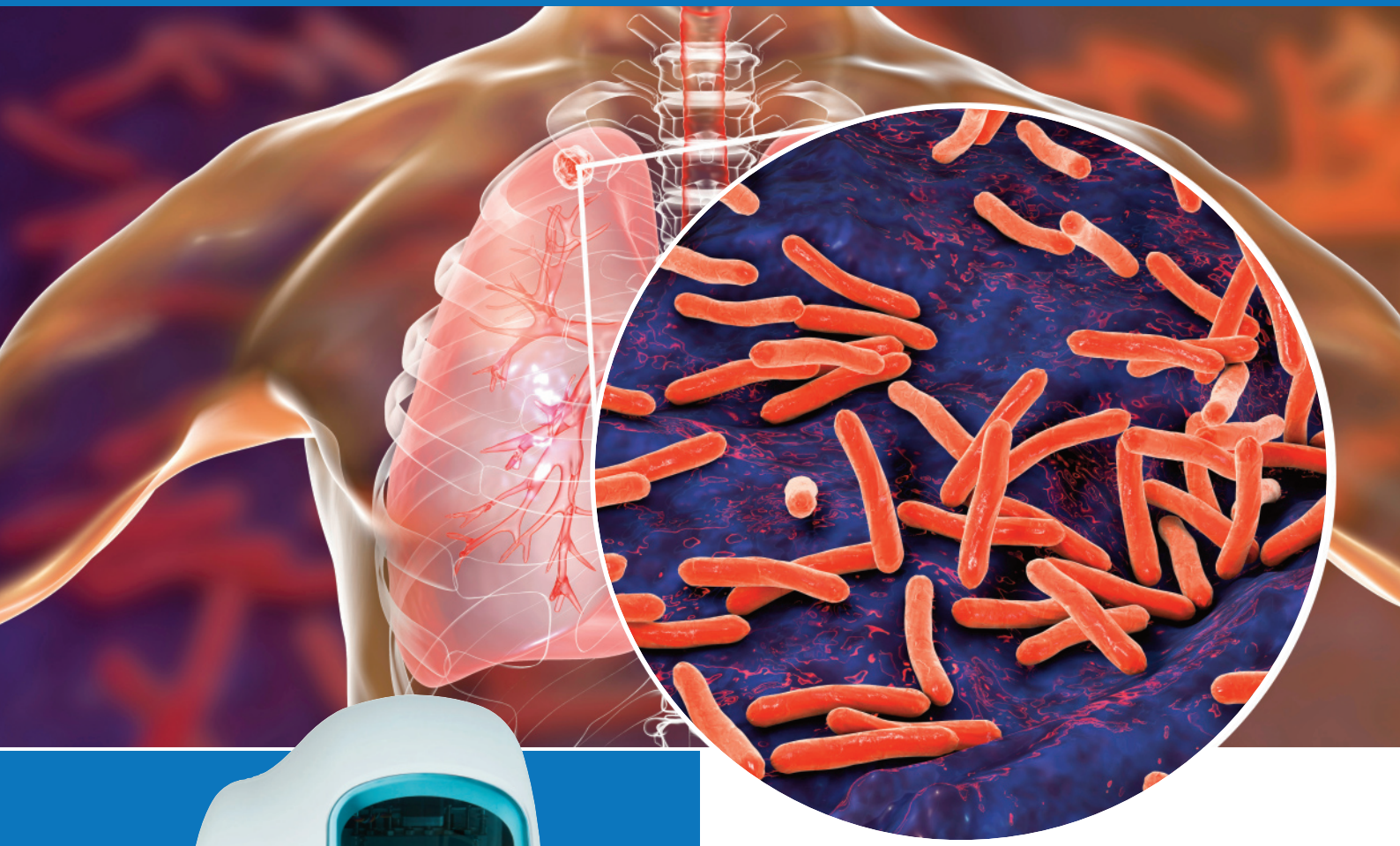
PATHFAST™

TB LAM Ag



TB Monitoring Marker

- Tuberculosis Bacterial Load Assay
- CLEIA technology
- Simple operation
- Rapid results

New diagnostic technology for better tuberculosis treatment monitoring in less than one hour

Tuberculosis: a grand global health challenge

Tuberculosis (TB) is a formidable global health challenge, ranking as the second infectious killer worldwide, following COVID-19 but surpassing HIV and AIDS. TB, primarily affecting the lungs, results from infection with *Mycobacterium tuberculosis complex* bacteria, such as *M. tuberculosis* and *M. africanum* [1,2].

