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Ministry of Health and Family Welfare
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OPERATIONAL MANUAL FOR ISONIAZID PREVENTIVE THERAPY

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Central TB Division
Directorate General of Health services
Ministry of Health and Family Welfare
Government of India, New Delhi

Basic Services Division
National AIDS Control Organization
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Government of India, New Delhi

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PREFACE

Tuberculosis (TB) is commonest opportunistic infection and foremost cause of death among people living with HIV(PLHIV).To mitigate the effect of dual burden of HIV and TB co-infection, the Ministry of Health and Family Welfare, Government of India through its National AIDS Control Organisation (NACO) and Central TB Dvision has been undertaking joint collaborative efforts as per the National Framework for HIV TB collaborative activities in India.

Isonaizid Preventive Therapy is one of the key interventions recommended by World Health Organisation to reduce the burden of TB in people living with HIV

The "National Framework for HIV-TB collaborative activities (Nov-2013)" and the "Standards of Tuberculosis care in India" recommend Isonaizid Preventive Therapy as one of the important startegy for prevention of TB among PLHIV as a important component of the package of care delivered by HIV and TB service providers for people living with HIV.

An e-consultative process was initiated to seek inputs and comments to develop **"Operational Manual For Isonaizid Preventive Therapy"** .The operational manual is intended to build the capacity of National AIDS Control Program (NACP) and Revised National TB Control Program (RNTCP) program staff at various level and provide operational guidance for implementation of Isonaizid Preventive Therapy in country .The use of this manual will assist NACP and RNTCP staff to deliver Isonaizid Preventive Therapy in effective manner.

Collaborative efforts of NACP, RNTCP and program partners in bringing out this operational manual are highly appreciable.

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Abbreviations and Acronyms

PLHIV	People Living with HIV
CLHIV	Children Living with HIV
RNTCP	Revised National Tuberculosis Programme
NACP	National AIDS Control Programme
CTD	Central TB Division
NACO	National AIDS Control Organisation
WHO	World Health Organization
UNAIDS	United Nations Programme on HIV/AIDS
HRG	High Risk Group
IDU	Injection Drug Users
SA-ICTC	Stand Alone Integrated Counselling and Testing Centre
F-ICTC	Facility Integrated Counselling and Testing Centre
LAC	Link ART Centre
TI	Targeted intervention
CBNAAT	Cartridge Based- Nucleic Acid Amplification Test
DMC	Diagnostic Microscopic Centre
WBT	Whole blood finger prick test
PITC	Provider Initiated Testing and Counselling
3 I's	Intensified TB Case Finding, Airborne Infection Control & Isoniazid Preventive Therapy
ICF	Intensified Case Finding
IC	Infection Control
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
PTB	Pulmonary TB
EPTB	Extra Pulmonary Tuberculosis
LTBI	Latent Tuberculosis Infection
DR-TB	Drug-Resistant TB
DOTS	Directly Observed Treatment Short course
PMDT	Programmatic Management of Drug Resistant TB
Z	Pyrazinamide
4 'S'	Four Symptoms Screening
DST	Drug Sensitivity Test
CPT	Cotrimoxazole Preventive Therapy

1: INTRODUCTION

Tuberculosis (TB) is the most common opportunistic infection amongst HIV-infected individuals. It is a major cause of mortality among patients with HIV and poses a risk throughout the course of HIV disease. Overall, the risk of developing TB is between 20 and 37 times greater among people living with HIV (PLHIV) than those who do not have HIV infection (WHO, 2010).The risk of TB in HIV-infected persons continues to increase as HIV disease progresses and immunity decreases.

It is estimated that there are 2.1 million people living with HIV in India with an estimated adult HIV prevalence of 0.27% (range: 0.2%–0.4%).TB accounts for 25% of deaths among PLHIV in India. Although only 5% of incident TB patients are HIV-infected, in absolute terms it means more than 100,000 cases annually, ranks second in the world and accounts for about 10% of the global burden of HIV-associated TB. HIV positivity among PLHIV varies from states /districts in the country, the proportion of HIV positive among TB patients over 10% in high HIV burden states to up to 40% in some high burden districts.

TB -HIV Coordination:

To mitigate the effect of dual burden of HIV and TB co-infection, the Ministry of Health and Family Welfare, Government of India through its National AIDS Control Organization (NACO) and Central TB Division (CTD) has been undertaking joint collaborative efforts since 2001. While joint HIV/TB activities started with differential strategies based on underlying HIV burden initially, the programme evolved over the years and currently implements uniform HIV/TB collaborative activities across the country. NACP and RNTCP have developed a policy of HIV/TB collaborative interventions based on experience gained during programme implementation in initial years, important operational research (OR) studies instituted by NACP and RNTCP and the WHO HIV/TB interim policy, for implementation across the country.

National Framework for Joint HIV/TB Collaborative Activities in India

Under the HIV-TB collaborative activities NACO and CTD jointly developed a National Framework for HIV/TB Collaborative activities in 2008 and 2009, which was updated in 2013, aiming to incorporate recent policies regarding HIV -TB. It included interventions that reduce the morbidity and mortality from TB in PLHIV. The salient features are as below.

1. **Emphasis on Integrated TB and HIV services e.g. HIV screening at RNTCP Diagnostic Microscopic Centre (DMC)**

2. **Focus on early detection and early care**

a. Early detection of TB in PLHIV

i. Early suspicion of TB–symptoms of any duration among PLHIV

ii. Use of an **expanded clinical algorithm for TB screening** that relies on presence of **four symptoms** (current cough, weight loss, fever or night sweats).

iii. Strengthen ICF at ART, Link ART centre (LAC) and Targeted intervention projects (TI) for High Risk Group (HRG) specially Injection Drug Users (IDU)

iv. Offering upfront Cartridge Based- Nucleic Acid Amplification Test (CBNAAT) among presumptive TB cases among PLHIV

b. Early detection HIV/TB

i. Enhance HIV testing facilities in settings with lack of co-located HIV and TB testing facilities, by establishing HIV screening services using whole blood finger prick test (WBT)

ii. Strengthen HIV testing of TB patients in high HIV prevalent settings by promoting establishment of Facility Integrated Counselling and Testing Centre(F-ICTC) where DMC exists

iii. Provider Initiated Testing and Counselling (PITC) among patients being evaluated by diagnostic smear microscopy presumptive TB cases in high HIV prevalent settings

c. Early Care

Promotion of 'single window delivery services' where in all HIV/TB patients get their TB medications from the ART centres along with ART drugs.

i. ART for HIV infected TB cases irrespective of CD4 count
ii. Prompt ART initiation- within 8 weeks of commencing Anti-TB treatment.
iii. Monitoring of timeliness of ART initiation through expanded ART reporting formats

3. Early detection and care of HIV infected Drug Resistant TB patients (DR-TB/HIV)

i. Strengthen HIV testing in presumptive DR-TB cases (Criteria C)
ii. Ensure access to culture and drug susceptibility testing for HIV infected TB patients
iii. Prompt linkage of HIV infected DR-TB cases to ART centres
iv. Prompt initiation of ART in HIV infected DR-TB cases

4. Prevention of TB among HIV infected adults and children

i. Implementation of IPT for all PLHIV (On ART + Pre-ART)
ii. Strengthen implementation of air borne infection control strategies.

5. Strengthen HIV/TB activities among children and pregnant women

6. Promotion of participation of private, NGO, CBO health facilities and affected communities working with NACP and RNTCP to strengthen HIV/TB collaborative activities.

The 3"I"s

1. Intensified Case Finding (ICF)

All clients attending ICTC/F-ICTC/TI/ART/LAC/LAC Plus should be screened for TB symptoms at every visit. Clients who have symptoms or signs, irrespective of their HIV status, should be referred to RNTCP for early diagnosis of TB and link patient with the treatment facilities for further management.

2. Isoniazid Preventive Therapy (IPT):

Isoniazid is the most effective bactericidal drug currently available. It protects both against progression of latent TB infection (LTBI) to active disease (reactivation) as well

as from reinfection when exposed to active TB case. People living with HIV who are unlikely to have active TB should receive at least six months of IPT as part of a comprehensive package of HIV care.

