ-CAP for implementation with specific recommendations that the supply of Bedaquiline drugs under the CAP must be provided free of cost by Janssen Pharma. DGHS, GoI assured the committee members that the negotiations would be done with Jehnson and Jehnson to provide drug free of cost to run the this CAP. The budgeted cost of INR 1.25 crores (excluding the cost of drugs) to cover for equipment, consumables, human resources, travel, stationaries, shipment, communication and overheads would be borne by ICMR/ Department of Health and family welfare.

Following Key decisions were taken based on presentation and discussions

- Programme to arrange for issue of stipulated courses of Bedaquiline through Janssen Pharmaceuticals (critical step)

- The First Meeting with PIs and the two oversight committee members proposed at NIRT Chennai with support from CTD and WHO with objective of
  - orientation in the BDQ-CAP Guidelines and
  - initiate DR TB Centers preparedness in 1st Quarter 2015
- Subsequent meetings on monthly basis at each of the participating DR TB centers on rotation basis proceeded with a day of site visits.

Agenda 17

Dr Amar Shah presented **"Pharmacovigilance Project".** The Pharmacovigilance is required as Regimens for drug-resistant TB are commonly associated with ADRs (based on Indian studies under programmatic settings), Use of ARVs in patients with TB associated with HIV (DDI), Advent of newer medicines to treat TB (Bedaquiline, Delamanid). To strengthen patient safety, safeguard patient's interest and ensure adherence to prescribed drug regimens programme need to put mechanisms in place. To take care of these issues programme is collaborating with Pharmacovigilance Programme of India (PvPI).

Following Key decisions were taken based on presentation and discussions.

- The program will systematically implement pharmacoepidemological system for Tuberculosis under the Revised National Tuberculosis Control Programme, India. Under this, Pharmacovigilance related to Anti TB drugs will be implemented in phased manner starting from DRTB cases, TB-HIV cases and then covering all drug sensitive TB cases. With help of NIRT, Chennai program will also continuously monitor pharmacokinetics of Anti TB drugs including anti TB drug in daily dosages. The Drug resistance pattern for anti TB drugs is being monitored on time-to-time basis by conducting drug resistance Survey at country level. However country will put up thrust on establishing the drug resistance surveillance system for continues monitoring of drug resistance pattern.

Agenda 18

Dr Ranjani Ramchandran presented **"Establishing Laboratory Surveillance Systems".** The need for strengthening surveillance for drug-resistant TB was

reiterated by the 2009 World Health Assembly resolution. A surveillance system based on routine DST of all TB cases is able to provide continuous information on drug resistance patterns among patient groups, able to accurately detect trends, as well as localized outbreaks. In settings where capacity is currently not available for routine DST of all TB patients, a surveillance system should be organized with priority on establishment of routine DST of cases at high risk for drug-resistant TB. At a minimum, a system of routine DST should be established among all previously treated TB cases, with country-specific prioritization of patient subcategories. Subcategories include cases after treatment failure, return cases after default, relapses, and other previously treated cases

Following Key decisions were taken based on presentation and discussions

- To establish six sentinel Sites of the country with geographical coverage for regional representation
- To do DST for first and second line
    - INH and RIF
    - If RIF resistant test for ID and FQ
    - SM and EMB every two cycles
    - Frequency at least twice a year

Agenda 19

Dr Ranjani Ramchandran, NPO Laboratories, WCO-India presented **"Quality Assurance Programme-RNTCP".** ISO 15189 is the international standard for medical laboratory quality and competence. Quality assurance – system designed to continuously improve reliability of lab services, efficiency, accuracy and to achieve required technical quality of lab diagnosis by supervision of peripheral labs by intermediate reference labs in turn by central or national reference labs.

Potential problems in the isolation and identification of M. tuberculosis can be greatly reduced by monitoring media and reagents before using them on clinical specimens. Routine monitoring and maintenance may minimize serious and costly breakdowns of equipment. Laboratory reports can be more accurate and expeditious as the use of inadequate media, equipment techniques and recording minimized. The quality assurance programme can serve as a learning exercise, enabling the recognition and

identification of problem areas that might otherwise have been overlooked. A good quality assurance programme will enhance the credibility of the laboratory

Following Key decisions were taken based on presentation and discussions

- Formation of a National Task Force – a composite team of microbiologists, biomedical engineers, technicians, design and HVAC specialists (on-call basis)

Agenda 20

Mrs. Smriti Kumar presented **"Drug Resistant TB Counsellor Project".** DR TB counselling project is a pilot project under GFATM Single Stream Funding Phase 2 project. Under this pilot Population Services International (PSI) is implementing the project under Project Axshya where PSI is a Sub Recipient of the Grant where TB Union is a Principal Recipient. Pilot of DR TB counselling at facility and home settings in 28 districts (Out of 60 PSI Project Axshya districts). Districts selected Based on the DR-TB patient load and in discussion with the Central TB Division and the Union.

The counsellors completed line listing of 78% of DR-TB patients registered since inception of DR-TB sites in Program Districts.>95% of DR-TB patients registered from own districts. Out of 5,914 on treatment cases, 3024 (52%) of cases has been counselled at least once. In case of own districts Out of 2,727 patients on treatment, 2089 (76%) of cases has been counselled. Out of 275 LFU cases from Own Districts 20% of LFU cases are retrieved.

Following Key decisions were taken based on presentation and discussions

- Programme to closely supervise and monitor the counseling project
- All the posts of DR TB Counselors to be filled under the programme
- District level counselors for DR TB to be scaled up

The meeting concluded with vote of thanks by Dr K S Sachdeva, ADDG-TB-CTD.