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# DEPARTMENT OF HEALTH AND HUMAN SERVICES

## DIVISION OF PUBLIC AND BEHAVIORAL HEALTH

*Helping people. It's who we are and what we do.*

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# Technical Bulletin

Date: April 25, 2022
Topic: Tuberculosis Rapid Detection DNA Tests, NAATs and PCRs: The Standard of Care When Evaluating Patients for Possible Pulmonary Tuberculosis.
Contact: Susan McElhany, DMD, Division of Public and Behavioral Health (DPBH) Tuberculosis (TB) Program
To: Health Care Providers, Health Care Facilities, Health Care Administration, Laboratories, Infection Prevention and Control Departments

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## Background

Rapidly identifying infectious respiratory or pulmonary tuberculosis (TB) disease is critical to reducing the transmission of this disease. Infectious TB is determined through chest radiograph interpretation combined with respiratory specimen analysis by routinely collecting three sputum specimens between 8 and 24 hours apart and evaluating these specimens for the presence of acid-fast bacilli (AFB). *Mycobacterium tuberculosis* (MTB) presence is confirmed through culture that may take weeks to complete. Culture is the gold standard for MTB identification and verification of diagnosis, but culture results can take up to six weeks. The Nucleic Acid Amplification Test (NAAT) or Polymerase Chain Reaction (PCR)-type test, which are rapid DNA analysis laboratory tests, can detect MTB genetic material (DNA) in a respiratory or sputum specimen within one day. The rapid results can expedite initiating appropriate TB disease treatment and management or the formulation of an alternative diagnosis when TB disease is ruled out.

## Purpose

The purpose of this technical bulletin is to help health care providers, health care administration, and clinical laboratory administration better understand the effective use of the rapid MTB NAA/PCR tests. This technical bulletin should also be used to develop health care facility-based protocols for appropriate ordering of these laboratory tests when TB disease is being considered and apply NAA/PCR results to clinical care and infection control measures. If rapid MTB NAA/PCR testing protocols can be successfully integrated into initial TB disease diagnostic and infection control protocols, then immediate anti-TB therapy can start and further spread of TB can be mitigated. Alternatively, isolation can stop in certain situations when infectious TB disease is ruled out.

## Standard of Care: Using NAA/PCR Tests to rapidly detect *Mycobacterium tuberculosis*

The Centers for Disease Control and Prevention (CDC) previously published "Report of an Expert Consultation in the uses of Nucleic Acid Amplification Tests for the Diagnosis of Tuberculosis" recommends NAA testing for TB to become the standard of practice for suspected TB patients. The DPBH TB Program, Southern Nevada Health District, Washoe County Health District, Carson City Health and Human Services, Rural Community Health Services, and the Nevada State Public Health Laboratory support the recommendation for rapid DNA detection tests, MTB NAA/PCR tests, as a standard of care for TB diagnosis and isolation procedures.

*****A NAA/PCR test should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established.** Regardless of AFB results, the MTB NAA/PCR test can assist with initiating appropriate treatment immediately and decreasing the potential for transmission while awaiting culture results.

The following guidance is provided for the effective use of rapid MTB NAA/PCR testing in individuals suspected of having TB disease, regardless of AFB smear result. Appendix A summarizes NAA/PCR use and interpretation algorithms (adapted from "Use of Xpert/Rif (NAATs/PCRs) - Algorithms"[1] ).

CDC and Nevada TB Program guidance for testing of sputum specimens with MTB NAA/PCR laboratory test

Patients initially evaluated for pulmonary TB, should undergo the following[1,2,3]:

- An MTB NAA/PCR test should be ordered for at least one respiratory specimen, preferably the first specimen, along with an AFB and culture; providers should not wait for AFB results to be returned to order a NAAT.
    - The Cepheid Xpert MTB/Rif® NAA test provides the additional benefit of rapid initial Rifampin resistance testing, valuable in decreasing transmission of multi-drug resistant TB.
- Providers must **ensure the NAA/PCR MTB test is additionally ordered** when ordering AFB and culture; the NAA/PRC tests are not automatic when AFB and culture are ordered. *See Appendix B for common Laboratories and their TB test names and codes.*
- When there is a higher suspicion of TB disease, providers should order a second NAA/PCR test along with the second sputum specimen collected for AFB and culture.
- Whether suspicion of TB disease is high or low, a total of three consecutive respiratory specimens collected between 8 and 24 hours apart including one in the early morning, should be tested for AFB and culture.
- Sputum/respiratory specimen collection for testing: Collect a minimum of 5 milliliters (≥ 5 ml) of quality sputum, not saliva, or bronchial fluid (breakdown: > 2 ml for NAAT, > 1 ml for AFB, > 2 ml culture).
- *NAA/PCR results should be incorporated with clinical information in making diagnostic and treatment decisions as outlined below.*

