Case finding and Diagnosis strategy

To achieve universal access to early accurate diagnosis of TB and enhancing case finding efficiency, identification of presumptive TB cases at the first point of care and linking them to the best available diagnostic tests is of paramount importance. Early case detection is vital to interrupt the transmission of TB disease as highlighted in the 12th five year plan for TB control in India.

Early identification of people with a high probability of having active TB (presumptive TB) is the most important activity of the case finding strategy. Screening and diagnosing patients with appropriate tests and strategies will largely determine the response to appropriate treatment.

Patients attending health institutions - government/private need to be systematically screened for symptoms of TB by the health care provider. Presumptive TB patients should be promptly identified and are to be referred to diagnostic facility for appropriate investigation using the RNTCP request form for examination of biological specimen.

Passive case finding alone can lead to missed cases or delayed diagnosis. Enhanced outreach activities to detect more TB cases are critical to universal access. Screening for TB has also to be undertaken at every point of contact with health care among key population including clinically and socially vulnerable group of people.

Definitions of presumptive TB

2.1 Presumptive Pulmonary TB refers to a person with any of the symptoms and signs suggestive of TB including cough >2 weeks, fever > 2 weeks, significant weight loss, haemoptysis, any abnormality in chest radiograph.

Note: In addition, contacts of microbiologically confirmed TB Patients, PLHIV, diabetics, malnourished, cancer patients, patients on immune-suppressants or steroid should be regularly screened for sign and symptoms of TB

2.2 Presumptive Extra Pulmonary TB refers to the presence of organ specific symptoms and signs like swelling of lymph node, pain and swelling in joints, neck stiffness, disorientation, etc and/or constitutional symptoms like significant weight loss, persistent fever for ≥2 weeks, night sweats.

2.3 Presumptive paediatricTB refers to children with persistent fever and/ or cough for more than 2 weeks, loss of weight*/ no weight gain and/ or history of contact with infectious TB cases**.

**History of unexplained weight loss or no weight gain in past 3 months; loss of weight is defined as loss of more than 5% body weight as compared to highest weight recorded in last 3 months.*

*** In a symptomatic child, contact with a person with any form of active TB with in last 2 years may be significant.*

2.4 Presumptive DR TB refers to those TB patients who have failed treatment with first line drugs, paediatric TB non responders, TB patients who are contacts of DR-TB (or Rif resistance), TB patients who are found positive on any follow-up sputum smear examination during treatment with first line drugs, previously treated TB cases, TB patients with HIV co-infection.

DIAGNOSTIC TOOLS

Tools for microbiological confirmation of TB

All efforts should be undertaken for microbiologically confirming the diagnosis in presumptive TB patients. Under RNTCP, the acceptable methods for microbiological diagnosis of TB are:

Sputum Smear Microscopy (for AFB):

- Zeihl-Neelson Staining
- Fluorescence staining

Culture:

- Solid (Lowenstein Jensen) media
- Automated Liquid culture systems e.g. BACTEC MGIT 960, BactiAlert or Versatrek etc.
- Drug Sensitivity Testing:
- Modified PST for MGIT 960 system (for both first and second line drugs)
- Economic variant of Proportion sensitivity testing (1%) using LJ medium (as a back up when indicated)

Rapid molecular diagnostic testing:

- Line Probe Assay for MTB complex and detection of RIF& INH resistance
- Nucleic Acid Amplification Test (NAAT) Xpert MTB/Rif testing using the GeneXpert system

Smear microscopy being the most commonly used method for microbiological diagnosis of TB for the last several decades, has had enormous value in TB diagnosis but with limited sensitivity, more so in children and PLHIV. Under RNTCP, two methods of microscopy are currently being used- ZN stain based microscopy using conventional microscope and Light Emitting Diode based Fluorescent Microscopy (LED FM).

Culture though highly sensitive and specific method for TB diagnosis, requires 2-8 weeks to yield results and hence alone does not help in early diagnosis. However culture will be used for follow up of patients on Drug Resistant TB treatment to detect early recurrence as part of using the indicator of relapse free cure.

Nucleic Acid Amplification Test (NAAT) provides accurate and rapid diagnosis of TB by detecting *Mycobacterium tuberculosis* (*M. tuberculosis*) and Rifampicin (Rif) resistance conferring mutations, in sputum specimen as well as specimen from extra-pulmonary sites. Presently, under RNTCP, its use is recommended for diagnosis of DR-TB in presumptive DR-TB patients and TB preferentially in key population such as children, PLHIV and Extra-pulmonary TB.

Other diagnostic tools

Radiography

Where available, CXR to be used as a screening tool to increase sensitivity of the diagnostic algorithm. Any abnormality in chest radiograph should further be evaluated for TB including microbiological confirmation. In the absence of microbiological confirmation, careful clinical assessment for TB diagnosis should be done. Diagnosis of TB based on X-ray will be termed as clinically diagnosed TB.

Tuberculin Skin Test (TST) & Interferon Gamma Release Assay (IGRA)

Standardized TST may be used as complementary test in children in combination with microbiological investigations, history of contact, radiology and symptoms. Interferon-Gamma Release Assays (IGRAs) are being used in place of skin test in low prevalence countries to detect TB infection. The exact advantage of IGRA in high burden countries like India is still not clear, hence these are not recommended for use for adults in diagnostic algorithm for tuberculosis in India.

Serological tests

The Government of India issued Gazette notification (vide 433E 7th June 2012) has banned the manufacture, importation, distribution and use of currently available commercial serological tests for diagnosing TB. These tests are not recommended for diagnosis of TB.

Process of Biological Specimen Collection & testing for microscopy

Medical Officers of health care facilities (governmental or non-governmental) should identify all presumptive TB from patients attending health facilities and refer them for examination using the RNTCP request form for examination of biological specimen. In Medical Colleges and other hospitals, indoor-patients suspected of TB should also be referred by the treating physician using the same RNTCP laboratory request forms.

Patients are given specimen containers with instructions to provide quality specimen which are then subjected for microscopy examination.

Two samples are collected within a day or two consecutive days. One sample is collected on the spot under supervision and other is collected early in the morning. The sputum containers should be labelled properly by writing the patient's laboratory serial number on the side of the sputum container and not on the lid. Sputum should be at least 2 ml in quantity and preferably mucopurulent. Results of sputum tests should be reported within a day. If needed, storage of sputum samples should be in cool place/ refrigerator. A smear is made, fixed and stained using the Ziehl-Neelsen staining / Fluorescence technique.