TB not only claims numerous lives but also leads to significant morbidity and impairments (e. g., mental disorders) in affected individuals, and results in substantial economic consequences [3]. **Each year, an estimated 10 million individuals are impacted by TB**, with a substantial number of cases occurring in low- and middle- income countries (Figure 1).

In 2023, several countries continue to face significant TB challenges within various WHO regions. These challenges are characterized by an incidence rate of ≥ 20/100, 000 population, categorizing the countries as high- burden nations. **Collectively, these countries account for 87% of all new TB cases worldwide, emphasizing the necessity for tailored interventions to address challenges specific to each WHO region and country (Figure 2)[3].**

Efforts to improve TB control, expand treatment coverage, and strengthen healthcare systems are critical to combating the global TB burden and moving closer to its elimination. Its important to consider that there are diverse challenges in addressing this gigantic global health issue as its prevalence and number of incident cases vary significantly across different WHO regions and countries [3].

The need for effective TB treatment monitoring

Monitoring TB patients is crucial for ensuring successful treatment outcomes and preventing the spread of the disease.

Monitoring TB patients allows healthcare providers to assess treatment response, make informed decisions, and prevent treatment failure or relapse[4]. Traditional monitoring methods, such as sputum smear microscopy, which is widely used, and culture, have limitations in terms of time, accuracy and sensitivity[5].
Accurate and timely monitoring plays a vital role in achieving effective TB management and reducing the burden of the disease. To address these challenges, the PATHFAST™ TB LAM Ag test offers a revolutionary solution for transforming TB monitoring.

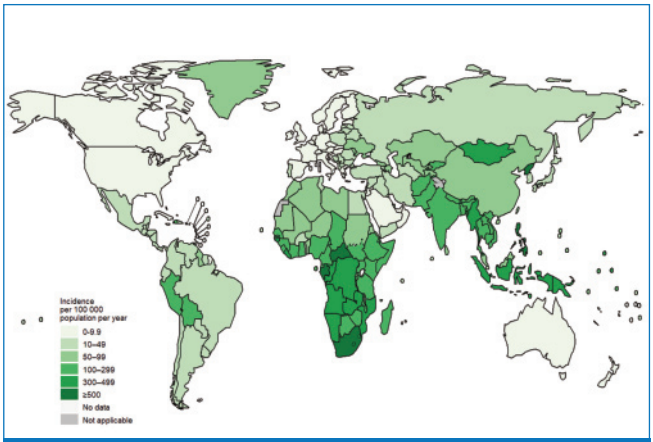


Figure 1: Estimated TB incidence rates by country in 2021
(Source: WHO global TB report 2022)

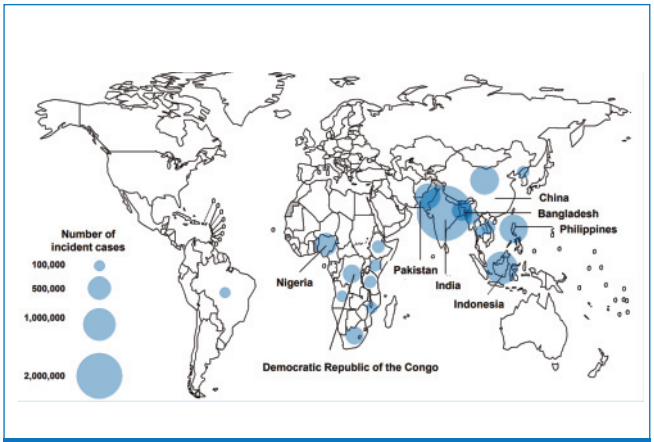


Figure 2: Countries with highest estimated TB incidence cases in 2021
(Source: WHO global TB report 2022)