Interpretation of MTB NAA/PCR Tests when establishing an initial diagnosis (*not for established TB diagnosis*)[2,3,4]

- **AFB smear-positive combined with NAA/PCR-positive**: Presume TB disease and initiate anti-TB treatment, pending culture results.
- **AFB smear-negative combined with NAA/PCR-positive*:** Order a NAA/PCR test along with the second specimen to confirm the NAA/PCR result; if two or more specimens are NAA/PCR-positive, presume TB disease and initiate treatment pending culture results. NAA/PCR detects about 75% of smear-negative/culture-positive disease, thereby greatly expediting diagnosis in these not uncommon cases.
- **AFB smear-positive combined with NAA/PCR-negative*:** Order a NAA/PCR test along with the second specimen to confirm the NAA/PCR result; if both NAA/PCRs are negative and the AFB is smear-positive, presume infected with non-tuberculous mycobacteria. Airborne isolation may be discontinued if consistent with other clinical findings (see Appendix A).
- **AFB smear-negative combined with NAA/PCR-negative*:** A second negative NAA/PCR has a negative predictive value approaching 98% for pulmonary TB in low-incidence settings such as most of the United States. While this does not entirely exclude TB disease, it may enable removal from isolation and expedite efforts to seek alternative diagnosis in instances with a low to moderate likelihood of TB disease.
  Airborne isolation may be discontinued if consistent with other clinical findings (see Appendix A).

***Use clinical judgment to determine whether to begin anti-TB treatment while awaiting results of culture and additional diagnostic testing.***

References and Resources:

1. Adapted from: National Tuberculosis Controllers Association and Association of Public Health Laboratories. Consensus statement on the use of Cepheid Xpert MTB/RIF®assay in making decisions to discontinue airborne infection isolation in health care settings. Available at: NTCA_APHL_GeneXpert_Consensus_Statement_Final.pdf (tbcontrollers.org)
2. Adapted from: 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 16;58(1):7-10. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm
3. Adapted from: Centers for Disease Control and Prevention (CDC). Report of an Expert Consultation of the Uses of Nucleic Acid Amplification Tests for the Diagnosis of Tuberculosis. Available at: https://www.cdc.gov/tb/publications/guidelines/amplification_tests/reccomendations.htm
4. Rice, J, Seifert, M., Moser, K. Rodwell, T. Performance of the Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis and rifampin resistance in a low-incidence, high-resource setting. PLoS One. 2017 Oct 9:12(10):e0186139.doi: 10.1371/journal.pone.0186139.
5. Association of Public Health Laboratories. Laboratory considerations for use of Cepheid Xpert MTB/RIF Assay. 2013. Available at: http://www.aphl.org/AboutAPHL/publications/Documents/ID_2013Nov_Cepheid-Xpert-Fact-Sheet.pdf

**Questions:** For questions regarding this Technical Bulletin, please contact Susan McElhany, DMD, at smcelhany@health.nv.gov.