3. Infection Control (IC) for prevention of TB in HIV care settings

There is the risk of transmission of tuberculosis infection occurring in health care facilities including the laboratory when patients remain undiagnosed and untreated for tuberculosis. This may be curtailed by early diagnosis and immediate initiation and adherence to RNTCP treatment regimens. This prompt and timely action will make infectious TB patients rapidly non-infectious.

It is now mandatory that any Infection Control plan of the facility should include infection control for TB and TB/ HIV. Broadly, infection control needs to be addressed at three different levels: administrative, environmental and personal.

2: INTENSIFIED TB CASE FINDING AT ART AND LINK ART CENTRES

TB screening - ICF at ART Centres

HIV-infected persons attending ART centres have a high prevalence of TB disease (6 to 8%). The incidence of TB among ART clients is also very high, even when on ART. Although ART reduces risk of incident TB, it remains many times higher compared to general population. In addition, HIV-infected clients having undiagnosed or untreated TB may seek care at ART centres and thus exposing other HIV-infected persons to the risk of acquiring TB. Therefore active effort for intensified TB case finding (ICF) at ART centres are critical for early suspicion and detection of TB, linkage to treatment and thus for prevention of transmission of infection to other clients. The national ART guidelines clearly state that all patients coming to ART centres should be actively screened for opportunistic infections, particularly tuberculosis. All people living with HIV should be regularly screened for four symptoms viz., current cough of any duration, fever of any duration, significant weight loss or drenching night sweats, during every visit to a health facility and every contact with a health-care provider. Those with history of coughing blood and sputum and with any pulmonary abnormality in chest X-ray should also be evaluated for TB. Similarly, Children Living With HIV (CLHIV) who have one or more of the following symptoms – failure to thrive, fever or cough of any duration or history of contact with a TB patient should be evaluated for TB.

Screening for TB is important regardless of whether the PLHIV is receiving IPT or ART. The presumptive TB cases identified at ART centres or Link ART centres should be prioritized and "fast-tracked" for evaluation by Senior Medical Officer (SMO)/Medical Officer (MO) to minimize opportunities for airborne transmission of infection to other PLHIV.

PLHIV suspected to have TB by MO, should be subjected to testing of sputum / appropriate specimen from a relevant extra-pulmonary site by Cartridge Based- Nucleic Acid Amplification Test (CBNAAT) and should be sent with the referral form (annex- IV) at the nearest facility for diagnosis. CBNAAT is the frontline test for diagnosis of TB among PLHIV & CLHIV. If

CBNAAT is not available, arrangements have to be made for collection and transportation of sputum specimen to the nearest CBNAAT site. If CBNAAT linkage is not available, then the patient should be evaluated with microscopy and Chest-X ray on the same day.

Smear negative TB and extra pulmonary TB (EPTB) is more common among people living with HIV and therefore a high level of suspicion is required. In the event of suspicion of Extra Pulmonary TB, the diagnostic algorithm as for HIV negative presumptive EPTB patients (annexure-II) may be followed. Similarly, refer to annexure -III for diagnostic algorithm for paediatric pulmonary TB.

Preferably, PLHIV should be offered TB and HIV diagnostic facility at the same premises as a "one-stop service" in order to reduce diagnostic delay and to link those not having any of the four symptom complex to IPT services.

In addition, the referrals presumptive TB cases should be recorded on an ART centre TB-HIV line list to facilitate coordination with RNTCP programme staff and to track the patient closely through the process of TB diagnosis and Directly Observed Treatment Short course (DOTS) initiation. It is also crucial that ART Centre staff members attend monthly HIV/TB coordination meeting. The HIV/TB monthly reporting format to be generated at ART centres is incorporated into the ART centre monthly report.

Information of all HIV infected TB patients in HIV care should be recorded in the ART centre HIV/TB register. These include TB patients detected by ART centre staff as well as those TB patients found HIV infected while on DOTS treatment and referred to ART centre by the RNTCP. TB-HIV register is an important monitoring tool to track timeliness of initiation of Co-trimoxazole preventive therapy (CPT) and ART the TB treatment outcome to modify ARV regimens as per guidelines. It is also important that ART centre staff carry this register when they attend monthly HIV/TB coordination meeting to update information on TB treatment outcome from RNTCP staff and share information pertaining to CPT and ART with them for recording into RNTCP TB registers.

PLHIV diagnosed to be suffering from TB are presumptive Multi Drug Resistant (MDR) cases and need to follow the algorithm for diagnosis of drug resistant TB (DR-TB) & management as per the Programmatic Management of Drug Resistant TB (PMDT) Guidelines in India.

TB screening - ICF at Link ART Centres (LAC)

The ICF activity is also implemented at all Link ART plus and Link ART centres in the country. As in ART centres LAC-Plus and LAC should 1) implement ICF using symptom screening on every encounter 2) promptly refer presumptive TB case to RNTCP diagnostic facilities, and 3) refer the patient to ART centre promptly if TB is detected for initiation of ART or modify current ARV regimen. Similar to ART centre, the LAC staff nurse /counsellor should maintain line-list, exchange with local RNTCP staff to seek information on TB diagnosis and treatment and complete the line-list.

The LAC Plus use same line-list format as the ART centre while at LAC the ICTC line-list format is used (since ICTC counsellor runs the LAC). The completed line-list from LAC-plus is merged with ART centre line-list whereas that from LAC is merged into ICTC line-list for the same period and monthly report is generated accordingly.

These mechanisms are designed considering operational feasibility but key point is if TB is detected among patients at LAC plus of LAC, they **must be promptly referred to ART centre** for further management.

Diagnostic Tools for TB diagnosis

All efforts should be undertaken for microbiologically confirming the diagnosis in presumptive TB patients.

Sputum Smear Microscopy (for AFB):

- Sputum smear stained with Zeil-Nelson Staining or
- Fluorescence stains and examined under direct or indirect microscopy with or without LED.

Culture:

- Solid(Lowenstein Jansen) media or
- Liquid media (Middle Brook) using manual, semi-automatic or automatic machines e.g. Bactec , MGIT etc.

Rapid diagnostic molecular test:

- Conventional PCR based Line Probe Assay for MTB complex or
- Real-time PCR based Nucleic Acid Amplification Test (NAAT) for MTB complex e.g. CBNAAT

Radiography

Where available, CXR to be used as a screening tool to increase sensitivity of the diagnostic algorithm. Any abnormality in chest radiograph may be evaluated for TB.

Diagnosis of Pulmonary TB

Pulmonary tuberculosis (PTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheo-bronchial tree. Diagnostic algorithm is annexed at Annexure I.

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 & Drug Sensitivity Test (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.

If CBNAAT testing facility is available, then it should preferentially be used for establishing the microbiological diagnosis. Diagnostic algorithm for Extra pulmonary TB is annexed at annexure II.

CBNAAT, having better sensitivity than smear examination in specimens from extra-pulmonary sites has been recommended as the preferential test for diagnosis, but not in urine, blood and stools. 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 Cerebro-Spinal Fluid (CSF), but lower in pericardial, ascetic 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.

Tissues, to be tested by CBNAAT should be collected without formalin.

Diagnosis of Paediatric TB

In children with presumptive paediatric TB, every attempt must be made to bacteriologically prove the 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. In case sputum specimen is not available, alternative specimens (Gastric lavage/ Induced sputum/ broncho-alveolar lavage) should be collected by a skilled health care provider, depending upon available infrastructure. CBNAAT is the preferred investigation of choice. If *M. tuberculosis* is detected, patient is diagnosed as microbiologically confirmed pulmonary TB.

If CBNAAT is not available, smear microscopy should be performed. In situations where *M. tuberculosis* is not detected on CBNAAT / smear microscopy is negative or not available, chest X-ray and Tuberculin skin test (TST) by Montoux 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. General antibiotics in particular situations as given in the diagnostic algorithm Fluroquinolones & Amoxycilin-Clavulanic acid must not be given. Diagnostic algorithm for Paediatric TB is annexed at Annexure III.

