

# DCLS Nucleic Acid Amplification Testing (NAAT) for *M. tuberculosis*



## Guidelines for the use of *M. tuberculosis* NAATs

CDC recommends that NAAT testing be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary tuberculosis (TB) when:

- A diagnosis of TB is being considered but has not yet been established
- The test result would alter case management or TB prevention activities, like contact investigations



## NAAT utilized at DCLS on Sputum Specimens

### Real-time PCR (non-FDA approved)

- Detects *M. tuberculosis* complex (MTBC) and *M. avium* complex (MAC)
- Direct specimen testing
  - 48-72 hour turn-around-time (TAT) from specimen receipt
  - If MTBC detected, sample reflexes to Xpert MTB/RIF
- Isolate testing
  - Used for identification of MTBC and MAC in culture

### Xpert MTB/RIF (FDA-approved)

- Detects *M. tuberculosis* complex (MTBC)
- Detects mutations associated with rifampin resistance
- If rifampin resistance detected, sample reflexes to CDC molecular detection of drug resistance testing

### NAAT should NOT be used on the following patients:

- Patients recently diagnosed with TB disease (patients with a previous positive MTBC result (NAAT and/or culture) in the past 12 months will not be tested again by direct real-time PCR at DCLS)
- Patients currently receiving anti-TB treatment (which can cause false-negative results)
- Patients recently treated for TB disease (which can cause false-positive result)

### Benefits of NAAT

- Greater positive predictive value (>95%) with AFB smear positive specimens as compared to smear alone
- Ability to rapidly detect the presence of *M. tuberculosis* in 50-80% of AFB smear-negative, culture-positive specimens
- Detects the presence of *M. tuberculosis* in days, compared to weeks in culture

### Importance of smear and mycobacterial culture

- Even if NAAT are performed, AFB smears and cultures should be performed on three respiratory specimens
- Culture remains the gold standard for diagnosis, and is still necessary for drug susceptibility testing and strain genotyping
- A negative NAAT result does not exclude the possibility of MTBC in culture
- A negative NAAT result for MTBC and a positive AFB smear are good indicators of the presence of nontuberculous mycobacteria



# DCLS Nucleic Acid Amplification Test (NAAT) Results



## Direct Specimen NAAT

### *M. tuberculosis* complex DNA and *M. avium* complex DNA

- Detected
- Not detected
- Inconclusive -DNA was not reliably detected; above the cut-off for a positive result. Possibly due to low amount of DNA, cross-reactivity
- Inconclusive due to inhibition - DNA presence not able to be determined due to inhibitors in the specimen

## Xpert MTB/RIF

### *M. tuberculosis* complex DNA

- Detected
- Not detected

### Rifampin resistance (only reported if *M. tuberculosis* complex DNA detected)

- No *rpoB* gene mutations detected; probably rifampin susceptible
- A mutation in *rpoB* gene has been detected; indicating possible rifampin resistance
- Presence of *rpoB* gene mutations cannot be accurately determined

## Culture Isolate NAAT

### *M. tuberculosis* complex DNA and/or *M. avium* complex DNA

- Detected

## Notification

- Same day verbal notification of the initial MTBC detected result (either direct specimen or culture isolate) and *rpoB* mutation detected result
- Preliminary laboratory report issued for all NAAT results

**NOTE:** Clinicians should interpret all laboratory results on the basis of the clinical situation. A single negative NAAT test result should not be used as a definitive result to exclude TB, especially when the clinical suspicion of TB is moderate to high. Rather, the negative NAAT test result should be used as additional information in making clinical decisions, to expedite testing for an alternative diagnosis, or to prevent unnecessary TB treatment. Consultation with a TB expert should be considered if the clinician is not experienced in the interpretation of NAAT tests or the diagnosis and treatment of TB.

## References

- Centers for Disease Control and Prevention (CDC). Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. MMWR Morb Mortal Wkly Rep.2009 Jan 16;58(1):7-10. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm>
- Los Angeles County TB Control Program. Guidelines for the use of *Mycobacterium tuberculosis* nucleic acid amplification tests, including Xpert MTB/RIF. September 15, 2015. Available at: <http://ph.lacounty.gov/tb/docs/NAATs/NAATGuidelines09-15-2015f.pdf>