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TECO®

Fast Cryptococcus neoformans Ag – Lateral Flow Assay

Instructions for use
English

CE

Catalogue No: TE 1085
UDI-DI 7640146270184

TE1085_AA-E_11/2024

TECOmedical AG

www.tecomedical.com

Symbol Description

Read electronic kit instructions

LOT

Lot number

Expiry date

Storage temperature

Not intended for self-testing
Or near-patient testing

Manufacturer

REF

TE 1085

UDI - DI

Unique Device Identifier

IVD

In Vitro Diagnostics

50

50 tests

Professional Use only
Not intended for self-testing or near-patient testing

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Any serious incident that has occurred in relation to this product shall be reported to TECOmedical AG and the competent authority of the Member State in which the user and/or the patient is established

Fast Cryptococcus neoformans Ag Lateral Flow Assay

CONT **Reagents and Materials Supplied:**

SYMBOL	DESCRIPTION	FORMAT
1	**Test cassette** Ready to use Cassette is for single use only DO NOT REUSE	50 bags (1 test cassette/bag)
C1	**Positive Control** Ready to use Range as indicated on data sheet	**1 x 2.0 mL**
C2	**Negative Control** Ready to use Range as indicated on data sheet	**1 x 2.0 mL**
	**eIFU indicator** Login address for electronic kit instructions	
	QR code on kit box lot-specific, for standard curve import	

Storage

Store the kit at 2–8℃ in a dark place. Do not freeze.

Intended Use

Fast Cryptococcus neoformans Ag Lateral Flow Assay is used for the detection of cryptococcal capsular polysaccharide antigen in human serum/cerebral spinal fluid (CSF), offering a diagnostic reference for cryptococcal meningitis infection.

Clinical Use

Cryptococcosis is a conditionally pathogenic deep fungal disease. The main *Cryptococcus* species causing human infection are *Cryptococcus neoformans* and *Cryptococcus gattii*, which quickly form thick pods and become more pathogenic after entering the body. It can infect any tissue and organ in the body, including the skin, lungs, and bones, most commonly the central nervous system, followed by the lungs and skin. The prevalence of cryptococcal infection has been reported to be about 5% to 10% in immunosuppressed patients and can be as high as 30% in AIDS patients, while in immunocompetent populations, the rate of cryptococcal infection is about 1 in 100,000. While traditional diagnostic methods include fungal culture and ink staining, the *Cryptococcus* capsular polysaccharide antigen test is a new indicator for the early diagnosis and therapeutic monitoring of Cryptococcal meningitis infections.

Limitations

- The *Fast* Cryptococcus neoformans Ag Lateral Flow Assay is a prescription-use laboratory assay that provides aid to the diagnosis of Cryptococcal meningitis infection.

- This product is intended for the qualitative detection of cryptococcal capsular polysaccharide antigen in human serum/cerebrospinal fluid (CSF) only and cannot be used for other samples.

- The test results are for reference only, and the separate test results should not be used as the sole basis for disease diagnosis.

- A positive result is only indicative of the presence of cryptococcal capsular polysaccharide antigen in the sample and cannot be used as a criterion for cryptococcal meningitis infection in the body. For diagnostic purposes, this test result should be used in conjunction with the clinical examination, medical history, and other findings

- A negative result does not exclude the possibility of cryptococcal meningitis infection as the product has certain detection limits.

References

[1] McFadden D, Zaragoza O, Casadevall A.
The capsular dynamics of *Cryptococcus* neoformans .
Trends Microbiol, 2006, 14（11）: 497-505

[2] Zaragoza O, Rodrigues M L, De Jesus , et al
The capsule of the fungal pathogen *Cryptococcus* neoformans.
Adv Appl Microbiol, 2009, 68 : 133-216.