Ending TB: UN and WHO's collaborative drive for a TB- free world

The UN and WHO's collaborative drive for a TB-free world have united in their commitment to eliminate TB globally during the UN High-Level Meeting (HLM) on TB, held in September 2018. The meeting resulted in a number of ambitious targets for TB elimination, including reducing TB deaths by 90% and TB incidence by 80% by 2030 (Figure 3). Their collaborative efforts encompass raising awareness about TB, offering financial and technical support, and advocating for TB eradication on a worldwide scale. Their shared vision is to make TB a thing of the past with collective assistance.

In 2018, the UN and WHO initiated the End TB Strategy, aimed at eradicating TB as a public health threat by 2030.
This strategy is built upon five pivotal pillars:

1. **Prevention:** Reducing initial TB infections.
2. **Early diagnosis:** Promptly detecting TB cases for swift treatment.
3. **Treatment:** Ensuring effective and accessible TB treatment for all in need.
4. **Care and support:** Providing comprehensive care, social support, and access to essential medicines for individuals with TB.
5. **Research:** Investing in innovative tools and approaches to TB control.

The UN and WHO actively collaborate with countries worldwide to implement this strategy by providing financial backing and technical guidance to assist countries in achieving TB elimination. Furthermore, the UN and WHO work diligently to ensure access to crucial services, including prevention, testing and treatment.
The UN hosted a second HLM in September 2023 to conduct a comprehensive review of global progress in the quest to end TB. This serves as a poignant reminder of the urgency to accelerate efforts, especially considering that over seven million lives have been lost to TB in the five years since the initial HLM in 2018. With collective determination and concerted action, TB can be eliminated as a looming public health threat.

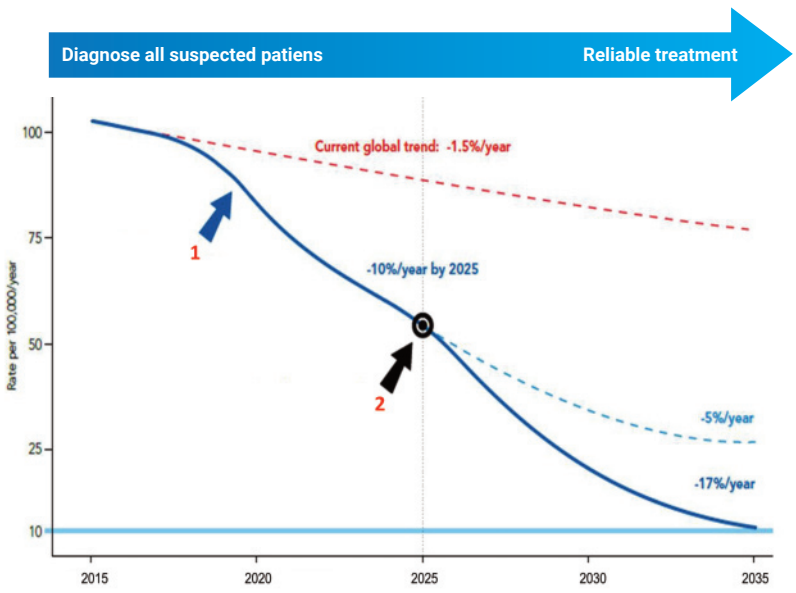


Figure 3: Desired decline in global TB incidence rates to reach the 2035 targets. (1) By 2020 the End TB Strategy involves optimizing the use of existing and upcoming tools, aiming to achieve universal health coverage and social protection.(2) Additionally by 2025, the End TB Strategy includes the introduction of new resources, such as a vaccine, novel drugs, treatment regimens and a point-of-care test for managing both active TB disease and latent infections.