Transport of Biological specimens

Arrangements should be made locally for transporting the specimens to the DMC and for sending the results to the referring health centres. The specimens should be packed carefully in a box to avoid spillage. Before sending the sputum specimens to the DMC, the person should verify that:

1. The accompanying dispatch list contains the necessary information for all patients and clearly identifies the referring health facility collecting the sputum.
2. The total number of sputum specimens corresponds to the total number in the accompanying dispatch list.
3. The Specimen Identification Numbers on the sputum containers correspond to those on the accompanying list.
4. One RNTCP request form for examination of biological specimen is to be enclosed for each patient.
5. The health worker should then mark the date of dispatch on the dispatch list, put the list in an envelope and attach it to the box outside.
6. Sputum specimens should be examined by microscopy not later than 2 days after collection. Once examined, the microscopy results should be reported on the same day.
7. The containers along with the sample MUST be disinfected with 5% phenol solution and disposed as per guidelines after the sputum smears results are recorded in the laboratory Register.
8. Refer SOP for sputum collection & transportation **(Annexure 3)**

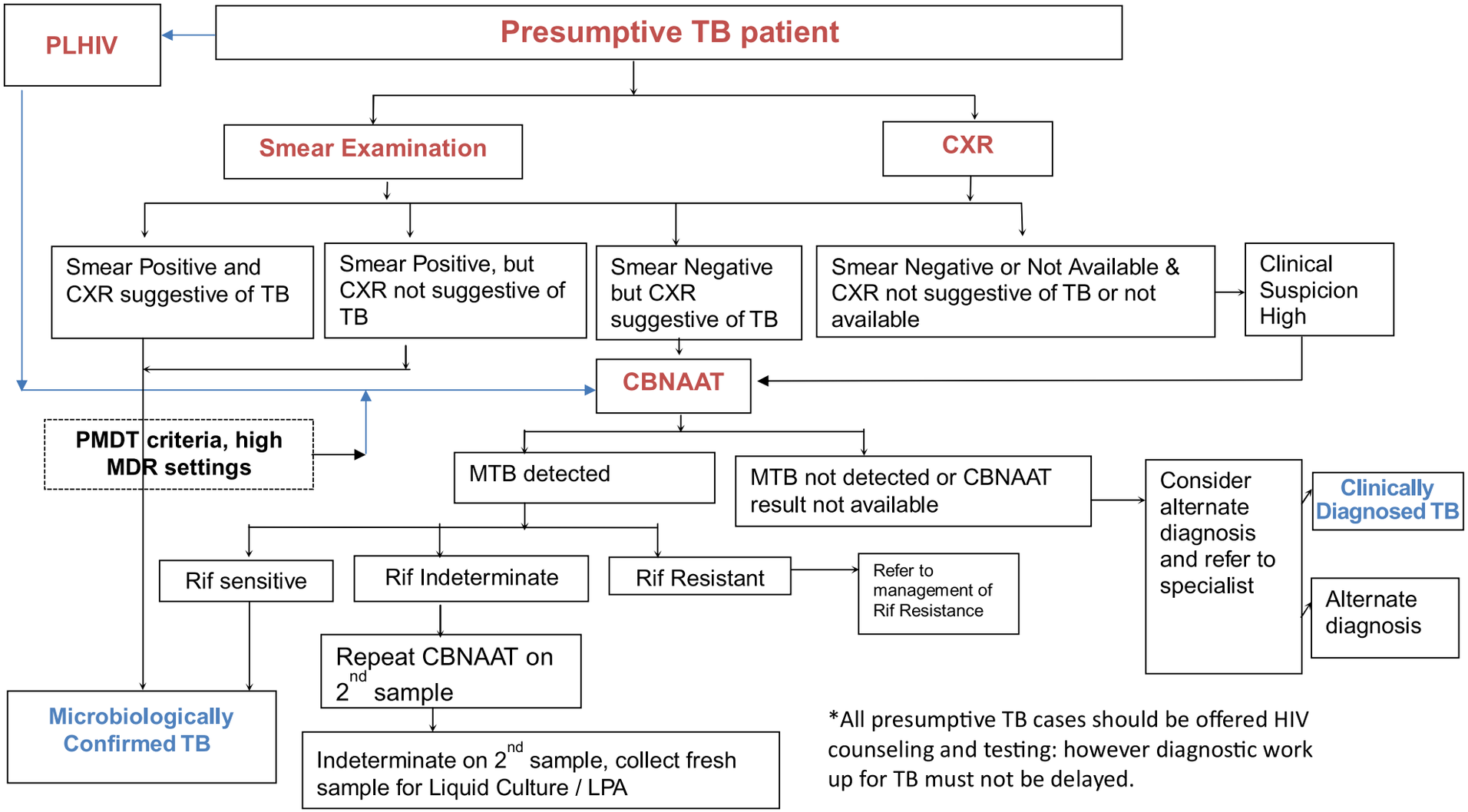
Smear preparation, Staining and Reading

Refer to SOPs of ZN Staining Techniques or Fluorescence Staining Techniques in (**Annexure 1 & 2)**

Diagnostic algorithm for pulmonary TB

All persons identified as presumptive TB patients in the health facility or those referred by other health care providers from the public / private health sector should be subjected to diagnostic tests as per the diagnostic algorithm(s).

Diagnostic algorithm for pulmonary TB



*All presumptive TB cases should be offered HIV counseling and testing: however diagnostic work up for TB must not be delayed.

Note for diagnostic algorithm for pulmonary TB

A. All presumptive TB (specifically for PTB symptoms) will undergo sputum smear examination (ZN/LEDFM). Two specimens will be collected (spot-early morning or spot-spot). If the first smear is positive and the patient is not at risk for Drug Resistant (DR) TB, he will be categorized as microbiologically confirmed TB (sensitivity status not known)

B. Smear positive and presumptive MDR TB (as per PMDT guidelines) and in settings of high MDR TB (e.g. MDR TB rates >5% among new case and >20% among re-treatment cases), a CBNAAT will be performed to rule out rifampicin resistance before initiation of treatment where patients will be categorized as microbiologically confirmed Drug Sensitive (DST) TB or RIF resistant TB.

C. If the first smear is negative, CXR may be considered and if reported as suggestive of TB, the 2nd sample will be subjected to smear and CBNAAT simultaneously.

D. Based on CBNAAT results, patients will be categorized as microbiologically confirmed Drug sensitive TB or Rif resistant TB, if negative move to differential diagnosis for other etiology or point F.

E. A RIF indeterminate result will get an additional CBNAAT to get a valid result and in case of indeterminate on second occasion, an additional specimen will be collected and sent to the nearest Intermediate Reference Laboratory (IRL) or Culture & Drug Susceptibility Testing (C&DST) centre for LPA or Liquid Culture & DST as appropriate.

F. Wherever the facilities are available, efforts should be made to obtain DST results of all drugs by collecting additional samples and sending to nearest C&DST. (Subject to laboratory capacity).

