

## TUBERCULOSIS DIAGNOSTICS

### LATERAL FLOW URINE

### LIPOARABINOMANNAN ASSAY (LF-LAM)

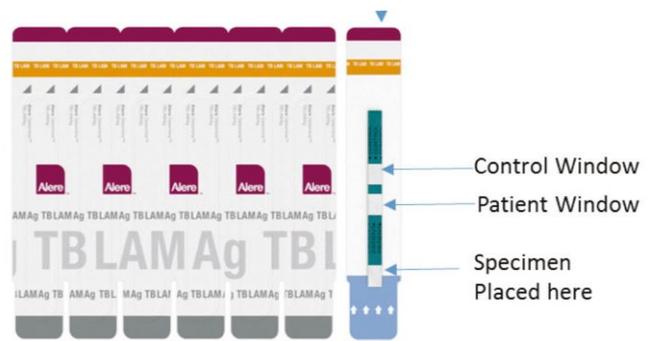
FOR THE DIAGNOSIS AND SCREENING OF ACTIVE TUBERCULOSIS IN PEOPLE LIVING WITH HIV

#### BACKGROUND

- Key global priorities for tuberculosis (TB) care and control include improving case-detection and detecting cases earlier, including cases of smear-negative disease which are often associated with co-infection with the human immunodeficiency virus (HIV) and with young age.
- Globally in 2015, there were an estimated 10.4 million new (incident) TB cases. People living with HIV accounted for 1.2 million (11%) of new cases.
- There were an estimated 1.4 million TB deaths in 2015, and an additional 0.4 million deaths resulting from TB disease among people living with HIV.

#### ABOUT THE TEST

- Determine™ TB LAM Ag test (LF-LAM) is an urine test for the detection of LAM antigen, a lipopolysaccharide present in mycobacterial cell walls, which is released from metabolically active or degenerating bacterial cells. LAM appears to be present predominately in people with active TB disease.
- The test is performed manually by applying 60 µL of urine to the Determine™ TB LAM Ag test strip and incubating at room temperature for 25 minutes. The strip is then inspected by eye. The intensity of any visible band on the test strip is graded by comparing it with the intensities of the bands on a manufacturer-supplied reference card. The reference card includes four bands (grade 1 representing a very low intensity band to grade 4 representing a high/dark intensity band).



Individual LF-LAM strip: Courtesy of Alere™

#### BENEFITS OF THE LF-LAM

- Urine-based testing has advantages over sputum-based testing because urine is easy to collect and store, and lacks the infection control risks associated with sputum collection.
- Presence of LAM in urine is indirectly related to human immune response, and its detection process is amenable to inexpensive point of care platforms.
- Owing to suboptimal sensitivity and specificity, current urinary LF-LAM assays are deemed unsuitable as a general screening or diagnostic test for TB.
- Unlike traditional TB diagnostic methods, however, LF-LAM demonstrates improved sensitivity in seriously ill\* HIV infected individuals, especially in those with low CD4 counts.

#### COSTS

- The test was initially marketed at \$3.50 per test. More information can be obtained from manufacturer <http://www.alere.com/en/home/product-details/determine-tb-lam.html>

# WHO RECOMMENDATIONS ON THE USE OF THE LF-LAM

[http://www.who.int/tb/areas-of-work/laboratory/policy\\_statements](http://www.who.int/tb/areas-of-work/laboratory/policy_statements)



## POLICY RECOMMENDATION

- Except as specifically described below for persons with HIV infection with low CD4 counts or who are seriously ill, LF-LAM **should not be used for the diagnosis of TB** (strong recommendation, low quality of evidence).
- LF-LAM may be used to assist in the diagnosis of TB in HIV positive adult in-patients with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a **CD4 cell count less than or equal to 100 cells/μL**, or HIV positive patients who are **seriously ill\*** regardless of CD4 count or with unknown CD4 count (conditional recommendation; low quality of evidence).

### Remarks

- This recommendation also applies to HIV positive adult out-patients with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a CD4 cell count less than or equal to 100 cells/μL, or HIV positive patients who are seriously ill\* regardless of CD4 count or with unknown CD4 count, based on the generalisation of data from in-patients.
- This recommendation also applies to HIV positive children with signs and symptoms of TB (pulmonary and/or extrapulmonary) based on the generalisation of data from adults while acknowledging very limited data and concern regarding low specificity of the LF-LAM assay in children.
- LF-LAM **should not be used as a screening test for TB**. (strong recommendation, low quality of evidence).

## IMPLEMENTATION CONSIDERATIONS

Even with targeted use of the LF-LAM assay (in HIV positive adult *in-patients* with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a CD4 cell count less than or equal to 100 cells/μL, or in HIV positive patients who are seriously ill\* regardless of CD4 count or with unknown CD4 count), the following implementation considerations apply:

- LF-LAM does not differentiate between the various species of mycobacterium and cannot be used to distinguish *Mycobacterium tuberculosis* from other species. However, in areas endemic for tuberculosis the LAM antigen detected in a clinical sample is likely to be attributed to *M. tuberculosis*.
- Implementation of LF-LAM in the targeted patient groups does not eliminate the need for other diagnostic tests as these tests have better diagnostic accuracy. Whenever possible, a positive LF-LAM should be followed up with a confirmation test such as Xpert MTB/RIF, line probe assay or bacteriological culture and drug-susceptibility testing.
- LF-LAM is designed to detect mycobacterial LAM antigen in human urine. Other samples (e.g. sputum, serum, plasma, CSF or other body fluids) or pooled urine specimens should not be used.
- LF-LAM test cards must be stored at 2-30°C until the expiration date. Kit components are stable until the expiration date when handled and stored as directed. Devices that have become wet or if the packaging has become damaged should not be used.