PATHFAST™ TB LAM Ag Test

PATHFAST™ TB LAM Ag test is a product for *in vitro* diagnostic use with the PATHFAST™ automated analyser for the **quantitative measurement of lipoarabinomannan (LAM) in human sputum**. PATHFAST™ TB LAM Ag test is intended to be used:

- as an aid to the diagnosis of TB
- by laboratory technician, nurse or physician
- in a hospital or clinical laboratory setting.

The PATHFAST™ TB LAM Ag test procedure is based on a chemiluminescent enzyme immunoassay and MAGTRATION*. All required components for performing the testing are packed in one reagent cartridge.

By loading PATHFAST™ TB LAM Ag cartridge into the *in vitro* diagnostic system PATHFAST™, the quantification of LAM can be accurately measured within 17 minutes.

LAM is a 17.5 kDa glycolipid present in the mycobacterial cell wall [6]. LAM can be detected in the sputum of TB patients, and LAM concentration correlates well with the score of smear microscopy and time to detect of a culture (Figure 4 and 5).

*MAGTRATION is a bound/free separation technology in which magnetic particles are washed in a pipette tip. It is a trademark or registered trademark of Precision System Science Co., Ltd.

Figure 4: Correlation of the LAM concentration with the liquid culture time to detect (TTD)

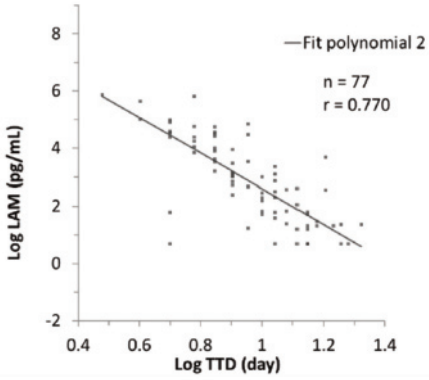
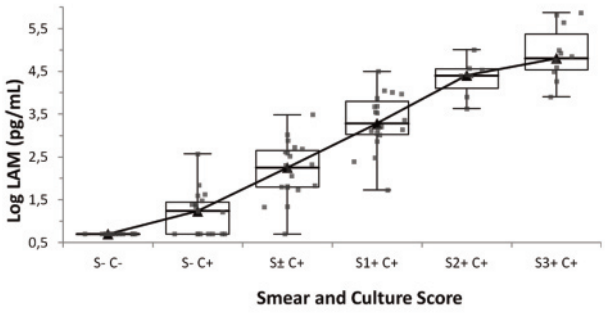
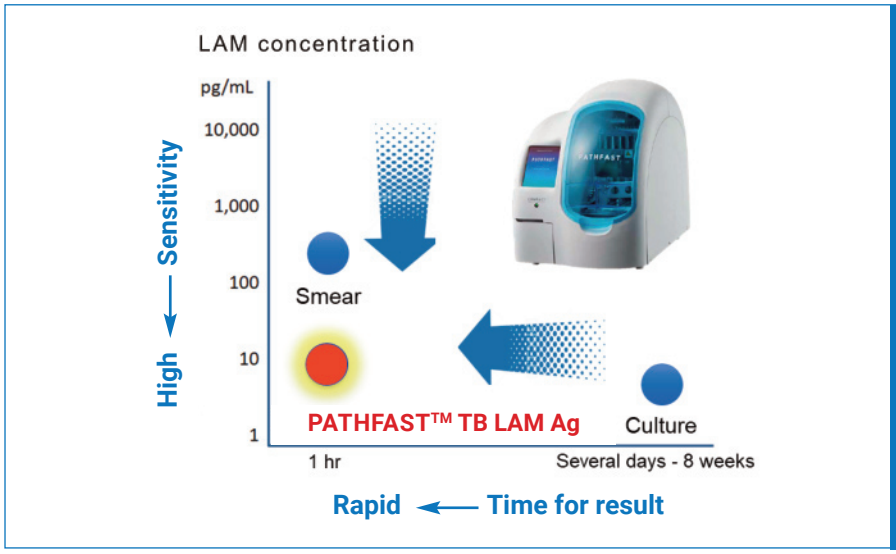


Figure 5: Correlation of the LAM concentration with the smear microscopy and culture score





Characteristics of laboratory test for TB treatment monitoring.
The smear microscopy has a low sensitivity. The culture provides definitive diagnosis of TB by establishing the viability of organisms; however it takes from several days to 8 weeks.

