

# DETERMINE™ TB LAM AG TEST

TECHNICAL INFORMATION NOTE

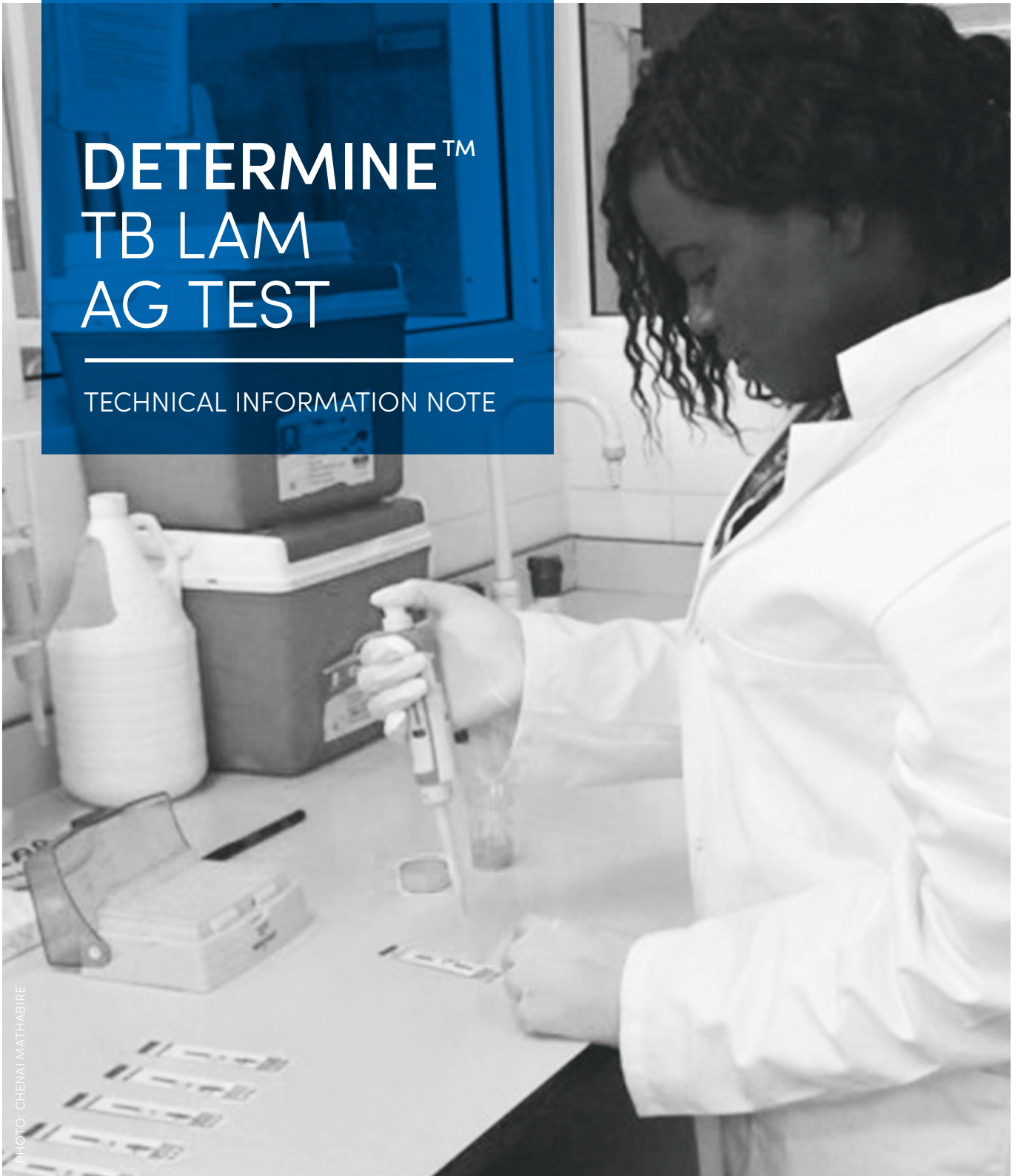


PHOTO: CHENAI MATHABIRE



Ensuring an uninterrupted supply of quality-assured, affordable anti-TB drugs and diagnostics to the world.

