Nucleic Acid Amplification Testing for Early Diagnosis of Tuberculosis

and Identification of Rifampin Resistance

Massachusetts Department of Public Health

Bureau of Infectious Disease and Laboratory Sciences

Division of Global Populations and Infectious Disease Prevention



**INTRODUCTION**

Nucleic acid amplification testing has become a standard of care for diagnosis of pulmonary tuberculosis and for guiding the management of persons suspected of having infectious tuberculosis in inpatient settings. This document highlights currently available FDA-approved testing platforms and reviews indications and appropriate use of these tests.

**NUCLEIC ACID AMPLIFICATION TESTS**

A nucleic acid amplification (NAA) test is a powerful tool to assist in the early diagnosis of tuberculosis (TB) and determination of drug resistance. Two NAA tests are approved by the U.S. Food and Drug Administration (FDA) and are available for testing respiratory specimens:

* **Hologic Amplified MTD test** (GenProbe): Sputum (spontaneous or induced) or bronchial specimens; patient on anti-TB therapy ≤ 7 days.
* **Xpert® MTB/RIF assay**: Sputum (spontaneous or induced) only; patient on anti-TB therapy ≤ 3 days; see below for bronchial specimens.

The Xpert® MTB/RIF assay also determines susceptibility to Rifampin (RIF). If RIF resistance is detected, a specimen should be sent to a reference laboratory to confirm the resistance by DNA sequencing as soon as possible.

**DEPARTMENT OF PUBLIC HEALTH RECOMMENDATIONS**

For initial diagnosis of Pulmonary TB, three sputum specimens should be collected 8-24 hours apart, with at least one obtained as an early morning specimen. Ideally, specimens should be collected before drug therapy is started[[1]](#footnote-1), since a few days of treatment may inhibit growth and prevent isolation of *M. tuberculosis* complex.

* **NAA testing should be performed on at least one respiratory specimen from each patient with signs and symptoms of active pulmonary TB disease for whom a diagnosis of TB is being considered but has not yet been established.** Clinical suspicion for tuberculosis should be high; this may be supported further by the presence of risk for tuberculosis infection and a positive Tuberculin skin test or an Interferon-gamma Release Assay (IGRA).
* Specimens also should be tested by both concentrated smear and culture. NAA testing does not replace the need for acid-fast bacilli (AFB) smear and culture. Smears are helpful in interpreting test results and cultures are necessary for confirmation of identification, determination of drug susceptibility, and genotyping.

The Massachusetts State Public Health Laboratory (SPHL) can perform smear, Xpert® MTB/RIF assay, culture, and drug susceptibility testing (DST). **The Xpert® MTB/RIF assay has been validated in accordance with the Clinical Laboratory Improvement Act (CLIA) by the SPHL for bronchial fluids and washes.** All positive smear, NAAT, culture, and DST results are reported via telephone to the ordering provider as soon as they become available. Preliminary and final reports are available on the MDPH Electronic Laboratory Reporting (ELR) web portal. To gain access to the ELR portal please contact SPHL at ELR.Support@massmail.state.ma.us.

**MOLECULAR DETECTION OF DRUG RESISTANCE**

The Centers for Disease Control and Prevention (CDC) offers a molecular detection of drug resistance (MDDR) testing service using DNA sequencing free of charge. The laboratory accepts NAA-positive concentrated sputum specimens as well as MTB culture isolates. The service can be accessed on request and with submission of specimens or isolates to the State Public Health Laboratory.

***Nucleic Acid Amplification testing is NOT used to monitor treatment responses***. These tests signal the presence of nucleic acid (DNA or RNA) but provide no indication of viability of the organisms nor of their ability to be transmitted.

**TB TESTING FOR RELEASE FROM AIRBORNE INFECTION ISOLATION (AII)**

The Xpert® MTB/RIF has been approved by the FDA to assist in decision-making regarding release of a patient with suspected infectious TB from AII. A protocol for this application has been developed by the National TB Controllers Association and the Association of Public Health Laboratories. The link to the protocol is included in the Resources section below.

**RESOURCES**

[Report of an expert consultation on the uses of nucleic acid amplification tests for the diagnosis of tuberculosis](http://www.cdc.gov/tb/publications/guidelines/amplification_tests/reccomendations.htm)

[Consensus Statement on the Use of Cepheid Xpert MTB/RIF Assay in Making Decisions to Discontinue Airborne Infection Isolation in Healthcare Settings](http://www.tbcontrollers.org/resources/airborne-infection-isolation/#.YCFWIDGSk2x)

For more information, contact the Massachusetts TB Program at 617-983-6970.

1. Commercial nucleic acid amplification (NAA) tests cannot be performed if patients have been on anti-tuberculous therapy for >3 days with the Xpert MTB/RIF assay or >7 days with the Amplified MTD test. [↑](#footnote-ref-1)