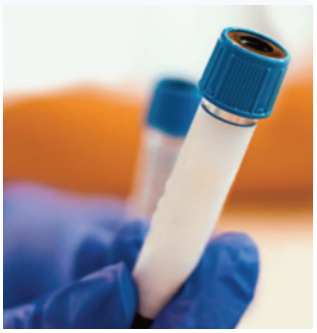
PATHFAST™ TB LAM Ag Procedure

1

Sample collection
Collect raw sputum from the patient following the general procedure for smear microscopy and culture

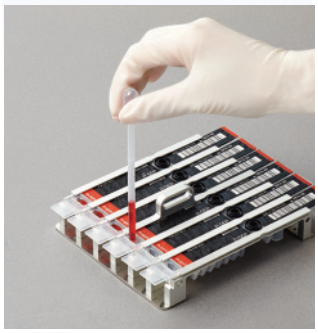
2

LAM extraction
Extract LAM from 200 µL of the raw sputum following the LAM extraction protocol [7]



3

Sample loading
Transfer 100 µL of the LAM extract into each sample well of the reagent cartridges



4

LAM measurement
Load the reagent rack into the instrument and start the assay. Get results in <17 minutes

Benefits of choosing PATHFAST™ TB LAM Ag test

PATHFAST™ TB LAM Ag test stands out with many benefits for TB treatment monitoring due to its numerous competitive advantages.

1. **Minimal containment requirements:** It doesn't demand high-level biosafety containment (e.g. BSL3 lab), making it ideal for resource-limited settings.
2. **Ease of use:** Its straightforward operation that requires minimal training, streamlining workflow.
3. **Quantitative precision:** It provides quantitative results allowing for a deeper understanding of TB treatment efficacy.
4. **High sensitivity:** It detects lower LAM concentrations, enabling TB treatment monitoring also in patients with low bacterial loads.
5. **Swift results:** With a turnaround time of less than an hour, it expedites clinical decision-making.
6. **Data-driven decisions:** Its quantitative nature enables tracking of LAM concentration changes over time.
7. **Cost-effective:** Considering its speed and accuracy, it offers a cost-effective solution for TB management.
8. **Could serve as a Point-of-Care test:** The test shows potential for use as a point-of-care test, possibly bringing TB diagnosis and treatment monitoring closer to patients in primary care facilities and clinics.
9. **Reagents "all in one":** Once the sample preparation is done, no water supply & drain system and no extra washing buffer & substrate bottles needed.

The highly precise, fast and compact chemiluminescence immunoassay analysis system

PATHFAST™ TB LAM Ag test utilizes advanced technology to detect and quantify LAM which is a specific component in the cell wall of *M. tuberculosis* in patient sputum samples. LAM is released during active TB infection. The test uses special antibodies that create a visible signal to indicate TB treatment success.

The PATHFAST™ analyzer employs a technology involving magnetic particles in a pipette tip. During the test, the sample interacts with specific antibodies and magnetic particles. After removing unwanted substances, a chemiluminescent substance (CDP-star) is added. The brightness produced during the test is used to calculate the LAM concentration in the sample (Figure 6).