**Stop TB Partnership**  
**GLOBAL DRUG FACILITY**

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# TECHNICAL INFORMATION NOTE

## DETERMINE™ TB LAM AG TEST

Diagnosis of TB in people living with HIV (PLHIV) using sputum-based tests is challenging, given the frequency of extrapulmonary TB in such patients combined with their frequent inability to expectorate sputum adequately. In PLHIV with advanced immunodeficiency, disseminated TB with renal involvement can result in the lipoarabinomannan (LAM) antigen being present in the urine. A urine-based test to detect LAM therefore has important utility among these patients. In November 2015, WHO issued policy guidance on the urine-based LAM assay, based on the evaluation of the commercially available Determine™ TB LAM Ag test. As a simple dipstick test with minimal biosafety hazards and training needs, it is currently the only truly point-of-care test for TB.

## SUPPLY INFORMATION

PRODUCT NAME	Determine™ TB LAM Ag test
GDF ITEM NUMBER	106642 (available in the GDF diagnostics catalogue)
MANUFACTURER	Abbott Laboratories, Lake Bluff, USA (formerly Alere Inc, Waltham, USA)
COST	USD \$3.50 / test strip (packaged in kits of 100 test strips: USD \$350)
SHELF LIFE	18 months
STORAGE CONDITIONS	2 – 30°C



For more information or to place an order contact  
[gdf@stoptb.org](mailto:gdf@stoptb.org)

## ACCESSORIES REQUIRED

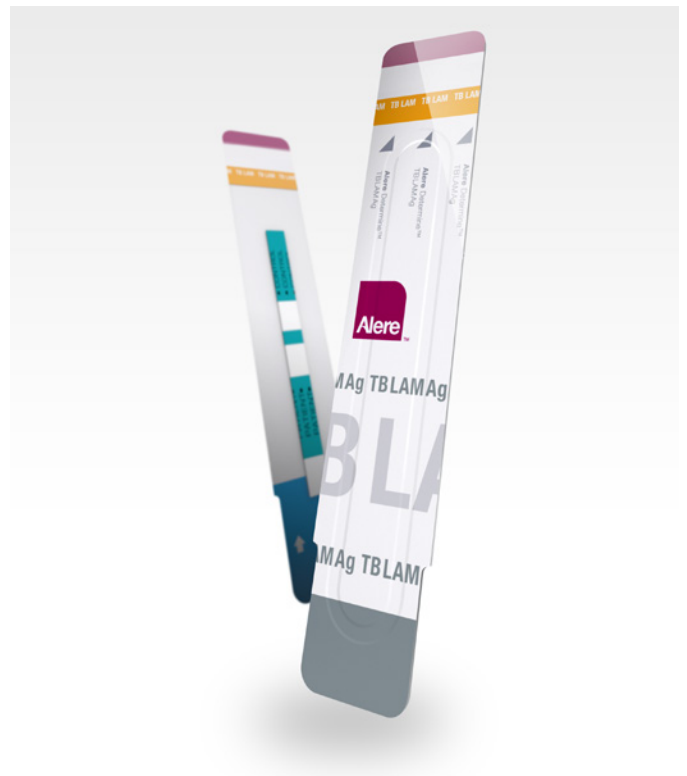
ITEMS INDICATED IN PACKAGE INSERT	GDF ITEM NUMBER	GDF ITEM DESCRIPTION	COST (IN USD)
Sputum containers	106525	80 ml each; 1,000 cups per pack	\$83.30
Pipette capable of delivering 60 µl	106055	Pipette capable of delivering 10-100 µl	\$226.94
Disposable pipette tips	106388	Pipette tips capable of delivering 10-100 µl; 1,000 tips per pack	\$72.75
Timer	106570	Mechanical timer	\$1.11

## FORECASTING SIZES OF ORDERS

→ To forecast the number of LAM test strips to procure for an initial shipment, data from HIV registers on numbers of patients stratified by CD4 count at planned implementation sites (hospitals and/or peripheral sites) should be used, if available:

- In settings where CD4 testing is routine, the number of patients registered annually with CD4 counts  $\leq 100$  cells/ $\mu$ l at the implementation sites should be multiplied by a factor to arrive at the number of people in this population group who would be evaluated for TB annually based on presence of signs or symptoms of TB or danger signs, and therefore in need of a LAM test.
  - In the absence of country-specific data to calculate the factor, 0.6 may be used as a default estimate of the proportion of this population group who would have signs or symptoms of TB or danger signs in a given year.<sup>1</sup>
  - The calculated number of tests may be used as a conservative estimate for the size of an initial order, given seriously ill patients with unknown CD4 counts would also be eligible for testing, and considering the 18 month shelf life of the test strips.
  - Data from any in-country pilot studies or verification studies should be used to refine the initial forecast.