3: ISONIAZID PREVENTIVE THERAPY

About 50% adult in the community have Latent TB infection (LTBI). Isonaizid Preventive Therapy (IPT) is one of the 3 I's globally recommended strategy for prevention of incident TB among HIV infected individuals. IPT is a key public health intervention for the prevention of TB among people living with HIV and has been recommended as part of a comprehensive HIV and AIDS care strategy by World Health Organisation (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), National Framework for HIV TB Collaborative activities in India (Nov 2013) and Standards of TB Care in India.

STANDARDS FOR TB CARE IN INDIA

Standard 10 : Addressing TB with HIV infection and other co morbid conditions

10.3 Isoniazid preventive therapy in HIV patients without active TB: People living with HIV (PLHIV) should be screened for TB using four symptom complex (current cough or fever or weight loss or night sweats) at HIV care settings and those with any of these symptoms should be evaluated for ruling out active TB.

All asymptomatic patients and those, in whom active TB is ruled out, should be offered Isoniazid Preventive Therapy (IPT) for six months.

What is Isoniazid Preventive Therapy?

Isonaizid Preventive Therapy is the administration of INH to individuals with latent TB infection in order to prevent progression to active TB Disease.

How does Isoniazid Preventive Therapy (IPT) benefit in People living with HIV?

Isoniazid is one of the most effective bactericidal, anti-TB drugs available at present. While it protects against progression of latent TB infection to active disease i.e. reactivation, it also prevents TB reinfection post the exposure to an open case of TB.

Evidence has shown that IPT is efficacious, safer than Rifampicin and Pyrazinamide containing regimens used for prevention of latent TB infection. IPT was also found to be effective in reducing the incidence of TB and death from TB in HIV-infected patients.

Several studies concluded that there is benefit in providing TB preventive therapy to people living with HIV. The efficacy of IPT in preventing active TB, relapse, reinfection and toxicity is as good as regimen include pyrazinamide, rifampicin and rifapantin.IPT reduces the overall risk of developing TB by 33% (relative effect 0.67; CI 0.51– 0.87).

National Institute of Research in Tuberculosis, Chennai conducted a prospective multicentric study with phased implementation, to assess the uptake and effectiveness of IPT in reducing TB incidence in a cohort of PLHIV enrolled into HIV care between 2012 and 2015 at 9 ART centres in 4 states of India as recommended by National Technical Working Group TB HIV. All PLHIV were screened for active TB using WHO's symptom-based screening algorithm (absence of current cough, fever, night sweats and weight loss) and for safety of Isoniazid (h/o chronic liver disease, seizures, heavy alcohol use). After counselling, eligible PLHIVs were supplied IPT (Tab. Isoniazid 300mg along with tab. Pyridoxine), to be taken daily for 6 months. IPT was found to be effective in reducing TB incidence by almost 50%, under programme conditions in India. Study findings conclude scaling up and strengthening IPT services, in addition to ART will have beneficial effect in reducing burden of TB among PLHIV, however attention is need to ensuring compliance.

Source: Phase II NIRT, Chennai IPT Study

How can we rule out active TB in PLHIV and provide IPT safely?

Exclusion of active TB is critically important before IPT is started.

The absence of all of current cough, night sweats, fever, or weight loss can identify a subset of adolescents and adults living with HIV who have a very low probability of having TB disease

that can reliably be initiated on IPT. This screening rule has a negative predictive value of 97.7% (95% CI [confidence interval] 97.4–98.0) at 5% TB prevalence among people living with HIV.
In children, the absence of poor weight gain, fever and current cough can identify children who are unlikely to have TB.

Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT.

Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB

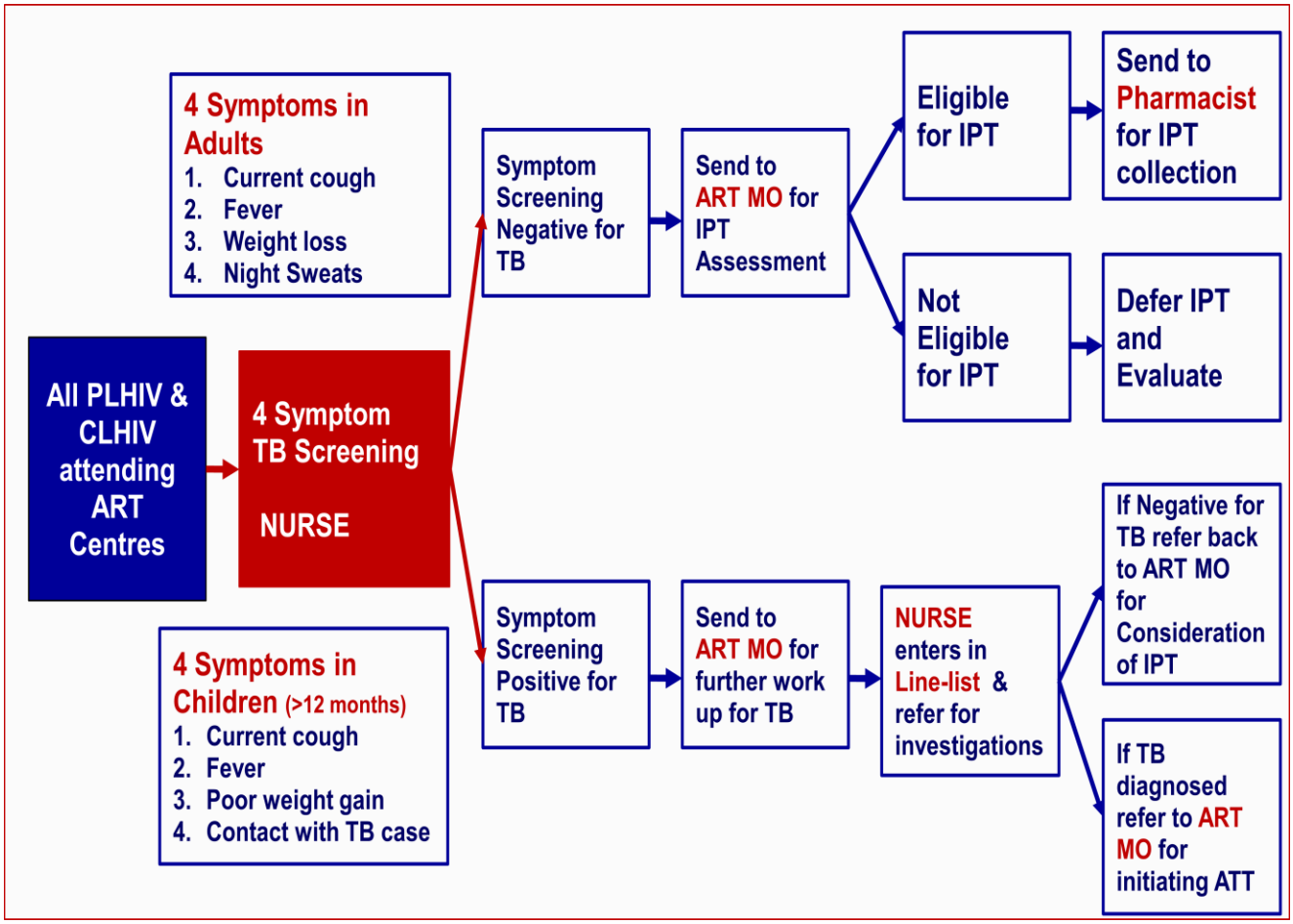
IPT work up

There are some contraindications for IPT like active hepatitis (acute or chronic), regular and heavy alcohol consumption, and symptoms of peripheral neuropathy. So IPT work up is essential before initiating IPT:

- Ask the patient for signs of liver disease (yellowness of eyes) and neuropathy (persistent numbness and burning sensation in the feet and hands).
- Examine the patient for jaundice and tenderness in the right upper quadrant of the abdomen.
- Where available, routine liver function tests/ALT should be offered, but lack of LFTs/ALT results should not delay the initiation of IPT in asymptomatic patients.
- If the patient does not have any abnormality based on the assessment above, assess for adherence using the criteria on the backside of the ICF/ IPT card

Tuberculin Skin Test (TST) is not a requirement for initiating IPT in people living with HIV (PLHIV).