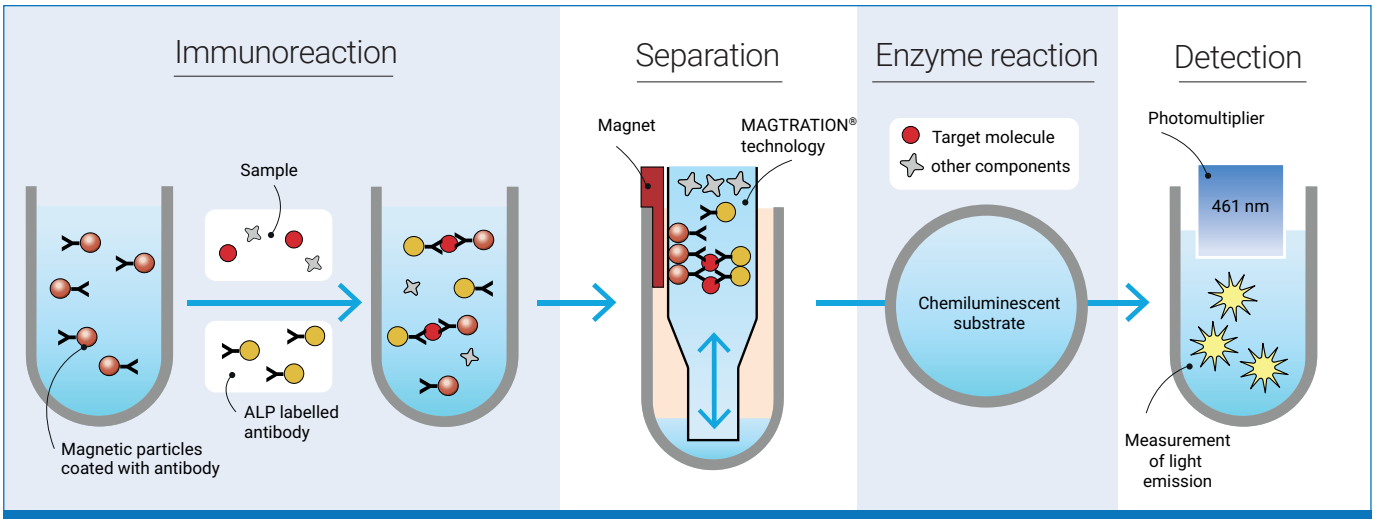


Figure 6: Principle of the PATHFAST TB LAM Ag Test. The test encompasses four-step process: immunoreaction, separation, enzyme reaction, and detection. In the immunoreaction step, specific antibodies interact with LAM antigen in patient sputum samples. The separation stage employs magnetic particles to isolate LAM-antibody complexes. Subsequently, an enzyme reaction occurs, amplifying the signal. Finally, in the detection phase, the luminescence intensity produced by the enzyme reaction is measured, providing a precise quantification of LAM concentration.

Specific performance data

Sensitivity (CI)*	Specificity (CI)*	PPV	NPV	Likelyhood Ratio (+)	Likelyhood Ratio (-)
88.8% (80.0-94.0%)	100% (83.9-100%)	100%	69.0%	+∞	0.113

Analytical sensitivity

Limit of blank (LoB): 3.03 pg/mL

Limit of detection (LoD): 6.67 pg/mL

Limit of quantitation (LoQ): 7.44 pg/mL (C.V. 20%)

Linearity

Five sputum-based QC samples at different levels of LAM (133, 3354, 30247, 45514, 53627 pg/mL) were serially diluted and measured. The recovery rate against the theoretical value was within 85% to 118% up to 53627 pg/mL.

Assay range: 10 - 50000 pg/mL

The assay range was set from the results of LoQ and linearity.

High dose hook effect

A sputum-based QC sample at a concentration of approximately 10000000 pg/mL was serially diluted and measured. There was no high dose hook effect for the samples with LAM values up to 10000000 pg/mL.

