



# Use of Interferon Gamma Release Assays to Detect Latent Tuberculosis Infection in Foreign-Born Persons – Recommendations from the Minnesota Department of Health

The purpose of this document is to provide guidance regarding the use of FDA-approved Interferon Gamma Release Assays (IGRAs) to test for latent tuberculosis (TB) infection (LTBI) in Minnesota, particularly among foreign-born individuals. In June 2010, the U.S. Centers for Disease Control and Prevention (CDC) issued updated guidelines for the use of IGRAs to test for LTBI.<sup>1</sup> These Minnesota Department of Health (MDH) recommendations do not differ from CDC's; they are intended to highlight the unique role that IGRA testing can play in preventing future TB disease in Minnesota, where 80% of reported TB cases occur among persons born in areas of the world where TB is common.

Treatment of LTBI using one of several acceptable drug regimens is effective in preventing infected persons from developing TB disease, if the prescribed medications are taken as directed.<sup>2</sup> However, completion of a lengthy course of LTBI treatment is a labor-intensive endeavor on the part of patients and providers, which makes achieving high LTBI treatment completion rates challenging. Medical and public health resources to enhance adherence to LTBI treatment are maximized when priority is given to treating infected individuals most at risk of developing TB disease. The use of IGRAs provides an opportunity to identify those individuals who are most likely to truly be infected with *Mycobacterium tuberculosis* (MTB) and therefore to benefit from LTBI treatment.

## The Minnesota Department of Health recommends the following:

- 1. IGRA testing is preferred over the tuberculin skin test (TST) for most foreign-born individuals age 5 years and older who have or may have received *Bacille Calmette Guerin* (BCG) vaccination.** The majority of foreign-born persons living in Minnesota come from areas of the world where the BCG vaccine is commonly used.<sup>3</sup> The TST can detect the presence of nontuberculous mycobacteria, including *M. bovis-BCG* (which is used to produce BCG vaccine), and therefore may be falsely positive in an unknown proportion of individuals. IGRAs use MTB-specific antigens that do not cross-react with BCG, and therefore, do not cause false positive reactions in BCG recipients. Anecdotal evidence indicates individuals whose LTBI diagnosis is based on positive IGRA results may be more accepting of the diagnosis and willing to take LTBI therapy than those with positive TST results, which individuals often attribute their prior BCG vaccination.
- 2. IGRAs should be used in accordance with guidelines published by the U.S. Centers for Disease Control and Prevention (CDC)<sup>1</sup>.** These recommendations state that “an IGRA may be used in place of (but not in addition to) a TST in all situations in which CDC recommends TST testing as an aid in diagnosing MTB infection, with preferences and special considerations.” These special considerations include children under age 5 years, individuals with compromised immune systems, recent contacts, and serial testing in occupational settings. For detailed recommendations, including guidance for interpreting the significance of indeterminate or discordant test results, refer to the CDC document or to a medical expert familiar with the use of IGRAs. These recommendations may be subject to revision as additional data become available.

3. **As with the TST, the use of IGRAs and interpretations of the test results must be combined with clinical judgment, including consideration of the individual’s risk factors for TB and the risks and benefits of LTBI treatment.** A negative or indeterminate TST or IGRA alone does not rule out the presence of LTBI and cannot exclude the possibility of TB disease in a patient with suspicious findings. Limited data exist on IGRA use in groups such as children younger than 5 years of age, persons recently exposed to TB, immunocompromised persons, and those who will be tested repeatedly (serial testing).
4. **Careful attention should be given to ensure that IGRA testing is performed and interpreted according to established protocols using FDA-approved test formats and in compliance with Clinical Laboratory Improvement Amendment (CLIA) standards.** Blood specimens must be collected in the proper tubes using proper handling and storage techniques, and laboratory processing must be performed within the required timeframes.
5. **Testing for LTBI using either method (i.e., IGRA or TST) should be performed only in individuals at risk for TB.** Universal TB testing among the general population and low-risk individuals is discouraged. Decisions to conduct screening should be based on an assessment of trends in the local epidemiology of TB in the community and on stipulations found in local laws or regulations governing certain types of facilities (e.g., health care agencies, correctional facilities).
6. **Regardless of the type of test used, targeted testing of persons at high risk for TB should be accompanied by a plan for providing necessary follow-up.** This plan should include resources for performing a chest x-ray and medical evaluation to rule out active TB, providing treatment for LTBI, and clinically monitoring patients during LTBI treatment.

**References and resources:**

1. Centers for Disease Control and Prevention. Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010. ([www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s\\_cid=rr5905a1\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s_cid=rr5905a1_e).) *MMWR* 2010; 59 (RR-5); 1-25.
2. Centers for Disease Control and Prevention. Targeted Testing and Treatment of Latent Tuberculosis Infection. ([www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm)) *MMWR* 2000; 49 (RR-6).
3. Country-specific information about BCG usage worldwide is available through McGill University and the Public Health Agency of Canada at [www.bcgatlas.org](http://www.bcgatlas.org).