Figure- 1: Patient flow for initial TB screening and for IPT at ART Centre



Regimen, Duration of IPT

Adult and Adolescent: Isoniazid 300mg + Pyridoxine 50mg (Vitamin B6) per day for 6 months

Children above 12 months: Isoniazid 10mg/kg + Pyridoxine 25 mg (Vitamin B6) per day for 6 months

Dosages of Isoniazid and Pyridoxine

IPT should be given at a dose of 10 mg/kg/day (maximum 300 mg) for duration of 6 months. Children should be weighed at every visit and their dose adjusted according to their weight.

Dose of INH for IPT

Weight range (kg)	Dose in mg	Number of 100mg INH tablets	Number of 300mg (Adult) tablet
<5	50	**½ tablet**	-
5.1-9.9	100	1 tablet	-
10-13.9	150	1½tablet **or**	**½ tablet**
14-19.9	200	2 tablets	-
20-24.9	250	2 ½ tablets	-
>25	300	3tabletsor **or**	1 tablet
Adults	300	3tabletsor **or**	1 tablet

Dosages for Pyridoxine

Weight(kg)	**Number of tablets of pyridoxine (50mg)**
1-13.9kg	Quarter tablet daily
14-25kg	Half a tablet daily
>25kg	One tablet daily
Adults	One tablet daily

Paediatric doses IPT

Weight range (Kg)	**Number of 100 mg tablets of INH to be administered per dose (total dose 10 mg/kg/day)**	**Dose (mg)**
<5	**½ tablet**	**50**
5.1–9.9	**1 tablet**	**100**
10–13.9	**1 ½ tablet**	**150**
14–19.9	**2 tablets**	**200**
20–24.9	**2 ½ tablets**	**250**
>25	**3 tablets or one adult tablet**	**300**

IPT dispensing and monthly collection

- **Patients on ART :**

Monthly collection of IPT from the ART centre, LAC-Plus or LAC along with monthly Collection of the ART

- **Patients in pre-ART care:**

Monthly collection of Isoniazid + Pyridoxine from the designated Stand Alone ICTC (SA-ICTC).

Procedure for Drug (INH) Dispense

- INH dispensing responsibility lies with Pharmacists and other health professionals (e.g health care workers (HCWs) at the ART Centres/LAC/LAC Plus& SA-ICTC)
- Dispense appropriate doses of Isoniazid to eligible patients at ART Centres/LAC/LAC Plus & SA-ICTC
- Ensure that there is availability of a six-month dose for each patient before initiation.
    - As much as possible, store the medicines for continuing patients at separate area to avoid stock outs.
    - Alternatively, a 6 month pack of INH can be labelled and earmarked for each initiated patient.
- Align INH refill appointments with ARV refill appointments i.e. if ARVs are dispensed for 2 months, then INH should also dispensed for 2 months.
- Patients should be counselled on adherence and monitored for side effects at every visit.

Is concomitant use of IPT with ART recommended?

Studies and a sub-analysis of data from randomized clinical trials, potential benefit of concomitant use of IPT with ART. (Table 2).

WHO Guidelines on IPT strongly recommends that IPT be given irrespective of immune status and whether or not a person is on ART. IPT initiation or completion should not be the cause for a delay in starting ART for eligible people living with HIV.

Table 1: Reduction in Tuberculosis risk **with IPT, ART and combined ART and IPT**

Studies	IPT alone	ART alone	ART plus IPT
Brazil	**68%**	**52%**	**80%**
South Africa	**13%**	**64%**	**89%**
Botswana	**65%**	**67%**	**97%**
ART has significant impact when combined with IPT			

Source: **AIDS 2007: 21: 1441-8; AIDS 2009, 23:631–636; Lancet 2011: 377:1588-98**

Can Co-trimoxazole be dispensed with IPT?

Co-trimoxazole and IPT can be safely co-administered.

Is IPT recommended for pregnant women living with HIV?

Pregnant women living with HIV are at risk for TB. Active TB Disease during pregnancy can impact on maternal and perinatal outcomes.

Evidence and experience from the pre-HIV and HIV era suggest that IPT is safe in pregnant women. WHO guidelines on IPT strongly recommends that pregnancy should not exclude women living with HIV from symptom-based TB screening and receiving IPT.

Does provision of IPT increase risk of drug resistance?

Results of a meta-analysis concluded that INH resistance is not significantly associated with the provision of IPT.

Providing IPT to people living with HIV does not increase the risk of developing INH-resistant TB. Therefore, concerns regarding the development of INH resistance should not be a barrier to providing IPT.

Clinical follow up and adherence to IPT:

- People living with HIV and receiving IPT should have regular clinical follow-up and should undergo regular screening using the TB symptom-based rule during every contact with a health-care provider.
- Proper counselling to be done to ensure adherence to IPT
- Conduct symptom based TB screening at every clinic visit for patients who have completed IPT.
- Update 12, 18, and 24-month TB status for every patient.
- If patients diagnosed with TB after completing IPT, manage according to RNTCP guidelines

Restarting IPT after interruption

Scenario	Action
If patient had discontinued INH for less than 1month in total and discontinued for any reason (like toxicity or loss to follow up)	Conduct adherence counselling, Address reasons for discontinuation. Conduct ICF and if asymptomatic. Restart INH afresh. Ensure they have completed a **6 month course**
After taking INH for more than 1month: If patient had discontinued INH for less than 1 month	Conduct adherence counselling, Address reasons for discontinuation Conduct ICF and if asymptomatic continue from where they let off Ensure they have completed a 6 month course
After taking INH for more than 1 month: If patient had discontinued INH for more than 1 month but less than 3 months	Conduct adherence counselling, Conduct ICF and if asymptomatic Restart INH Ensure they complete a 6 month course within 9 month period
If patient discontinued for 3 months or more, or had discontinued more than once	Do not re-initiate IPT

IPT in special circumstances

Scenario	Action
Patients previously treated for TB *(Secondary prophylaxis*)	• All PLHIV who have just successfully completed treatment for TB disease should receive INH for an additional six months. • All CLHIV who have been successfully treated for TB and are living in settings with a high TB prevalence and transmission should receive IPT for an additional six months. IPT can be started immediately after the last dose of anti-TB therapy or at a later date.
IPT with ART *(Secondary prophylaxis)*	• Combined use of IPT with ART for all PLHIV irrespective of ➢ the degree of immune suppression ➢ previously been treated for TB ➢ pregnancy • Combined use of IPT with ART is recommended for all CLHIV. • ART should not be delayed while starting or completing a course of IPT (WHO, 2010).

Patient on IPT develops TB during IPT treatment	• If patient develop TB symptoms during IPT treatment do the following. Evaluate patients for TB. Do DST for drugs H,R,O and K. Treat according to resistance pattern. • If the patient is sensitive to all the drugs then based on history and duration of IPT decide following. • If patient has taken a anti-TB treatment in the past OR patient has taken the IPT for more than 30 days then provide patient a Cat- II (retreatment) treatment. • If patient has consume the IPT for less than 30 days than provide that patient cat-I (treatment for new case) treatment.
Patients develop TB after treatment	• Treat TB episode as per previous TB treatment history and Rif resistant pattern (wherever available)
IPT and Pregnancy	• Pregnant woman living with HIV should not be excluded from symptom-based TB screening and receiving IPT • Isoniazid is safe in pregnancy. Start IPT in all HIV positive pregnant women irrespective of their gestation period. • Advise women to complete IPT if a woman becomes pregnant while taking IPT. • Assure patient that IPT is safe while breastfeeding.
IPT and MDR-TB	• Contact of MDR TB and PLHIV who have completed DRTB treatment are not eligible for IPT.
IPT in children born to smear positive mothers:	• If a baby is born to a microbiologically confirmed TB mother, assess the newborn for TB.Non-specific features suggestive of neonatal TB include: Fever, low birth weight, hepato- splenomegally ,irritability, feeding intolerance. • If the child has none of the above, give IPT for 6 months. • Withhold BCG until 2weeks after completion of IPT.

