I. **BACKGROUND**

In February 2015, the U.S. Food and Drug Administration (FDA) approved a modification on the Package Insert for the Cepheid GeneXpert® MTB/RIF Nucleic Acid Amplification (NAA) Assay to allow the use of test results in making decisions concerning Airborne Infection Isolation (AII). FDA approval for this purpose was only provided for the Cepheid GeneXpert® MTB/RIF Nucleic Acid Amplification and only applies to its use in the decision to discontinue AII in healthcare settings. Other NAA tests currently in use have not been approved by the FDA for this purpose.

In April of 2016, the National Tuberculosis Controllers Association (NTCA) and the Association of Public Health Laboratories (APHL), in partnership with Hospital Infection Preventionists and Respiratory Therapy experts, published a Consensus Statement on the Use of Cepheid GeneXpert® MTB/RIF Assay in Making Decisions to Discontinue Airborne Infection Isolation in Healthcare Settings for presumptive pulmonary TB. This consensus statement was generated out of concern for the lack of detail in the modified package insert.

The Virginia Department of Health (VDH), Division of Tuberculosis and Newcomer Health (DTBNH) has developed the following guidelines for Virginia’s health care providers, based on the NTCA/APHL Consensus Statement. The purpose of the guidelines is to aid in the application and interpretation of the GeneXpert Assay in decisions concerning AII. This guideline does not constitute endorsement of GeneXpert or any other product.

As many as 30% of smear-positive mycobacteria cases in the United States may result from non-tuberculous mycobacteria (NTM). When applied and interpreted appropriately, the use of the GeneXpert assay at the clinical delivery site can assist providers in rapidly distinguishing between infectious TB disease and NTM, speed time of release from AII, and result in cost savings for inpatient units.

**For questions or assistance in interpreting test results and decisions regarding the release of specific persons from AII, please contact our Division of Tuberculosis and Newcomer Health at 804.864.7906.**
II. PRECAUTIONS IN THE USE OF THE GENEXPERT ASSAY FOR AII DECISIONS

- FDA approval for the use of GeneXpert in the decision to discontinue AII applies only to AII in healthcare facilities.
- These guidelines discuss the use of the GeneXpert® MTB/RIF Assay as a decision tool in releasing patients with presumptive infectious pulmonary TB from AII. These guidelines should not be confused with protocols on using the assay for diagnostic purposes.
- The use of the GeneXpert® assay as a tool in determining the appropriateness of releasing a patient from AII does not replace the need to collect a series of three sputa for acid-fast bacilli smear and culture for diagnosis, drug susceptibility testing, and genotyping.
- The decision to remove a patient with a negative GeneXpert result from AII must consider the clinical and radiographic presentation, the clinician’s suspicion for TB, and the risk of possible transmission of TB from an infectious patient to others. Such a decision should not be based on sputum test results alone.
- The sensitivity of sputum testing for TB using GeneXpert is subject to variability from a variety of factors, including poor specimen quality, inappropriate transport and/or processing of the specimen, errors in performance of the assay, or errors in labelling or reporting.
- Sputum quality is critical both for the diagnosis of pulmonary TB and for the performance of this assay. Sputum may be spontaneously expectorated after deep coughing, or induced following facility-approved procedures for sputum induction with deep inhalation of aerosolized saline and deep coughing. This often requires focused instruction and/or coaching of the patient by the provider supervising the sputum collection.
- FDA approval for the use of GeneXpert as an aid in decisions to discontinue AII for presumptive pulmonary TB applies only when the assay is performed on expectorated or induced samples. It does not include other types of samples (i.e. tissue, bronchoscopy).
- NAA testing should not be used to monitor response to treatment or to release newly confirmed TB patients from AII.
  - NAA determines the presence of genetic material and not viability of organisms.
  - NAA tests have remained positive for years in persons who have completed appropriate treatment for TB disease and been shown to be cured of the disease.
  - The Centers for Disease Control and Prevention has published guidelines on when persons with infectious TB disease can be released from isolation: [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm) (See Box 3).
III. THE INTERPRETATION OF GENEXPERT RESULTS

1. **Positive GeneXpert Result:** *M. tuberculosis* complex detected.
   - Diagnosis of TB is highly likely. A second specimen is not needed.
   - Continue AII until deemed non-infectious during hospital stay or discharged to home isolation.
   - Start TB medications and report the positive result to the local health department.
   - Individuals begun on treatment for presumptive infectious TB should remain in AII until:
     - Active TB disease is fully ruled out and treatment is terminated, OR
     - Criteria for release from AII once treatment is started are met: [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5412a1.htm) (See Box3) OR
     - The person is discharged from the healthcare facility.

2. **Negative GeneXpert Result:** *M. tuberculosis* complex not detected.
   - **Smear Positive for Acid Fast Bacilli (AFB)**
     - If the first GeneXpert result is negative, a second specimen collected at least eight hours after the first specimen should be tested.
     - If the second GeneXpert result is negative, the positive microscopy results likely indicate the presence of non-tuberculous mycobacteria (NTM). Infectious TB is not likely. AII can be discontinued.
   - **Smear Negative for AFB**
     - If the first GeneXpert result is negative, a second specimen collected at least eight hours after the first specimen should be tested.
     - If the second GeneXpert result is negative, decisions regarding AII should be based on clinical suspicion.
   - **Discordant AFB Sputum Smears**
     - If smears are discordant (i.e. one AFB positive, one AFB negative), decisions regarding AII should be based on clinical suspicion.

3. **Invalid GeneXpert Result:** An invalid result represents a failure of the assay.
   - This is a rare event, estimated to occur with 1 – 2% of all specimen runs.
   - If an invalid result is reported with the initial specimen, repeat the test on a new specimen.
   - If the second result is also invalid, use AFB smear results and clinical judgment to make the decision to discontinue AII. Consider release from AII if infectious TB is no longer a significant clinical consideration.
IV. REFERENCES


5. CDC. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings, 2005. MMWR 2005;54 (No. RR-17)


V. REFERENCES, CONTINUED