[3] Chinese Journal of Mycology, Editorial Board.
Expert consensus on the diagnosis and treatment of cryptococcal infections.
Chinese Journal of Mycology, 2010, 5(2):65-68+86

[4] Wang Luxia, Shi Lingbo, Chen Wanshan et al
Early diagnosis of cryptococcal polysaccharide antigen by latex agglutination in cryptococcal meningitis and cryptococcal pneumonia.
Laboratory Medicine, 2008(1):55-57.

Assay Principle

This product uses double antibody sandwich fluorescence immunochromatography to detect cryptococcal capsular polysaccharide antigen in human serum/cerebral spinal fluid (CSF). The cryptococcal antibody labeled with fluorescent microspheres and the chicken IgY antibody labeled with fluorescent microspheres are coated on a fluorescent pad, and the test line (T) and quality control line (C) are coated with cryptococcal antibody and anti-chicken IgY antibody, respectively.

– Positive samples: the cryptococcal capsular polysaccharides will combine with the fluorescent microsphere-labeled cryptococcal antibody to form a complex and migrate further along on the nitrocellulose membrane; the cryptococcal antibody coated on the test line (T) interact with the above complexes and display a fluorescent band; the fluorescently labeled chicken IgY antibodies display a fluorescent band on the quality control line (C) in combination with the anti-chicken IgY antibody.
- Negative samples: no immune complex will be formed, no band will appear at the test line (T), and only a band will appear at the quality control line (C). The control line (C) should always display a fluorescent band during the test, which is the criteria to check if the test works correctly also as an internal control standard.

Read the detection area with a fluorescence immunoassay analyzer to get a fluorescence signal, interpreting the antigen concentration.

Materials Required and not Supplied

- Pipettes 100 µL – 1000 µL
- Polypropylene centrifuge tubes 1.5 mL
- Vortex mixer
- Timer
- Fluorescence Immunoassay Analyzer: Model FIC-Q100N

Warnings and precautions

This kit is intended for in vitro use by professional persons only.

Follow the instructions carefully.

Observe expiry dates stated on the labels. Use reagents within 30 minutes after opening of the kit. Refer to" Materials Safety Data Sheet" for more detailed safety information.

Material of animal origin used in the preparation of this kit has been obtained from animals certified as healthy, but these materials should be handled as potentially infectious.

TECOmedical AG is not liable for loss or harm caused by non-observance of the kit instructions.

1. For in vitro diagnostic use.
2. Treat all specimen samples as potentially biohazardous material.
   Follow General Precautions when handling the contents of this kit and any patient samples.
3. Disposal of containers and unused contents should be done in accordance with federal and local regulatory requirements.
4. Use the supplied components as an integral unit prior to the expiration date indicated on the package label.
5. Store assay components as indicated.

Preparation and stability of samples

Collect samples according to standard laboratory procedures. Avoid cross - contamination among samples. Sample labeling should be clear and correct without mistake. Avoid using samples with severe hemolysis and high viscosity.

Sample Type

The assay is validated for serum and Cerebrospinal Fluid (CSF).

Sample transportation

Sample transportation in sealed tubes, free from air contact and should comply with national biosafety requirements

Stability

Maximum 72 hours at 2-8°C

Maximum 15 months at -20°C
Maximum 5 freeze/thaw cycles

Assay procedure

All samples are assayed in singlicate. Test should be performed as quickly as possible. Long-time exposure of test to air and moisture will cause invalid results performing the assay.

Allow all components to stand at room temperature (20–25°C). Test cassette is recommended to be used within 0.5 hour after opening the bag.

Prepare the FIC-Q100N fluorescence immunoassay analyzer according to the Operational Guide.
Note: Scan the QR code on the box to import the correct standard curves.

TEST PROCEDURE

- Carefully refer to the instruction for use before performing the test.
- Before testing, ensure that all kit components and samples are at room temperature.
- Place test cassettes on a flat and clean bench; slowly dispense 100 µL of sample or control into the sample pad well labelled "**S**".
- Read and record the results with the fluorescence immunoassay analyzer after 20 minutes (No longer than 25 minutes, as abnormal results may occur).