4: RECORDING AND REPORTING OF IPT

The step wise recording and reporting of IPT is detailed below:

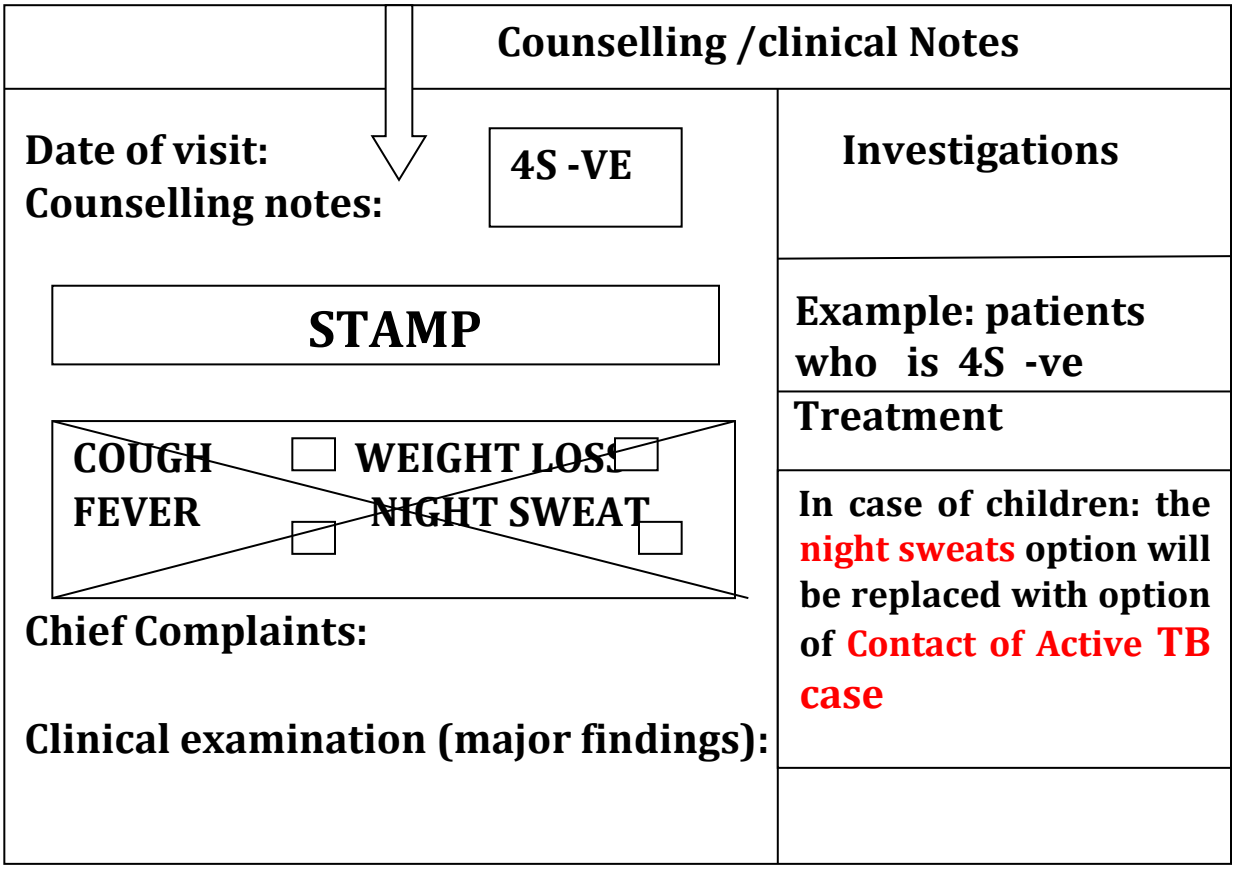
Staff Nurse will further screen all patients referred by counsellor and validate the 4s status to assess the eligibility for IPT, the same should be recorded using a detailed stamp

A large cross (X) should be placed over the stamp for all the 4s –ve patients

Stamp of 4S Screening

The S/MO will further screen all patients for 4 symptoms (both 4S+ & 4S-) and will document 4S status in column 19 of Section 13 of white card

- **4S-ve patients are to be considered for IPT and IPT status has to be documented in column 9**
-



IPT status

Initiated on IPT during this visit (I)

Contraindicated (Cont)

On IPT (IPT)

IPT stopped due to medical /other reasons (ST)

IPT full course completed (Comp)

White Card at ART Centre

White Card (SMO/MO)

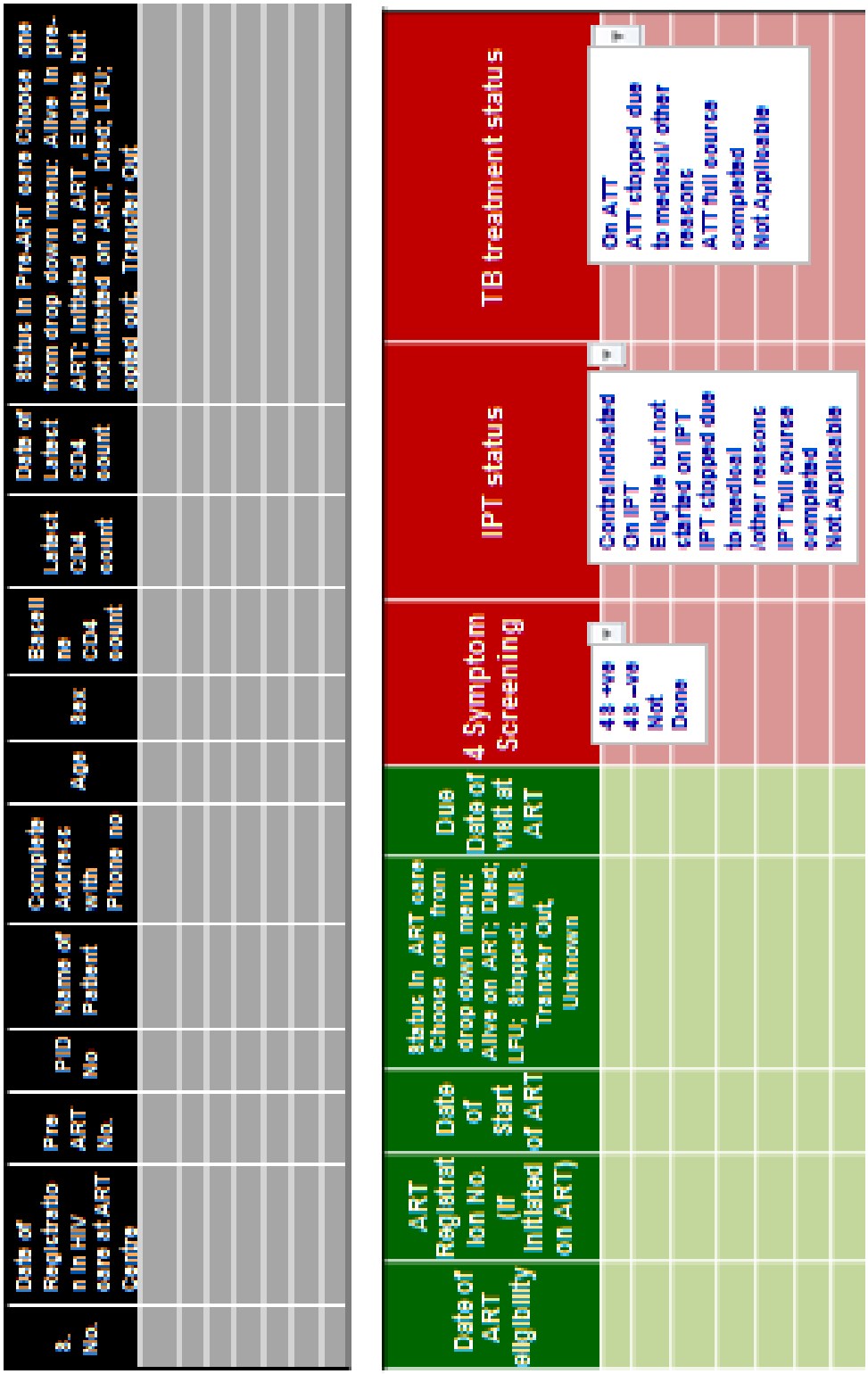
4S-Ve PLHIV, Start IPT if not contraindicated