G. If the both sputum smears and CXR are negative, and physician is still suspecting TB, he will refer patient to pulmonology expert / chest specialist.

H. All key population (PLHIV, Children, EPTB, etc.) will preferentially get an upfront CBNAAT as per approved algorithm for PLHIV and TB HIV patients, pediatric TB and Extra pulmonary TB.

I. The algorithm does not mandatorily decide the “order to DO” the tests / investigations. If needed / available, appropriate tests may be done simultaneously but “order of consideration” for different types of test / investigation results should be as per the algorithm. (e.g. If available, smear for AFB and CXR may be done simultaneously to avoid diagnostic delay / patient's day loss. But, smear results will be prioritized over CXR to make an early diagnosis). If patient walks in with the latest CXR, the same may be considered to reduce the diagnostic delay.

J. All diagnostic health care facilities should have TB labs that are quality assured by competent authority.

Diagnosis of Extra-pulmonary TB

Extra pulmonary tuberculosis (EPTB) refers to any microbiologically confirmed or clinically diagnosed case of TB involving organs other than the lungs such as lymph nodes, pleura, bones and joints, meninges of the brain, intestine, genitourinary tract, etc. A high level of suspicion of EPTB is important in patients with suggestive symptoms and signs.

All efforts should be made to establish microbiological confirmation in case of presumptive EPTB. Appropriate specimens from the presumed sites of involvement must be obtained from all presumptive EPTB patients for CBNAAT / Smear Microscopy / Culture & DST for *M. tuberculosis* / histo-pathological examination, based on type of specimen and availability of facilities. CBNAAT is preferred over other tests. Chest X-ray, Ultrasonography, Computerised Tomography (CT) Scan, Magnetic resonance imaging (*MRI*) are other investigations which can be used as supporting tools for diagnosing EPTB.

Sensitivity of CBNAAT for TB diagnosis, when compared to liquid culture as a 'Gold Standard', is high in FNAC / biopsy specimen from lymph nodes, biopsy specimen from other tissues and cerebrospinal fluid (CSF), but lower in pericardial, ascitic and synovial fluid samples and still lower in pleural fluid. A positive CBNAAT result provides useful confirmation but a negative test does not always rule out TB, since the sensitivity of liquid culture itself in extra-pulmonary specimen is not very high. The laboratory SOP should be referred while using CBNAAT for extra-pulmonary samples. Tissues, to be tested by CBNAAT should be collected **without** formalin. Tissue samples should only be processed at laboratories with appropriate bio-safety requirements. **(Annexure 5)**

Note on Diagnostic Algorithm for Extra Pulmonary TB

1. CBNAAT in specimen from extra-pulmonary sites provides the following results:
   a. *M. tuberculosis detected, Rifampicin sensitive*: Diagnosis of microbiologically confirmed EPTB is made.

   b. *M. tuberculosis detected Rifampicin indeterminate*: a repeat CBNAAT test is performed on the 2nd specimen. If found to be indeterminate on the repeat test, an additional specimen should be collected and sent to the nearest RNTCP certified lab for culture and DST.

   c. *M. tuberculosis detected, Rifampicin resistance*: patient should be treated as per PMDT guidelines;

   d. *M. tuberculosis not* detected: The patient should be evaluated for TB based on clinical, radiological findings and other investigations like histo-pathological examination, ultra sonogram etc. In the event of a decision to treat with anti TB drugs, a diagnosis of clinically diagnosed TB can be made. Otherwise, an alternate diagnosis should be sought.

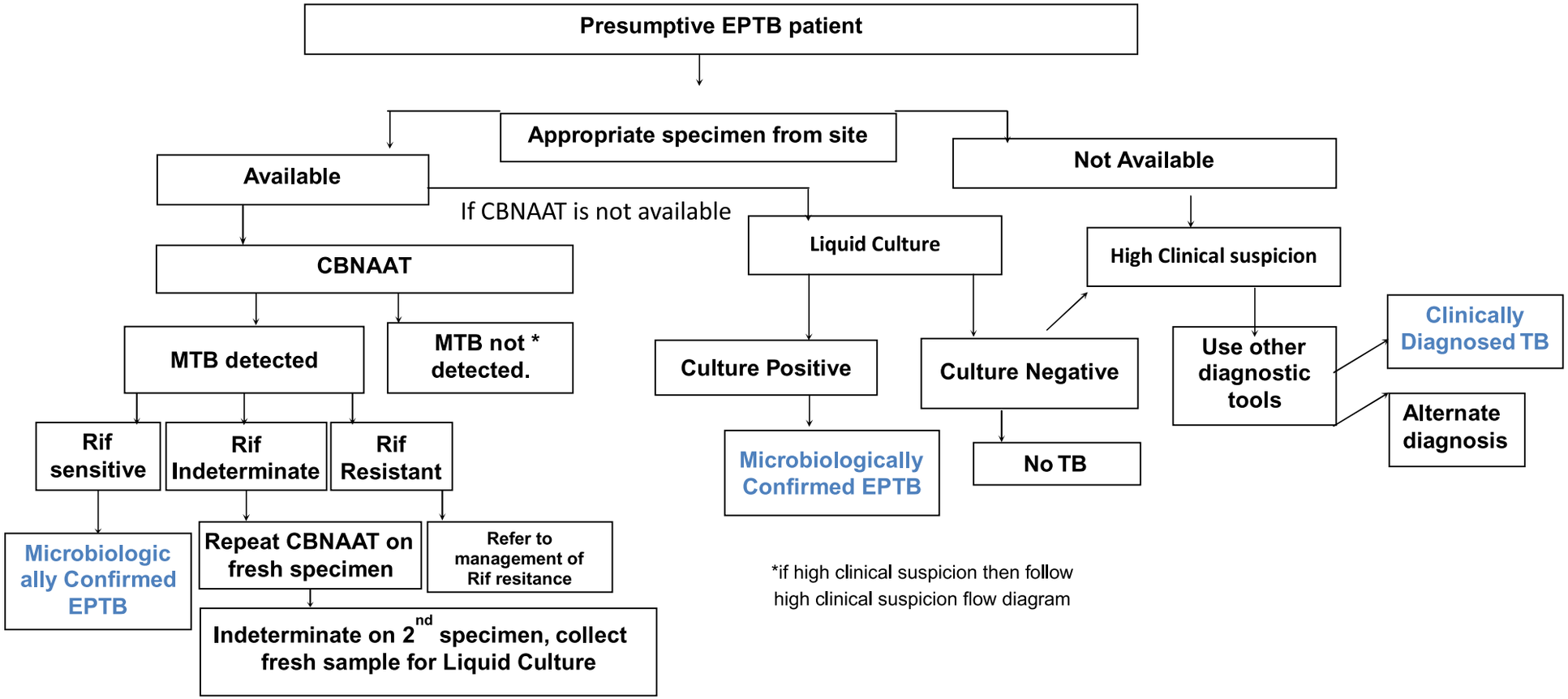
   e. Invalid test: a repeat CBNAAT test is performed on the 2nd specimen, if available.

   f. Error/No result: a repeat CBNAAT test is performed on the same sample.