QUALITY CONTROL

- The fluorescence immunoassay analyzer will calculate the signal of Control Line (C) automatically. If it fails, it will show "Invalid result". The test needs to be repeated.
- Recommendations are at least one control measurement per kit, or at least as a monthly run with controls.

Interpretation of results

The following cut off limits were identified in the population studied to obtain the performance characteristics; however, each laboratory may wish to establish their own cut off values and negative and positive interpretation with their patient population:

- Concentration value ≥0.5 ng/mL are considered to be positive for cryptococcal meningitis.
  Note: For all positive patients, it is recommended that a new aliquot of the same sample (serum/ cerebrospinal fluid) be repeated.
- Concentration value <0.5 ng/mL are considered to be negative for cryptococcal meningitis.
  Note: A negative result may indicate that the patient's result is below the detectable level of the assay. Negative results do not rule out the diagnosis of cryptococcal meningitis. Repeat testing is recommended if the result is negative, but the disease is suspected.
- This assay is intended to be used as an aid in the diagnosis of cryptococcal meningitis. Positive results obtained with this assay should be considered in conjunction with other clinical examination, medical history and other findings

Test Performance

Diagnostic Sensitivity and Specificity

The *Fast* Cryptococcus neoformans Ag Lateral Flow Assay uses a clinical research method that compares the assessment reagents with clinical diagnosis results on the same serum / CSF samples and compares the consistency of the results. The clinical agreement study evaluated a total of 310 serum and 350 CSF samples**.**
The diagnostic sensitivity of the CSF is 100% and the diagnostic specificity is 100%; the diagnostic sensitivity of the serum is 97% and the diagnostic specificity is 98.10%.

Test reagent results	Clinical diagnosis for CSF		
	Positive	Negative	Total
Positive	150	0	150
Negative	0	200	200
Total	150	200	350
Diagnostic sensitivity	150/150 = 100.0% (95% CI: 97.5% - 100.0%)		
Diagnostic specificity	200/200 = 100.0% (95% CI: 98.1% - 100.0%)		
Overall Percent Agreement	(150+200)/350 = 100.0% (95% CI: 98.9% - 100.0%)		

Test reagent results	Clinical diagnosis for serum		
	Positive	Negative	Total
Positive	97	4	101
Negative	3	206	209
Total	100	210	310
Diagnostic sensitivity	97/100 = 97.0% (95% CI: 97.5% - 99.0%)		
Diagnostic specificity	206/210 = 98.1% (95% CI: 95.2% - 99.3%)		
Overall Percent Agreement	(97+206)/310 = 97.7% (95% CI: 95.4% - 98.9%)		

Sensitivity

To evaluate the lowest limit of detection (LOD), first the limit of blank (LOB) was determined: 2 blank references (sample diluent) were tested with each of 3 batches of kits for 3 days each, with 2 replicates per day for each of the 3 instruments (2 blank references x 3 instruments x 3 days x 2 replicates/day x 3 batches = 108 results).

The LOB was calculated to be 0.08 ng/mL and five low-value reference products (for each serum and cerebrospinal fluid) were tested with 3 batches of kits, for 3 days, and 2 replicates were done per sample per day (5 reference product × 3 days × 2 replicates/day × 3 instruments = 90 results/batch). The LOD value of the three batches of kits was 0.100 ng/mL, so LOD was set at 0.10 ng/mL.

Precision

(Intra and Inter assays)

4 clinical serum samples and 4 clinical cerebrospinal fluid samples (1 negative sample, 1 critical-positive sample, 1 medium-positive sample, 1 strong-positive sample) were tested on 3 different instruments, 2 operators for each instrument (6 operators in total), 3 different batches for 5 days and 5 replicates per sample per day (3 instruments x 3 kit batches x 5 days x 5 replicates/day = 225 results per sample) in order to obtain within lot and between lot precision.

The CVs of repeatability, indoor precision, and inter-batch precision for positive and strongly positive samples in the three instruments were all less than 15% which meets requirements (repeatability CV $\leq$ 15%, inter-batch CV $\leq$ 20%).