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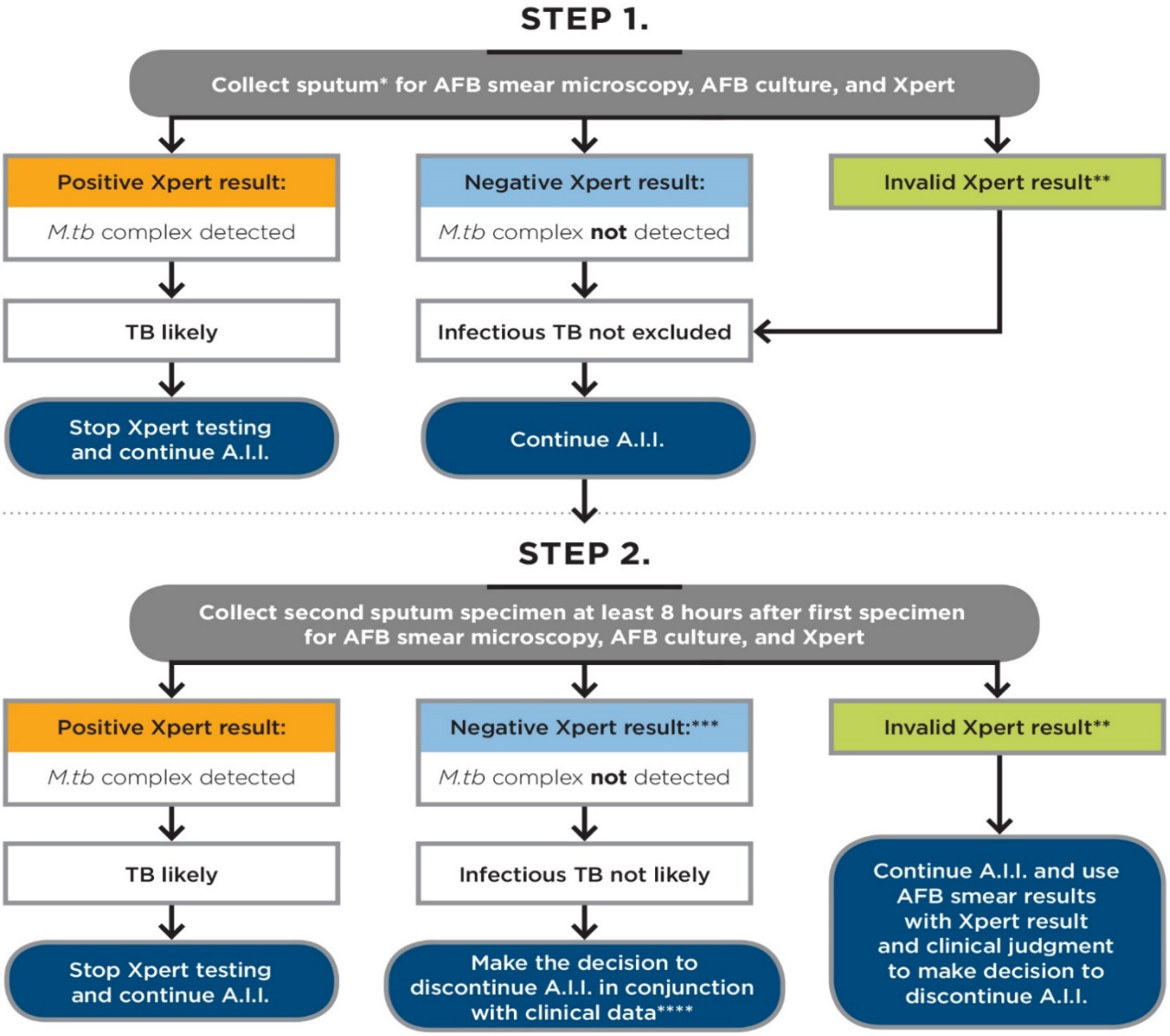
# Use of Xpert (NAAT/PCR) in Discontinuing Airborne Infection Isolation†

Adapted with permission from the National Tuberculosis Controllers Association and Association of Public Health Laboratories




***M. tb:*** *Mycobacterium tuberculosis* **A.I.I.:** Airborne infection isolation

* First morning specimen preferred to maximize diagnostic yield of AFB sputum smear, culture, and Xpert.

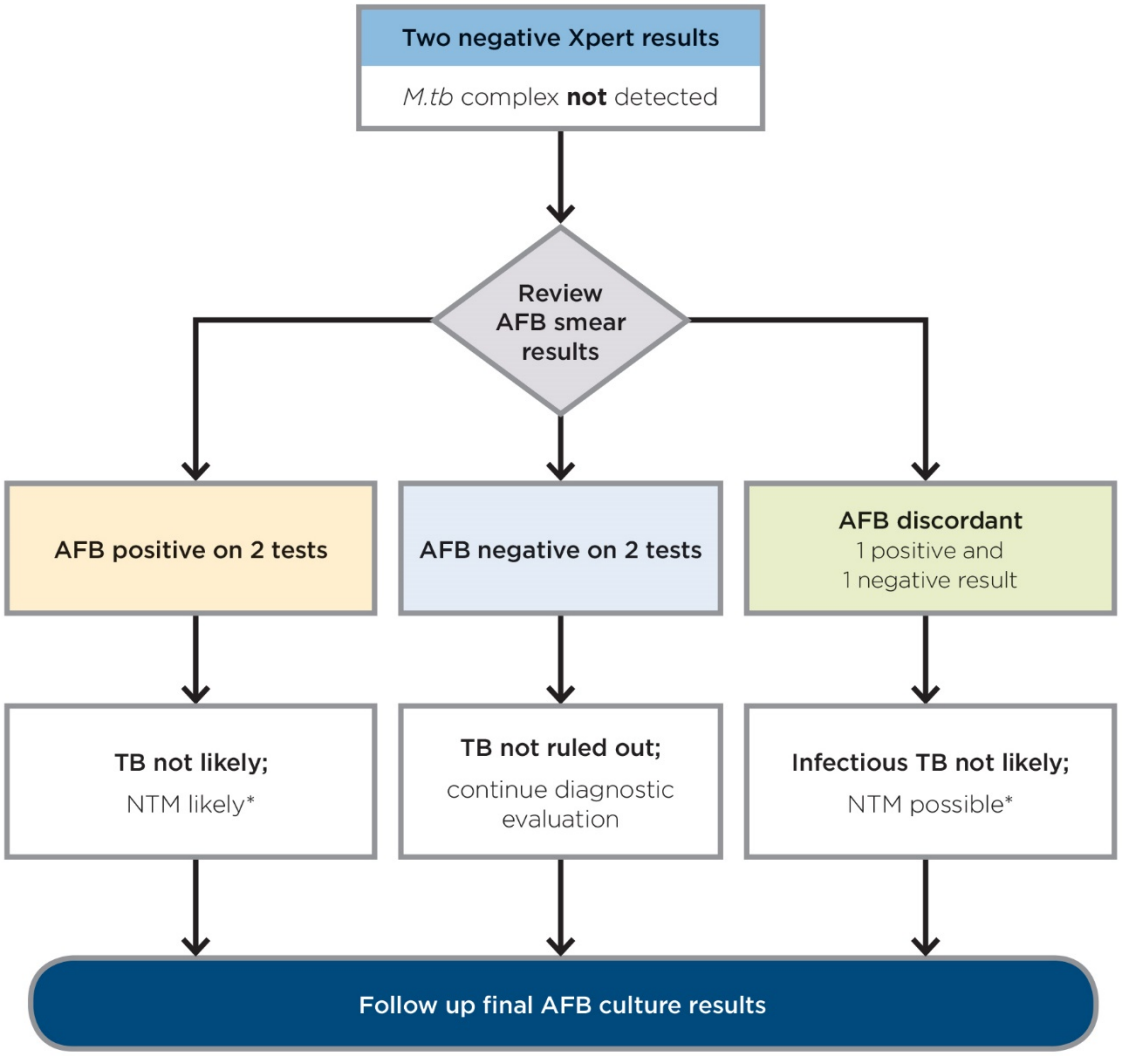
** Most laboratories/protocols will automatically retest leftover sample if an initial invalid (failed) result is obtained; in such cases, a reported invalid result reflects repeat testing of a single specimen.