2. In case CBNAAT is not available, liquid culture needs to be performed. If culture is positive then diagnosis of microbiologically confirmed EPTB is made. Further work up may be done for all EPTB patients if they fall under the criteria of presumptive DR TB.

3. If investigations like CBNAAT/smear microscopy/culture turn out to be negative or if appropriate specimen is not available for these investigations, consultation with a specialist followed by other tests such as histo-pathology, radiology, cytology, biochemical examinations, etc., may be undertaken. In the event of a decision to treat with a full course of anti-TB drugs, diagnosis of clinically diagnosed EPTB is made.

Diagnostic Algorithm for Extra Pulmonary TB



Diagnosis of Paediatric TB

In children with presumptive paediatric TB, every attempt must be made to microbiologically prove diagnosis through examination of appropriate respiratory / non-respiratory specimens with quality assured diagnostic tests. Diagnosis of tuberculosis should not be made only on clinical features and further investigations are always necessary to establish the diagnosis.

In case of suspicion of pulmonary TB, sputum examination should be carried out among children who are able to give good quality specimens. CBNAAT is the preferred investigation of choice. If CBNAAT is not readily available or testing is not possible even by referral, smear microscopy should be performed. If *M. tuberculosis* is detected, by either of methods patient is diagnosed as microbiologically confirmed pulmonary TB.In situations where *M. tuberculosis* is not detected or specimen is not available, chest X-ray and Tuberculin skin test (TST) by Mantoux technique using 2 TU of PPD RT 23 should be done. For interpretation and further course of action, refer to the diagnostic algorithm for childhood pulmonary TB.

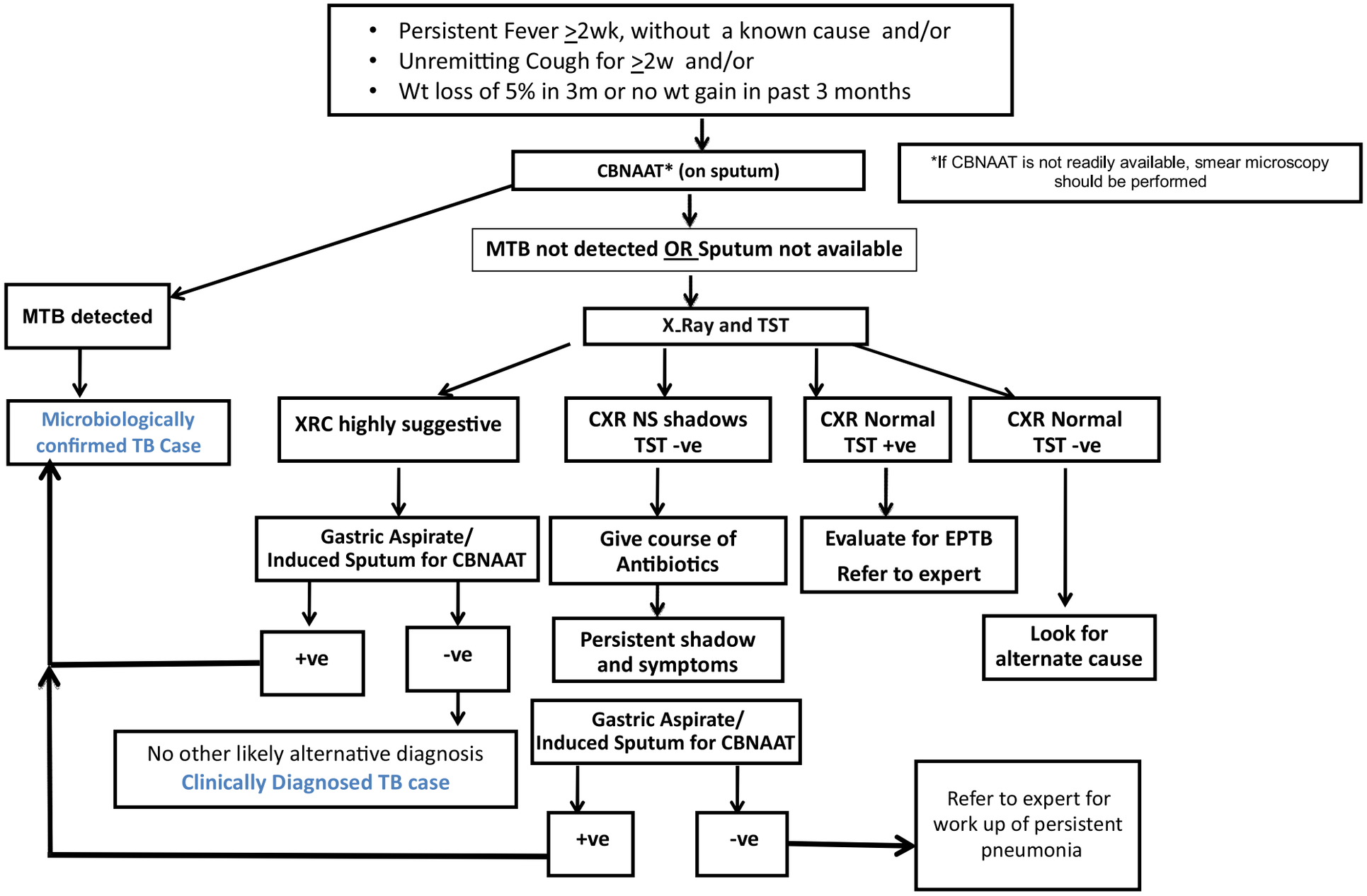
Notes on diagnostic algorithm

1. This algorithm is for children who are likely to have drug sensitive disease i.e. have not received ATT previously ever and are not presumptive drug resistant TB cases (lost to follow up, recurrent, treatment failure, HIV).
2. Proper Characterization of symptoms is very important starting point. Weight loss or not gaining weight should always be documented with appropriate and proper weighing.
3. Where CB NAAT is doable, smear examination may not be done. Whenever smear is used for diagnosis at least 2 samples should be sent while a single sample is subjected to CB NAAT. If a specimen is positive by any of these methods, the disease is labelled as Microbiologically confirmed TB.
4. Highly suggestive Chest X-ray refers to skiagrams showing either Miliaryor lymphadenopathy (hilar or mediastinal) or chronic fibro-cavitatory shadows. If the radiological picture is highly suggestive of TB, then proceed to do further investigations irrespective of the TST result as the sensitivity of the test is not 100%.
5. Non Specific Chest X-ray: Refer to patterns other than highly suggestive like consolidations, in homogenous shadows or bronchopneumonia, etc.
6. Whenever indicated, alternative specimens (Gastric aspirate/ Induced sputum/ broncho-alveolar lavage) should be collected by a skilled health care provider, depending upon available infrastructure and sample should be subjected to CBNAAT.
7. Antibiotics like linezolid or any quinolone or Amoxycilin-Clavulanic acid should not be used as they have anti-TB action.
8. Children with persistent symptoms, non specific shadows and negative smears and negative other samples (GA/IS) by CB NAAT should be referred to experts for further work up of persistent pneumonia.
9. All TB cases diagnosed must be offered testing for HIV.
10. Instructions for administering PPD vials are placed at (**Annexure 6)**
11. Whenever Rif Resistant result is reported on CBNAAT further management should be carried out as per the guidelines on Drug Resistant TB