PATHFAST™ for tuberculosis, critical care and sepsis diagnostics

Product List

	Item number	Pack size
SYSTEM		
PATHFAST™ Immunoanalyzer Analyzer for the detection of biomarkers for tuberculosis, cardiac,emergency parameters and sepsis	300929	1 x 1
CONSUMABLES AND ACCESSORIES		
PATHFAST™ pipette tips	300936	5 x 42 units
PATHFAST™ waste box	300950	10 units
REAGENT KITS FOR TB DIAGNOSTICS		
PATHFAST™ TB LAM Ag	PF1231-K	60 tests
PATHFAST™ TB LAM Ag Control	PF1231C	2 level, 1ml, 2 bottles
REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS		
PATHFAST™ hs-cTnI	PF1241-K	60 tests
PATHFAST™ Myoglobin	PF1021-K	60 tests
PATHFAST™ CK-MB	PF1031-K	60 tests
PATHFAST™ D-Dimer	PF1051-K	60 tests
PATHFAST™ NTproBNP	PF1061-K	60 tests
PATHFAST™ hsCRP	PF1071-K	60 tests
REAGENT KITS FOR SEPSIS DIAGNOSTICS		
PATHFAST™ B·R·A·H·M·S PCT	PF1221-K	60 tests
PATHFAST™ B·R·A·H·M·S PCT Control	PF0221C	2 level, 1ml, 2 bottles
PATHFAST™ Presepsin	PF1201-K	60 tests
PATHFAST™ Presepsin Control	PF0201 C	2 level, 1ml, 2 bottles

References

[1] WHO, (2023): Tuberculosis: fact sheets. Geneva, Switzerland.
[2] Gagneux, S., (2018): Ecology and evolution of Mycobacterium tuberculosis. Nat Rev Microbiol., 16(4):202-213.
[3] WHO, (2022): Global tuberculosis report. Geneva, Switzerland.
[4] WHO, (2022): WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update. Geneva, Switzerland.
[5] Horne, D. J., et al., (2010): Sputum monitoring during tuberculosis treatment for predicting outcome: systematicreview and meta-analysis. Lancet Infect. Dis., 0(6):387-94.
[6] Venisse, A., (1993): Structural features of lipoarabinomannan from Mycobacterium bovis BCG. Determination of molecular mass by laser desorption mass spectrometry. J. Biol. Chem., 268(17):12401-11.
[7] Instruction for use (IFU) PATHFAST™ TB LAM Ag.

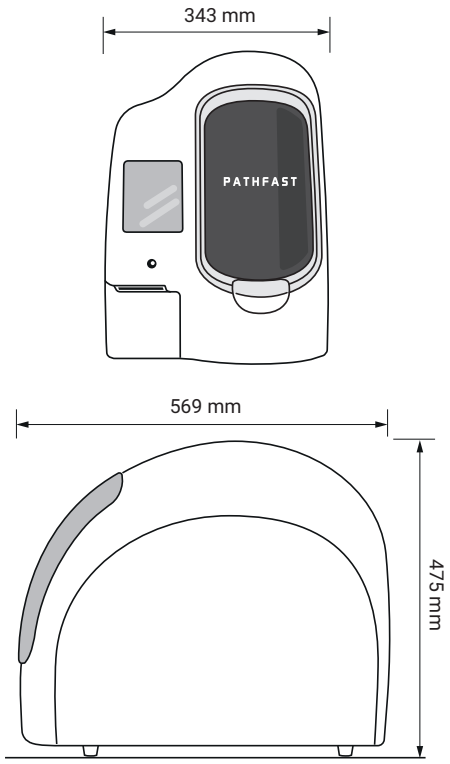
PATHFAST™

www.pathfast.eu

PATHFAST™ Technical Specifications

Instrument type	Desktop Immunoassay Analyzer
Throughput	Up to 6 samples or parameters per run
Measuring time	<17 minutes for 6 samples using emergency markers or PATHFAST™ Presepsin
Sampling material	Whole blood, plasma, serum
Measuring principle	Chemiluminescence enzyme immunoassay technology (CLEIA) and Magtration® technology.
Reaction temperature	37 °C
Sample volume	100 µl
Data storage	Patient data: 1000, QC data: 1800, CAL data: 300
Datatransfer	ASTM and Fixed standard
Weight	28 kg
El. requirements	100 - 240 V AC (50/60 Hz)
Power consumption	360 VA
Monitor/keyboard	LCD touch-screen
Printer	Integrated
PC	Integrated, Handheld Barcodereader included
Interface	RS-232C and Ethernet Port
Calibration	Factory calibration, 2-point calibration every 4 weeks
24-h operation (stand-by)	Recommended

PATHFAST™ Dimensions



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