- In the absence of data from registers or in settings where CD4 testing is not routine, data from any in-country studies on estimated numbers of patients stratified by CD4 count should be extrapolated to the planned implementation sites. The proportion of this population group with CD4 counts  $\leq 100$  cells/ $\mu$ l who would be expected to have signs or symptoms of TB or danger signs in a given year would need to be estimated in order to calculate the number of tests needed annually.
  - Alternatively, any data available from studies on the proportion or number of PLHIV classified as having advanced HIV disease (AIDS) may be used.
- For subsequent forecasting exercises, the number of PLHIV estimated nationwide to have CD4 counts  $\leq 100$  cells/ $\mu$ l multiplied by the aforementioned factor (default estimate of 0.6) should be considered as a target to phase in over time when implementation sites include all hospitals and peripheral sites. Data that become available on actual test consumption rates should be used to refine the forecast.
- Operational research may also be considered using the test with a threshold of CD4 counts  $\leq 200$  cells/ $\mu$ l or as a screening tool among all PLHIV admitted to hospitals.



<sup>1</sup> WHO proposes a default factor of 0.3 to estimate the proportion of all PLHIV who would have signs or symptoms of TB in a given year, assuming patients are clinically screened on average twice a year and 15% of screened patients would have signs or symptoms (WHO Framework of indicators and targets for laboratory strengthening under the End TB Strategy, 2016, WHO/HTM/TB/2016.18). The higher default factor of 0.6 proposed herewith is due to the target patient group having low CD4 counts.

## WHO POLICY RECOMMENDATIONS (NOVEMBER 2015)

WHO recommends use of the LAM test to assist in the diagnosis of TB in two specific population groups:

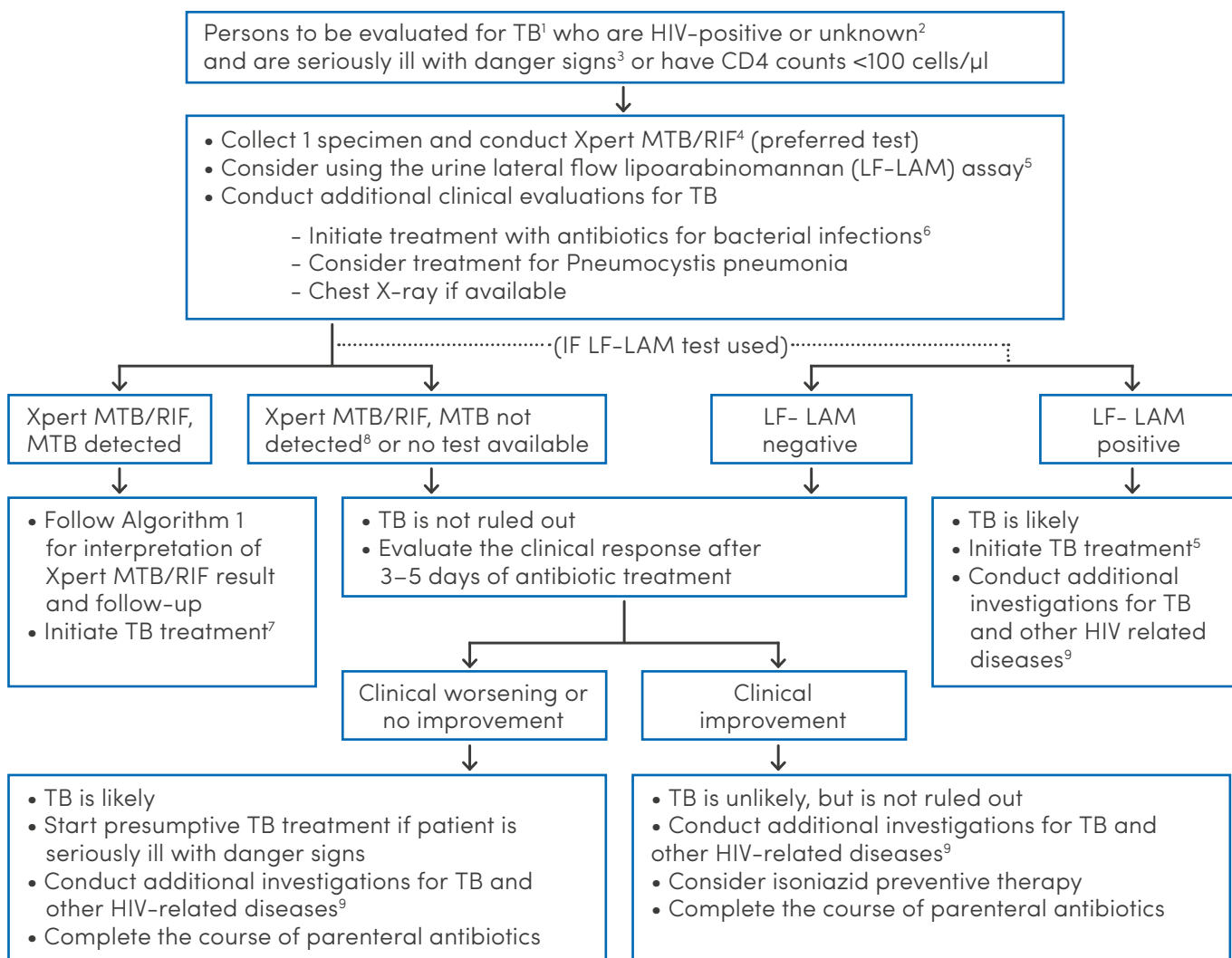
- People living with HIV who have signs or symptoms of TB and a CD4 count  $\leq 100$  cells/ $\mu$ l
- People living with HIV who are “seriously ill” regardless of CD4 count or if the CD4 count is unknown. “Seriously ill” is defined based on 4 danger signs: respiratory rate  $>30$ /min, temperature  $>39^{\circ}\text{C}$ , heart rate  $> 120$ /min and unable to walk unaided.