All presumptive DR TB patients should be appropriately followed up with PMDT guidelines. In case of suspicion of Extra Pulmonary TB, the diagnostic algorithm as given in section above may be followed.

There is no role for inaccurate / inconsistent diagnostics like serology (IgM, IgG, IgA antibodies against MTB antigens), various in-house or non-validated commercial PCR tests and BCG test. Currently there is no role of IGRAs in clinical practice for the diagnosis of TB.

Diagnostic algorithm for Pediatric Pulmonary TB



Diagnosis of Drug Resistant TB

Drug resistant TB is a laboratory based diagnosis and is performed either by phenotypic Drug Susceptibility Testing using solid / liquid culture or genotypic testing for detection of resistance by Line Probe Assay / Cartridge Based Nucleic Acid Amplification Tests like Xpert MTB/Rif. CBNAAT detects resistance to only Rifampicin while LPA detects resistance to both Rifampicin and Isoniazid.

Genotypic testing is much faster than phenotypic methods, as these are not growth based tests. DST results by Solid LJ media has a turnaround time (TAT)of upto 84 days, Liquid Culture (MGIT) upto 42 days, LPA upto 72 hours and CBNAAT by 2 hours.

Under RNTCP, access to either CBNAAT or LPA is available **and should be used for diagnosis of DR-TB.**Refer to RNTCP Laboratory manual of Standard Operating Procedures for culture and DST, LPA and CBNAAT testing.

For CBNAAT, a single specimen is required for testing. The need for a second specimen for CBNAAT arises in case the result is "Invalid" or "Rif Indeterminate". For "Errors", "No Results" the test can be repeated on the same specimen after appropriate trouble shooting as per the user manual. Two specimens should be collected (spot-early morning or spot – spot) for examination by LPA which can be performed directly on sputum specimen which are positive on microscopy or on culture isolates of specimen which were negative on microscopy.

All efforts must be made to optimize the utilization of all locally available genotypic diagnostic capacity.

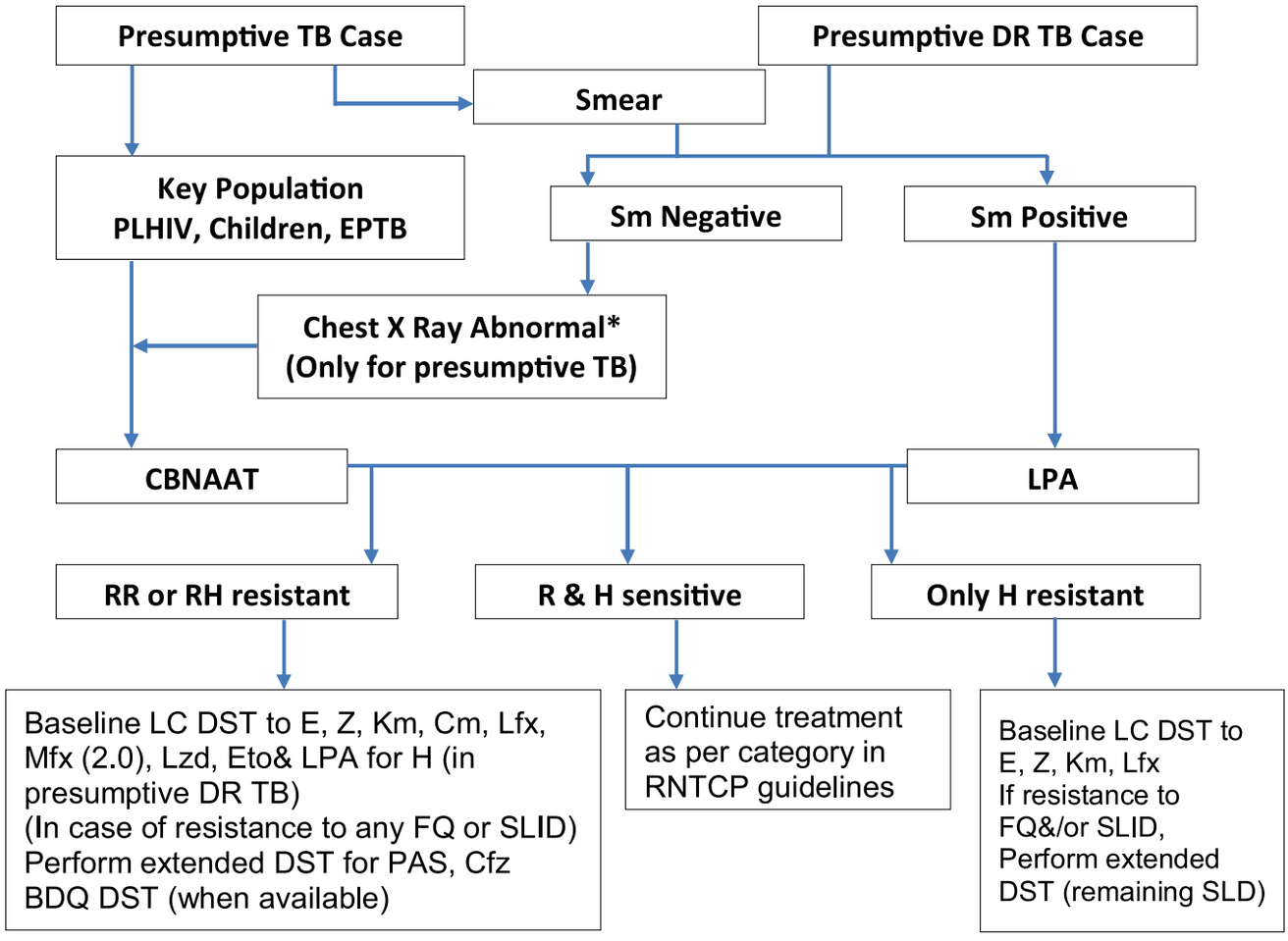
If Rifampicin Resistance is confirmed by CBNAAT or LPA, start Standardized Regimen for MDR TB and perform Liquid Culture DST at baseline to Levofloxacin and Kanamycin.