*** If this result is Negative following an initial invalid result in Step 1 and infectious TB still is clinically suspected, a repeat test (repeat Step 2) using a new specimen, if available, is recommended in order to improve sensitivity. Alternatively, the clinician may use the single Negative Xpert result from Step 2 with smear results and clinical information to make the decision to discontinue or maintain A.I.I.

**** **Note:** This process does not rule out tuberculosis with 100% certainty. Refer to Appendix IIIb *Application of AFB Smear Microscopy to Negative Xpert Results* to assist in diagnostic evaluation.

†Adapted from: National Tuberculosis Controllers Association and Association of Public Health Laboratories. Consensus statement on the use of Cepheid Xpert MTB/RIF®assay in making decisions to discontinue airborne infection isolation in healthcare settings. Available at: NTCA_APHL_GeneXpert_Consensus_Statement_Final.pdf (tbcontrollers.org)

# Application of AFB Sputum Smear Microscopy to Negative Xpert (NAAT/PCR) Results†




**NTM:** nontuberculous mycobacteria

# Laboratory Coding for AFB Sputum Smear Microscopy, AFB Culture, and Xpert (NAAT/PCR) Testing

Laboratory Commonly Used, Alphabetic, followed by Test Description and Codes for
First sputum specimen recommended tests ordered and code(s):
AFB Sputum Smear with Culture with NAAT (all-in-one) - *OR*- AFB Sputum Smear with Culture ***and*** NAAT (stand-alone)

## ARUP

Acid-Fast Bacillus (AFB) Culture and AFB Stain with Reflex to *Mycobacterium tuberculosis* Complex Detection and Rifampin Resistance by PCR [Comprehensive panel includes acid-fast bacillus culture and stain; positive smears reflex to PCR amplification of *M. tuberculosis* complex species and rifampin resistance.]

TEST CODE: 0060738

## Clinical Pathology Laboratories (CPL)

ACID FAST SMEAR AND CULTURE

TEST CODE: 6130

***and***

M Tuberculosis PCR, Respiratory (requires 7 ml raw sputum specimen as opposed to standard >5 ml)

TEST CODE: 5273

## LabCorp

1) Acid-Fast (Mycobacteria) Smear and Culture with Reflex to Identification and Susceptibility Testing

TEST CODE: 183764

***and***

*2) Mycobacterium tuberculosis* Complex Detection and Rifampin Resistance, NAA Without CAP-mandated Culture

TEST CODE: 183456

## Nevada State Public Health Lab

1) Acid-Fast Bacillus Culture and Smear

*No Test Code*, Use Test Name

***and***

2) *Mycobacterium tuberculosis* Complex Detection and Rifampin Resistance by PCR or NAA

*No Test Code*, Use Test Name

## Quest

*1) Mycobacteria,* Culture, with Fluorochrome Smear with reflex to Identification and susceptibilities [Includes *Mycobacteria* Culture; Concentration; Acid-Fast Bacilli Stain]

TEST CODE: 4554

***and***

2) *Mycobacterium tuberculosis* Complex, PCR, Respiratory

TEST CODE: 30298