4S+Ve PLHIV if found as TB

13 Follow Up

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18		20
Sl.No.	Date of Visit	Date of next visit(Due Date)	Weight (kg)	Height (cm) of child	Functional Status WAB **	WHO Clinical Stage	Opportunistic Infection (Code)2	Drugs prescribe for Opportunistic Infection /Prophylaxis		Antiretroviral Drugs	No. of Pills remaining with the patients	Adherence to ART (%)22	Any other medicine prescribed	TB treatment (Y/N)	ART Side effects(Code)	Concurrent condition e.g. STI	Pregnancy(Y/N)	Condoms given (Y/N)	Remarks/ Referrals	Staff Signature
								CPT (Yes/No)	Others (with dose)	Regimen										
									IPT (1)										4S+Ve	
									IPT										4S-Ve	

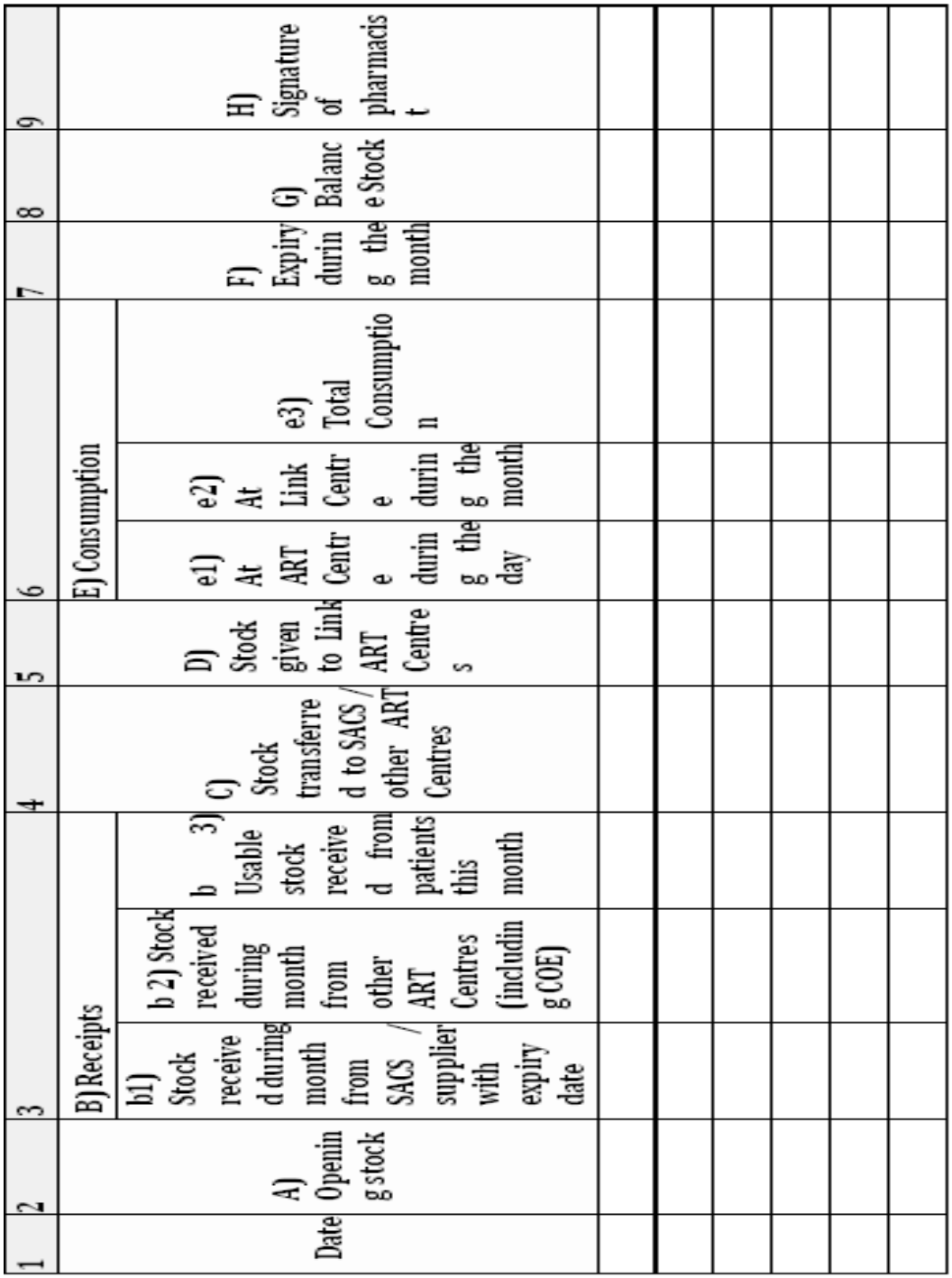
Revised Master line list at ART Centre should be updated as below:



The IPT related information should be reported in the 4.d section of the Monthly progress report (MPR) sent by ART Centre.

3 b. HIV/TB -Intensified TB Case Finding			
TB Diagnosis & Treatment			
(From Completed HIV/TB Line-List- 1 month prior to reporting month)			
3b.1) Number of PLHIV attending ART Centre during the month (Pre ART and ART)			
3b.2)Out of above number of PLHIV screened for 4 symptoms			
3b.3) Out of above, number of PLHIV with presumptive TB (those with anyone/more symptoms out of 4S)			
3b.4) Out of above, number of PLHIV with presumptive TB referred from ART centre for TB diagnosis			
3b.5) Out of above, number of PLHIV with presumptive TB, tested for TB diagnosis			
3b.6) Out of the above number of PLHIV diagnosed as having TB :	**In Pre ART Care at time of TB diagnosis**	**Already on ART at time of TB diagnosis**	**Total**
(i) Pulmonary TB (Microbiologically confirmed)			0
(ii) Pulmonary TB (Clinically diagnosed)			0
(iii) Extra-Pulmonary TB (Microbiologically confirmed)			0
(iv) Extra Pulmonary (Clinically diagnosed)			0
3b.7) Total PLHIV Diagnosed with TB	0	0	0
3b.8) Out of **(3b.7),**, number of TB patients receiving RNTCP treatment			
3b.9) Out of **(3b.7),**, number of TB patients receiving Non-RNTCP treatment			
3b.10) Out of **(3b.7),** number of TB patients with RRTB (Rif Resistant TB)			
3b.11) Out of **(3b.10),** number of TB patients with RRTB (Rif Resistant TB) receiving Cat IV treatment			
3 c. Treatment of HIV in HIV TB co-infected PLHIV			
(From the HIV- TB register data -2 months prior to reporting month)			
3c.1) Total number of TB patients enrolled in HIV/TB register 2 months prior to reporting month			
3c.2) Out of **(3c.1)** number of TB patients initiated on CPT			
3c.3) Out of **(3c.1)** number of TB patients initiated on ART			
3 d. IPT Status (From Master Line List of Reporting Month)			
3d.1) Number of PLHIV newly initiated on IPT during this month			
3d.2) Number of PLHIV completed IPT during this month			

The Pharmacist at ART centre should document receipt and consumption of INH IN Drug Stock register in RNTCP Drugs section and report monthly to RNTCP:



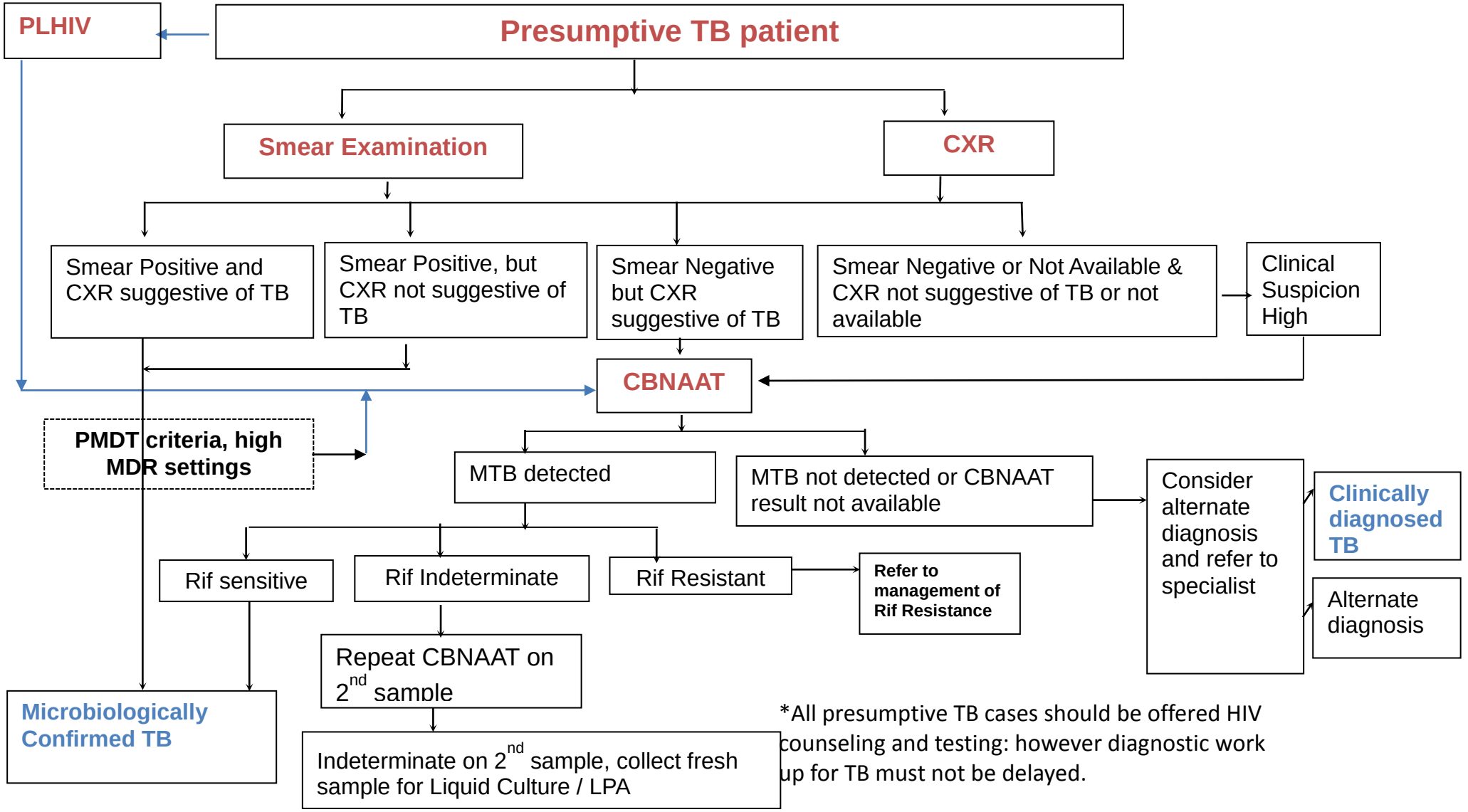
1	2	3		4	5	6		7	8	9
		B) Receipts				E) Consumption				
Date	A) Opening stock	b1) Stock received during month from SACS / supplier with expiry date	b 2) Stock received during month from other ART Centres (including COE)	b 3) Usable stock received from patients this month	C) Stock transferred to SACS / other ART Centres	D) Stock given to Link ART Centres	e1) At ART Centre during the day	e2) At Link Centre during the month	e3) Total Consumption	F) Expiry during the month	G) Balance Stock	H) Signature of pharmacist

References:

1. WHO. Guidelines for intensified Tuberculosis case-finding and Isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva, Switzerland, World Health Organization, 2011
2. WHO. Guideline for National Programmes and other stakeholders Geneva, Switzerland, World Health Organization, 2012.
3. WHO. Global tuberculosis control: a short update to the 2010 Report. December 2009. Geneva, Switzerland, World Health Organization, 2010.
4. Guidelines for Tuberculosis preventive therapy among HIV infected individuals in South Africa.2010.
5. Central TB Division. RNTCP Technical & Operational Guideline 2016. CTD Ministry of Health and Family Welfare, Government of India, New Delhi, 2016.
6. National Framework for Joint HIV/TB Collaborative Activities: November 2013 National AIDS Control Organisation; Ministry of Health and Family Welfare, Government of India, 2013.
7. Integrated training module for TB HIV collaborative activities 2015; National AIDS Control Organisation; Ministry of Health and Family Welfare, Government of India, New Delhi, 2015.
8. C. Padmapriyadarsini, P.K. Bhavani, L. Sekar et al; Effectiveness of Isoniazid Preventive Therapy in Reducing Incidence of Tuberculosis among PLHIV in Programme Settings in India; IPT Study Phase II (under publication) National Institute for Research in Tuberculosis ; Ministry of Health and Family Welfare, Government of India,2016.

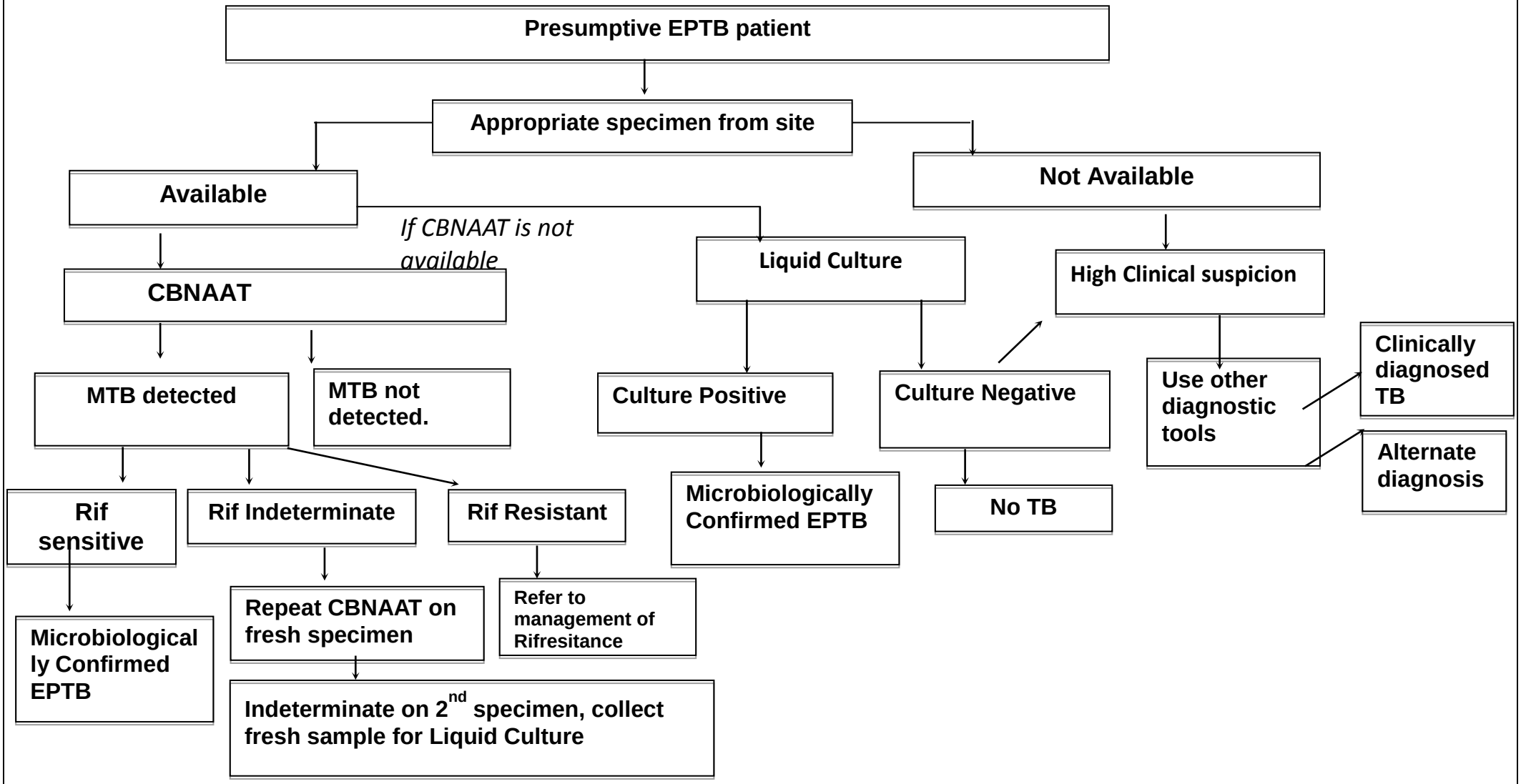
Link for TB HIV publications, National AIDS Control Organisation, MoHFW, GoI
http://www.naco.gov.in/NACO/Quick_Links/Publication/Basic_Services/