As guided by the diagnostic algorithm above, wherever the facilities are available, efforts should be made to obtain DST results of all the drugs intended to be used in regimen, by collecting additional samples and sending to nearest C&DST. (Subject to laboratory capacity which is dynamic and will be expanded in a phased manner).The programme has introduced Bedaquiline through conditional access programme initially at six sites with diagnostic protocol comprising of extended sets of DSTs. This diagnostic Algorithm for Bedaquiline containing and optimized background regimen is as follows

If Rifampicin Resistance is confirmed by CBNAAT or LPA, start Standardized Regimen for MDR TB and perform Liquid Culture DST at base line to Levofloxacin, Moxifloxacin, Kanamycin, Capreomycin, Ethambutol, Ethionamide, Linezolid and Pyrazinamide along with LPA for Isoniazid on sample /culture isolate (reported as KatG or inhA mutation to decide on use of INH) with the next available specimen.
If resistance is detected to any second line injectable and/or fluoroquinolones, extended DST is performed for Para Amino Salicylic acid, Clofazamine and Bedaquiline (whenever available) and treatment modified accordingly.

If Rifampicin sensitive is detected by CBNAAT among presumptive DR-TB cases, send sample for LPA or liquid culture. All Isoniazid sensitive patients after testing with LPA or those while awaiting results of LPA should continue treatment with first line drugs as per RNTCP guidelines. If Isoniazid resistance is detected by LPA, report of result must also mention Kat G or INH-A mutation. Furthermore, Liquid Culture DST will be performed for Ethambutol, Pyrazinamide, Kanamycin, and Levofloxacin. If resistance is detected to second line injectable and/or fluoroquinolones, perform DST for remaining second line drugs as mentioned above. Initiateor modify treatment as per Drug susceptibility test results.

Diagnostic Algorithm for Bedaquiline containing and optimized treatment regimen



- If RR by CBNAAT, in addition to other drugs, H resistance (by LPA) to be done and treatment modified accordingly.
- For samples reported by LPA – report must mention H- resistance by Kat G or INH A mutation.
- For new patients (those who do not fit in the definition of presumptive DR-TB case diagnosed as TB with RR by CBNAAT – a second CBNAAT test will be offered along with liquid culture DST

** Those who do not fit in the definition of presumptive DR-TB case*

Intensified TB Case Finding

Intensified case finding activity (ICF) is basically a provider initiated activity with the primary objective of detecting TB cases early by active case finding in targeted groups and to initiate treatment promptly. It can target people who anyway have sought health care with or without symptoms or signs of TB and also people who do not seek care. Increased coverage can be achieved by focusing on clinically, socially and occupationally vulnerable populations who have greater risk of TB. It must be remembered that 'Screening' is a dynamic process and the prioritization of vulnerable groups, choice of screening approach and screening interval should be regularly reassessed by the programme. Decisions on when and how to screen for TB, which vulnerable groups to prioritize and which screening tool to use will depend on the vulnerable group, the capacity of the health system, and the availability of resources.

Screening Tools

The most sensitive screening tool needs to be used to improve the pre-test probability of the subsequent diagnostic test and to reduce the number of people who need to undergo further diagnostic evaluation; and it may be different for different vulnerable groups or settings. Options for the screening tools include symptom screening and chest radiography. The following table shows the sensitivity and specificity of the screening tool options.

Pooled sensitivity and specificity of different screening tools for Pulmonary tuberculosis (TB), using culture-confirmed pulmonary TB as the gold standard

	Screening tests		Sensitivity %	Specificity %
	Primary Screening	Cough >= 2 weeks	56.2 (46.7, 65.4)	95.3 (94.4, 96.1)
		Any symptom	66.0 (56.3, 74.5)	93.8 (92.7, 94.8)
		Any symptom OR history of ATT	71.2 (64.8, 76.75)	92.7 (91.7, 93.6)
		CXR as initial screening tool	76.6 (70.8, 81.6)	97.3 (96.5, 97.9)
		Cough >= 2 weeks OR CXR any abnormality	94.3 (91.1,96.4)	93.1 (92.3,93.8)
	Secondary screening	CXR among those having Cough >= 2 weeks	66.8 (60.5, 72.7)	87.8 (83.7, 91.0)
		CXR among those having any symptom	65.0 (58.8, 70.7)	89.8 (85.8, 92.7)
		CXR any abnormality among those having any symptom OR H/o ATT	67.1 (61.7-72.1)	86.7 (82.3-90.2)

Screening strategies

1. Community screening can be done by:
Inviting people to attend screening at a mobile facility or a fixed facility. Invitations may target specifically people within a given vulnerable group, those

- who have had recent close contact with someone who has TB and people with symptoms of TB
- Going door to door to screen households

2. **Institutional screening**

- In Health care facilities : Systematically perform active screening of vulnerable individuals attending hospitals and other health care institution
- In congregate settings: Systematically perform active screening of vulnerable individuals in shelters, old age homes, refugee camps, correctional facilities and other specific locations such as workplaces.

Recommendations on Vulnerable groups to be screened

A vulnerable group is any group of people in which the prevalence or incidence of TB is significantly higher than in the general population. The recommended vulnerable groups to be considered for intensified case finding may be classified as follows:

Clinical	Social	Geographical
Clients attending HIV Care Settings	Prisoners	Urban Slums
Substance abuse including smokers	Occupations with risk of developing TB	Hard to reach areas
Co-morbidities like Diabetes Mellitus, Malignancies, patients on dialysis and on long term immunosuppressant therapy	People in Congregated settings – night shelters, De-addiction centres, Old age homes	Indigenous and tribal populations
Health Care Workers		
Household & Workplace Contacts		
Patients with Past History of TB		
Malnourished		
Antenatal mothers attending antenatal clinics/MCH clinics		

For the groups classified above; the rationale of intensified case finding activities in the particular vulnerable group, the screening tool recommended and the strategy for screening are discussed in **Annexure 7.**

In all settings where intensified case finding is undertaken, systematic TB **recording and reporting** needs to include the following:

- A special register with individual-level information for each person screened may be used to obtain refined data about subcategories of persons within a vulnerable group.
- A register of all presumptive TB cases (Presumptive TB register) who undergo further diagnostic evaluation (if a register is used to collect individual-level information for all people who are screened, then this information can be included in it)
- A column in the laboratory registers for noting whether the tested patient was identified through screening, and to which risk group the patient belongs;
- A column in the treatment registers to note whether the patient was identified through screening, and to which risk group the patient belongs

Adopting a well thought **ACSM** strategy and integrating it with the planning process for ICF will result in a multiplier effect in case finding efforts.