The LAM test is not recommended for TB screening or for diagnosis of active TB disease in the general population.

## RESOURCES AVAILABLE: CURRENT NORMATIVE AND PRACTICAL GUIDANCE

- **2015 WHO Global TB Programme Guidelines on use of the LAM assay**
- **2017 WHO HIV Department Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy:** Includes the LAM test as a component of the package of care for people with advanced HIV disease
- **2017 GLI Model TB Diagnostic Algorithms:** Includes the LAM test in Algorithm #4, for evaluating persons for TB among PLHIV who are seriously ill with danger signs or have CD4 counts  $\leq 100$  cells/ $\mu$ l (see next page)
- **2016 GLI Information Note:** Describes a study finding LAM-guided TB treatment initiation reduces mortality in HIV-positive hospital inpatients; includes case studies on use of the LAM test
- **2017 TAG Activist's Guide to the TB LAM Test and TAG Webinar on Expanding its Use**

# POSITIONING OF THE LAM TEST (LATERAL FLOW LAM ASSAY) IN ALGORITHM 4 OF THE GLI MODEL TB DIAGNOSTIC ALGORITHMS



<sup>1</sup> Persons to be evaluated for TB include adults and children with signs or symptoms suggestive of TB or with a chest X-ray with abnormalities suggestive of TB. This algorithm may also be followed for the detection of MTB using CSF, lymph node and other tissue specimen from persons being evaluated for extrapulmonary TB.

<sup>2</sup> PLHIV (People living with HIV/AIDS) include persons who are HIV positive or whose HIV status is unknown, but who present with strong clinical evidence of HIV infection in settings where there is a high prevalence of HIV or among members of a risk group for HIV. For all people with unknown HIV status, HIV testing should be performed according to national guidelines. For all adults living with HIV/AIDS regardless of CD4 cell count or clinical stage, ART should be recommended and initiating co-trimoxazole preventive therapy should be considered.

<sup>3</sup> Danger signs include any one of the following: respiratory rate >30 per minute, temperature >39°C, heart rate >120 beats per minute, or unable to walk unaided.

<sup>4</sup> The Xpert MTB/RIF test is the preferred initial diagnostic test. For persons being evaluated for pulmonary TB, sputum is the preferred specimen.

<sup>5</sup> The LF-LAM assay may be used to assist in diagnosing active TB in both in- and out-patients who are seriously ill with danger signs, regardless of CD4 count. Testing with the LF-LAM assay may be especially useful for patients unable to produce a sputum specimen. Whenever possible, a positive LF-LAM should be followed up with other tests such as Xpert MTB/RIF. While awaiting results of other tests, clinicians could consider initiating TB treatment immediately based on the positive LF-LAM and their clinical judgment.

<sup>6</sup> Antibiotics with broad-spectrum antibacterial activity (except do not use fluoroquinolones) should be used.

<sup>7</sup> Initiate a treatment with first-line or second-line TB drugs based on the Xpert MTB/RIF result. See Algorithm 1.

<sup>8</sup> If the Xpert MTB/RIF test does not detect MTB, the test can be repeated using a fresh specimen. See Algorithm 1 for a discussion of possible followup testing for an Xpert MTB/RIF result of MTB not detected.

<sup>9</sup> Further investigations for TB may include chest X-ray, additional clinical assessments, a repeat Xpert MTB/RIF using a fresh specimen, or culture. If the patient is being evaluated

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