ANNEX I:Diagnostic algorithm for pulmonary TB

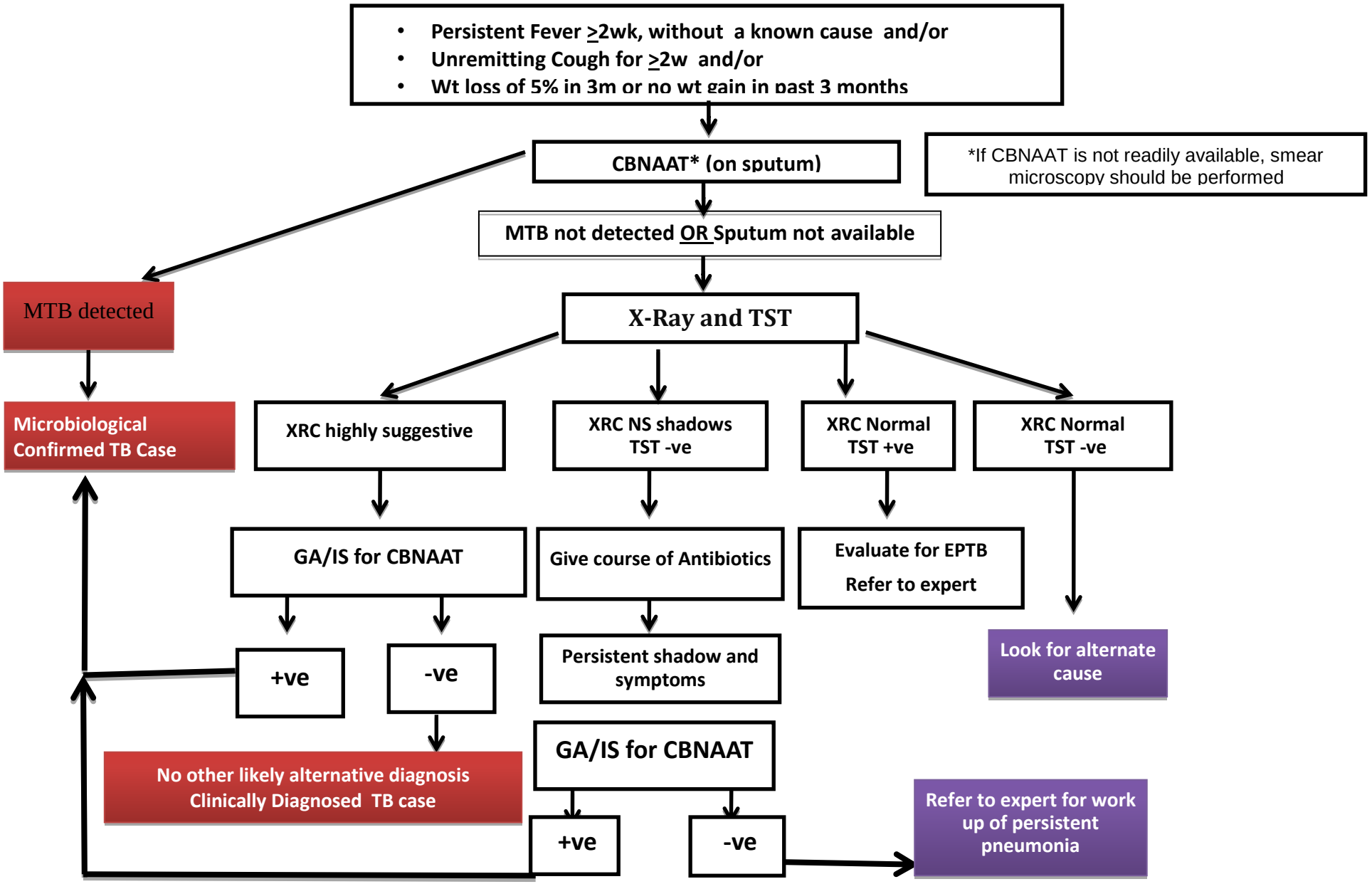


*All presumptive TB cases should be offered HIV counseling and testing: however diagnostic work up for TB must not be delayed.

ANNEX II: Diagnostic Algorithm for Extrapulmonary TB



ANNEX III: Diagnostic Algorithm for Paediatric TB



ANNEXURE IV: RNTCP Referral Form TB

RNTCP Request Form For Examination Of Biological Specimen For TB
(Required for Diagnosis of TB, Drug Sensitivity Testing and Follow up)

Patient Information			
Patient Name		Age (in yrs)	Gender: ☐ M ☐ F ☐ TG
Patient Mobile No. or other contact no.		Specimen Date of Collection (DD/MM/YY).....	Sputum ☐ Other(specify) ☐
Patient address with landmark		HIV Status: ☐ Reactive ☐ Non Reactive ☐ Unknown	
		High Risk Group: ☐ Contact of TB/DRTB Case ☐ Diabetes ☐ Tobacco ☐ Smoker ☐ Prison ☐ Miner ☐ Health –care worker ☐ other (Specify).....	

Name referring facility (PHI/DMC/DR-TB Centre/Laboratory/ Others): Health Establishment ID(NIKSHAY):.....	CDL NIKSHAY ID: ___.____._.C._____ RNTCP TB Reg No._____ Or ☐ Not Applicable
State:_____ District:_____ Tuberculosis Unit (TU):_____	

Reason for Testing:

Drug Sensitive TB	
Diagnosis (NIKSHAY ID_____)	Follow up (Smear and culture)
H/o anti TB Rx for > 1month: ☐ YES ☐ NO	RNTCP TB Reg No._____ NIKSHAY ID:_____
☐ Presumptive TB	Regimen : ☐ New ☐ Previously Treated
☐ Private Referral	Reason: ☐ End IP ☐ End CP
☐ Presumptive NTM	Post Treatment: ☐ 6M ☐ 12M ☐ 18M ☐ 24M

Drug Resistant TB		
Drug Susceptibility Testing(DST)		Follow-Up (Smear and Culture)
☐ Presumptive MDR TB (provide first line DST	☐ New ☐ Previously treated ☐ At diagnosis ☐ Contact of MDR/RR TB ☐ Follow-up SM +ve ☐ Private referral ☐ Discordance resolution	PMDT TB Reg No._____ DR TB NIKSHAY ID:_____ Regimen: ☐ Regimen for H Mono/Poly resistant TB ☐ Regimen for MDR/RR -TB ☐ Regimen for MDR/RR -TB + FQ/SLI resistant ☐ Regimen for XDR-TB ☐ Regimen with Bedaquiline for MDR TB+ FQ/SLI resistance ☐ Regimen with Bedaquiline for XDR-TB ☐ Regimen with Bedaquiline for failure of regimen for MDR -TB ±FQ/SLI resistant ☐ Regimen with Bedaquiline for failure of regimen for XDR-TB ☐ Regimen for mixed pattern resistance Treatment ☐ Month ☐ Week:_____
☐ Presumptive H mono/poly (provide first and second line DST)		
☐ Presumptive XDR TB (provide first and second line DST)	☐ MDR/RR TB at Diagnosis ☐ ≥4 months culture positive ☐ 3month for persistent culture positive(treatment month_____) ☐ Culture reversion ☐ Failure of MDR/RR-TB regimen ☐ Recurrent case of second line treatment ☐ Discordance resolution	

Test Requested:

☐ Microscopy ☐ CBNAAT ☐ Culture ☐ DST ☐ Line Probe Assay ☐ Gene Sequencing
☐ Other (Please Specify):_____

Requestor Name, Designation and Signature:_____

Contact Number:_____ Email ID:_____

Results: **CDL NIKSHAY ID Generated:__-___-_-C-__-_____**

Microscopy (☐ ZN ☐ Florescent)							
	Lab Sr. No.	Visual appearance	Result				
			Negative	Scanty	1+	2+	3+
Sample A							
Sample B							

Date tested: _____ Date Reported: _____ Reported by: _____

(Name and Signature)