Utilizing Mobile Medical Units for screening presumptive TB patients in identified and hard to reach areas. Using Information, Communication &Technology (ICT) tools to enhance case finding are some the examples of innovation in ICF which can be adapted.

Laboratory Quality Assurance

Quality Assurance (QA): A System designed to continuously improve the reliability and efficiency of laboratory services. The Quality Assurance activities include:

- Internal Quality Control (IQC)
- External Quality Assurance (EQA)
- Quality Improvement (QI)

For Smear Microscopy

The nationwide network of designated sputum smear microscopy laboratories provide appropriate and accessible quality assured TB diagnostic services. To meet the recommended standards of diagnostic practices for TB, the programme provides quality reagents and equipment to the laboratory network. A system has been designed for EQA of sputum smear microscopy and for supervision and monitoring of the diagnostic systems by the RNTCP which is carried out by Senior TB Laboratory Supervisor (STLS) locally and by the Intermediate (State level) and National Reference Laboratory at higher levels.

The NRLs work closely with the IRLs, monitor and supervise the IRL's activities and also undertake periodic training for the IRL staff in EQA, Culture & DST activities. Three microbiologists and four laboratory technicians have been provided by the RNTCP on a contractual basis to each NRL for supervision and monitoring of laboratory activities. The NRL microbiologist and laboratory supervisor / technician visit each assigned state at least once a year for 3 to 4 days as a part of on-site evaluation under the RNTCP EQA protocol

The IRL ensures the proficiency of staff in performing smear microscopy activities by providing technical training to district and sub-district laboratory technicians and STLSs. The IRLs undertake on-site evaluation and panel testing to each district in the state, at least once a year.

Designated Microscopy Centre (DMC) is the most peripheral laboratory under the RNTCP network. For DMC and its supervisory staff, quality improvement trainings conducted periodically focus on issues such as human resources, trainings, AMC for binocular microscopes, quality specifications for ZN stains, RBRC blinding and coding issues, bio-medical waste disposal, infection control measures etc.

Internal Quality Control (IQC): of microscopy is a process of effective and systematic internal monitoring of the performance of bench work in the microscopy laboratory against established limits of acceptable test performance. This is accomplished by checking:

a) Instruments: binocular/fluorescence microscopes, weighing machines, water baths etc.
b) New lots of staining solutions.
c) Smear preparation, staining, examination, grading, recording, reporting and storage.
d) Appropriate disinfection and disposal.

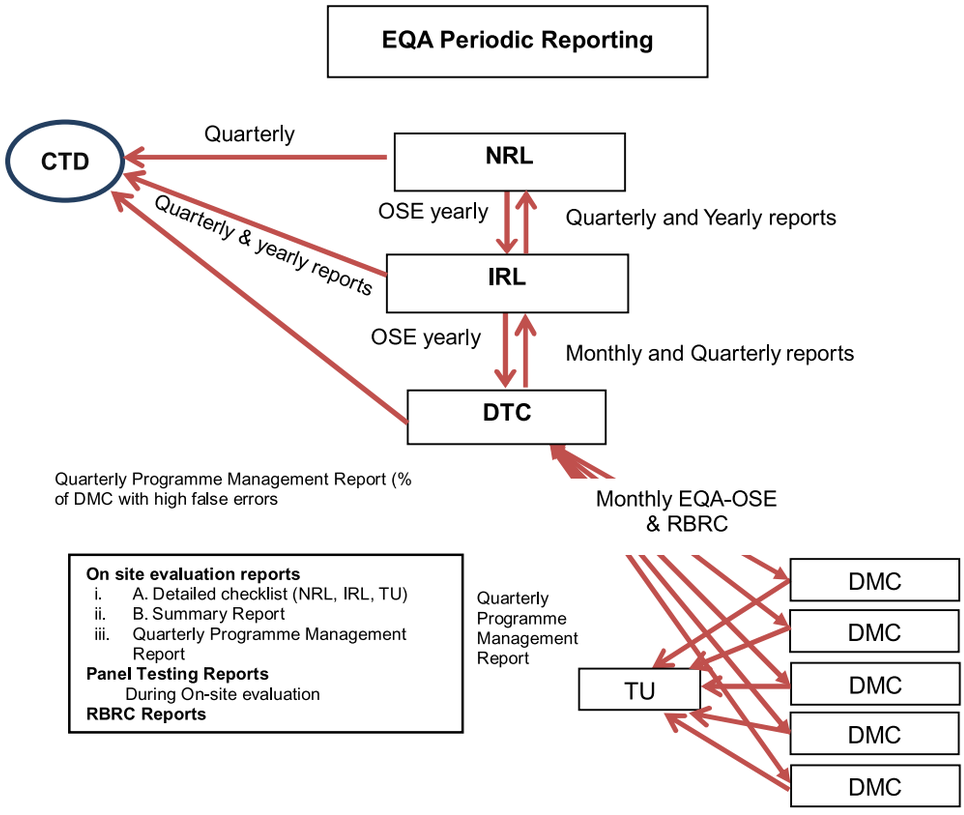
External Quality Assessment (EQA): EQA is a process to assess laboratory performance which includes:

- On-site evaluation (unblinded reading of smears, QC and process of smear microscopy)
- Panel Testing (PT of lab personnel during OSE)
- Random blinded re-checking of routine smears

EQA also allows participant laboratories to assess their capabilities by comparing their results with those obtained in other laboratories in the network

Quality Improvement (QI): A continuous process by which all components of smear microscopy are carefully analyzed for improving the diagnostic services. Data Collection, analysis and problem solving are the key components of this process.

The schematic representation of the EQA reporting process is shown below:



Quality assessment methods under RNTCP have been implemented for more than a decade now and it is therefore necessary to revise the modalities to the present day scenario as well as to have mechanisms to routinely monitor the quality parameters. Monitoring quality of sputum smear microscopy depends on the:

- Evaluation of entire process of smear microscopy.
- Quality of data collection, analysis and correct interpretation of the results.
- Identifying defects, followed by remedial action.
- Quality Improvement largely relies on effective on-site evaluations.

The mechanisms involved as well as appropriate data collection is revised periodically in consultation with the National Reference Laboratories. For further details refer to Guidelines for Quality Assurance of Smear Microscopy.

