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State of California—Health and Human Services Agency
California Department of Public Health

EDMUND G. BROWN JR.
Governor

AFL 10-23

September 9, 2010

TO: General Acute Care Hospitals
Acute Psychiatric Hospitals
Skilled Nursing Facilities
Intermediate Care Facilities
Home Health Agencies
Primary Care Clinics
Psychology Clinics
Intermediate Care Facilities for the Developmentally Disabled
Intermediate Care Facilities for the Developmentally Disabled - Habilitative
Psychiatric Health Facilities
Adult Day Health Centers
Chemical Dependency Recovery Hospitals

SUBJECT: Procedure for Requesting Program Flexibility for the Use of Interferon Gamma Release Assay (IGRA) Blood Tests to Identify Mycobacterium Tuberculosis Infection in California Health Care Workers

What are Interferon Gamma Release Assay (IGRA) Blood Tests?

For many years the Mantoux tuberculin skin test (TST) has been the basic screening test for detecting latent tuberculosis (TB) infection (LTBI) in health care workers. However, there have been some limitations including, the need to measure the response (induration) within 48-72 hours after the application of the TST as well as inaccuracies and errors in determining if the response meets the definition of a positive TST. IGRAs are designed to detect immunologic responsiveness associated with Mycobacterium tuberculosis infection and therefore are similar to the Mantoux TST using a purified protein derivative (PPD).

In 2005, the Food and Drug Administration (FDA) approved an in vitro laboratory diagnostic test, QuantiFERON ®- TB Gold (QFT-G) to aid in diagnosing Mycobacterium tuberculosis infection and the Centers for Disease Control and Prevention (CDC) subsequently released guidelines (MMWR; 54 [No. RR-15]:49-55). Two additional IGRA tests were FDA-approved in 2007 and 2008 respectively: QuantiFERON ® – TB Gold-In- Tube (QFT-GIT) manufactured by Cellestis Limited and T-Spot ® manufactured by Oxford Immunotech Limited.

In 2010, the CDC published updated guidelines for using IGRAs to detect Mycobacterium tuberculosis infection (MMWR; 59 [No. RR-5]: 1-25). The guidelines are available on the CDC website at: CDC - Morbidity and Mortality Weekly Report. The CDC recommends that an IGRA or a TST may be used without preference for periodic screening of persons who might have occupational exposure to Mycobacterium tuberculosis with special considerations regarding conversions and reversions. IGRAs should be performed and interpreted pursuant to the established protocols of the FDA-approved test formats.

The CDC advises that because TST, QFT-G, QFT-GIT, and T-Spot each measure different aspects of the immune response, use different antigens and interpretation criteria, the test results might not be interchangeable. Nonetheless, different tests can yield different results. Therefore, the CDC also recommends that an IGRA or a TST may be used without preference to test recent contacts of persons known or suspected to have active TB with special considerations for follow-up testing. It is important to note, that the IGRAs are not the preferred test for children less than 5 years of age.

Use of IGRA blood tests such as QFT-G, QFT-GIT, and T-Spot for screening health care workers for Mycobacterium tuberculosis infection requires a grant of program flexibility from the California Department of Public Health's Licensing and Certification Program, since the TST is required by regulation (California Code of Regulations (CCR), Title 22, all chapters – see attachment). However, use of FDA- approved IGRAs for screening patients, residents, or clients upon admission to a health care facility does not require program flexibility because the test method is not specified in the regulation. Therefore, the facility may choose either the IGRA blood test or the TST for patient, resident and client LTBI screening.

Requirements for Submitting a Request for Program Flexibility to Use IGRAs

1. The facility must submit a letter to the Licensing and Certification district office with jurisdiction over the facility signed by the hospital administrator or designee requesting that program flexibility be granted for the use of an IGRA blood test such as QFT-G, QFT-GIT, or T-Spot for health care worker screening for Mycobacterium tuberculosis infection.
2. Accompanying the flexibility request, the facility must submit a policy specifying the IGRA blood test to be used in screening health care workers for LTBI. The policy must comply with current standards of practice for LTBI screening as defined by the California Occupational Safety and Health Administration (Cal-OSHA) for new employee, annual and post-exposure testing.