Quality Assurance for Culture and DST:

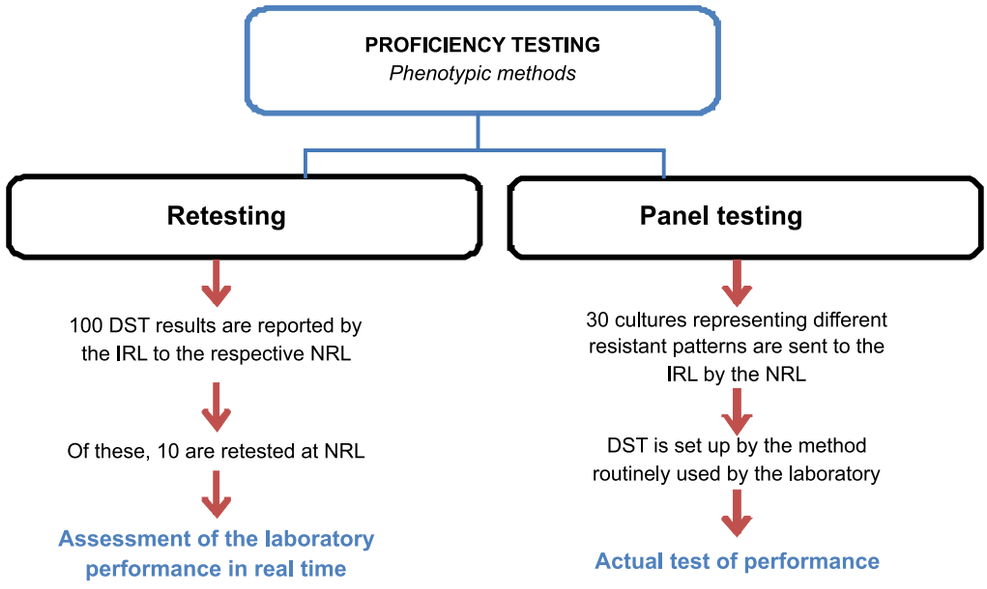
The components of quality assurance for Culture and DST include Internal Quality Control (IQC) and External Quality Assessment mechanisms.

Internal Quality control of LJ media is performed as a routine laboratory protocol and involves testing each batch of media for contamination as well as the use of control strain (H37RV) for growth parameters. IQC for MGIT is instrument guided. External quality assessment is not performed for culture.

Internal quality control of DST involves use of control strain (H37RV) as well as mono resistant strains (R mono and H mono) with every batch of DST performed.

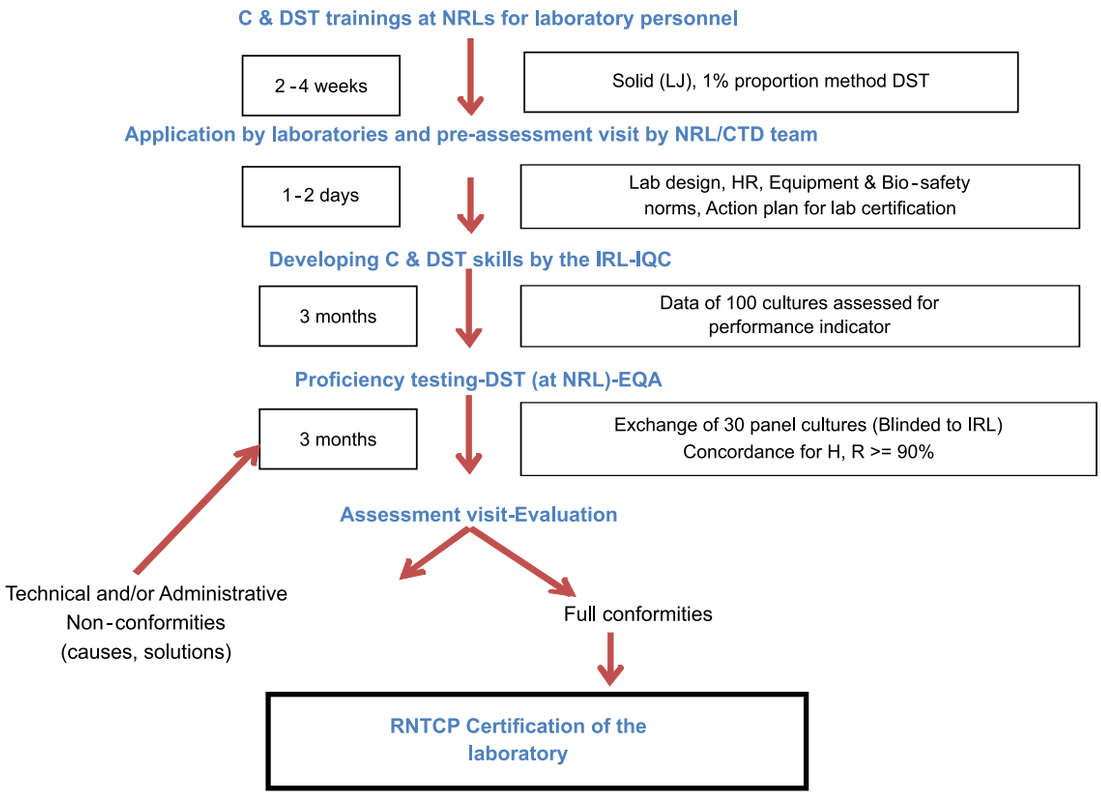
External quality control for both LJ as well as MGIT is performed in two stages, initial retesting as one time activity where the NRL retests ten strains out of hundred performed by the participating laboratory. This is assessment of the laboratory in real time. As a second stage the participating laboratory is required to perform DST for thirty panel strains received annually from the NRL. This is the actual test of performance. For further details refer to Guidance for accreditation of laboratories under RNTCP for Mycobacterial Culture & DST.

Schematic representation of Proficiency Testing:



Schematic representation of the process of Certification:

RNTCP Certification process for TB culture and DST laboratories



Quality assurance for LPA:

Initially, the NRL retests DNA extracts of twenty strains out of 50 performed in duplicates at the participating laboratory. This is followed by annual proficiency testing with panel strains.

PT Benchmark:

- Invalid LPA results – Less than 10%
- Contamination of negative control – Clean in all runs
- Internal Concordance – Greater than 95%
- External Concordance – Greater than 95%

Quality assurance for CBNAAT:

Each CBNAAT cartridge contains internal controls: Sample Processing Control (SPC) and Probe Check Control. If Probe Check fails, then the test is stopped, and an Error result is obtained. Troubleshooting is required based on the error code generated. Error rates higher than 5% should be investigated.

SPC must be:

- Positive when the result is **MTB Not Detected.**
- SPC can be negative or positive when the result is **MTB Detected.**
- The test result is **invalid** if the SPC is negative.

On site visits to CBNAAT sites should be planned at regular intervals to assess laboratory performance by district, state, IRL, NRL, CTD using the available standardized supervisory checklist for CBNAAT. CBNAAT sites in the districts should be visited by IRL/NRL during their EQA visits. Poorly performing sites should be prioritized for on-site visits.