The policy must specify the group of employees in which the IGRA will be used (i.e., new employee LTBI screening, annual or post-exposure screening). The CDC guidelines outline situations in which testing with both IGRA and TST may be considered.

The policy must include a statement that employees will be informed in writing of the limitations of using IGRAs as defined by most current recommendations by the CDC or the California Tuberculosis Controllers Association (if applicable).

The CDC currently identifies the following limitations:

(a) As with a negative TST result, negative IGRA results should not be used alone to exclude Mycobacterium tuberculosis infection in persons with symptoms or signs suggestive of TB disease. The presence of symptoms or signs suggestive of TB disease increases the likelihood that Mycobacterium tuberculosis infection is present, and these circumstances decrease the predictive value of a negative IGRA or TST result. Medical evaluation of such persons should include a history and physical examination, chest radiograph, bacteriologic studies, serology for human immunodeficiency virus (HIV), and, when indicated, other tests or studies.

(b) Limited data is available regarding the use of IGRAs in immunocompromised persons. The performance of IGRAs, in particular their sensitivity and rate of indeterminate results, has shown inconsistencies in persons who, because of impaired immune function, are at increased risk for Mycobacterium tuberculosis infection progressing to TB disease. Impaired immune function can be caused by HIV infection or acquired immunodeficiency syndrome (AIDS); current treatment with immunosuppressive drugs including high-dose corticosteroids, tumor necrosis factor-alpha (TNF-a) antagonists, and drugs used for managing organ transplantation; selected hematologic disorders (e.g., myeloproliferative disorders, leukemias, and lymphomas); specific malignancies (e.g., carcinoma of the head, neck, or lung); diabetes; silicosis; and chronic renal failure. All of these conditions or treatments have been known, or suspected to, decrease responsiveness to the TST, and they might decrease the responsiveness to an IGRA. Consequently, as with a negative TST result, negative IGRA results alone might not be sufficient to exclude Mycobacterium tuberculosis infection in these persons.

(c) With any of the testing methods, persons who have a negative test or result can still have LTBI. Those who have a negative result, are likely to have LTBI, and who are at greater risk for severe illness or poor outcomes if TB disease occurs might need treatment or closer monitoring for disease. Potential examples include, but are not limited to, those who are immunocompromised because of HIV infection, or those who will undergo treatment with TNF-a antagonists and other conditions or risk factors for progression of infection to active TB disease.

For questions regarding this All Facilities Letter or TB related questions, please contact Jan Young at (510) 620-3029, jan.young@cdph.ca.gov or for CCR Title 22 specific questions contact Carol Turner at (916) 324-1261, carol.turner@cdph.ca.gov.

Sincerely,

Original Signed by Kathleen Billingsley, R.N.

Kathleen Billingsley, R.N.
Deputy Director

California Code of Regulations, Title 22 Chapters Requiring the Use of the TST (PPD) for Screening Employees for LTBI
Chapter 1. General Acute Care Hospitals. § 70723. Employee Health Examinations and Health Records.
Chapter 2. Acute Psychiatric Hospitals. §71523. Employee Health Examinations and Health Records.
Chapter 3. Skilled Nursing Facilities. § 72535. Employees' Health Examination and Health Records.
Chapter 4. Intermediate Care Facilities. §73525. Employees' Health Examination and Health Records.
Chapter 6. Home Health Agencies. §74723. Employee's Health Examinations and Health Records.
Chapter 7. Primary Care Clinics. §75051. Health Examinations and Health Records of Persons Working in the Clinic.
Chapter 7.2. Psychology Clinics. §75335. Employee Health Examinations and Health Records.
Chapter 8. Intermediate Care Facilities for the Developmentally Disabled. §76539. Employee' Health Examination and Health Records.
Chapter 8.5. Intermediate Care Facilities/Developmentally Disabled – Habilitative. §76919. Employees' Health Examination and Health Records.
Chapter 9. Psychiatric Health Facilities. §77121. Employee Health Examinations and Health Records.
Chapter 10. Adult Day Health Centers. §78429. Employee Records.
Chapter 11. Chemical Dependency Recovery Hospital Licensing Regulations. §79331. Employee Health Examinations and Health Records.
Chapter 12. Correctional Treatment Centers. §79795. Employee Health Examinations and Health Records.

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Page Last Updated : October 7, 2017