The positive detection rate of critical positive samples is $\geq$ 95%, the negative detection rate for negative samples was 100%.

Interferences

Controlled test of potential interfering substances showed that there was no interference in the under-mentioned concentrations.

Substance	Concentration
Hemoglobin	≤5 mg/mL
Bilirubin	<300 mg/L
Cholesterol	<10 mg/mL
Triglyceride	<7.5 mmol/L
Voriconazole	40 µg/mL
Amphotericin b	1 mg/mL
Caspofungin	0.27 mg/mL

Rheumatoid factor, anti-nuclear antibody, anti-double-stranded DNA antibody did not interfere with the test results.

Cross reaction

No false positive Cryptococcus Neoformans Ag test results were observed on 10 specimens from each of the following disease states or specific conditions, respectively:

Cross reactant / Interfering substance	Result
Positive Candida antigen	Negative
Positive Aspergillus antigen	Negative
Syphilis	Negative
Toxoplasma gondii	Negative
Rubella	Negative
Cytomegalovirus	Negative

Hook effect

The Glucuronoxylomannan antigen, at a concentration of 50 000 ng/mL, was diluted to the following concentrations of 10 000, 5 000, 1 000, 500, 250, 100 and 50 ng/mL then tested in triplicates in three batches of reagents to check whether there is a hook effect. Fluorescence intensities are shown in relative fluorescence units (RFU).

Capsular Polysaccharide concentration (ng/mL)	Batch Nr 200201 Average RFU	Batch Nr 200202 Average RFU	Batch Nr 200203 Average RFU
50	67459	59518	70597
100	107876	109681	109096
200	168005	160350	164392
500	233128	231455	235703
100	267278	262600	262155
500	313078	307249	321293
10000	324066	323552	334298
50000	331746	350182	337750

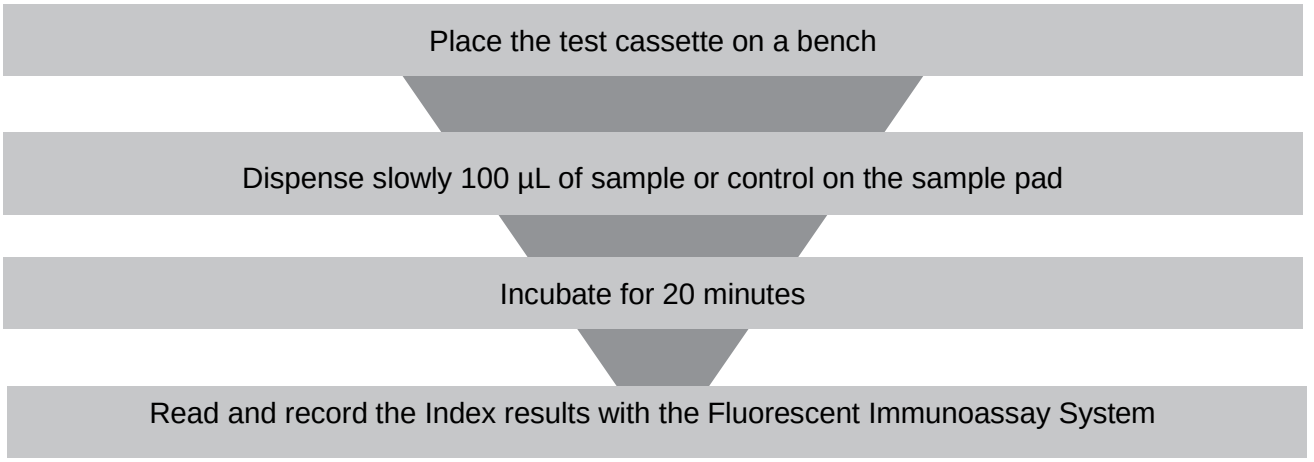
It can be seen from the above experimental results that there is no hook effect up to the concentration of Capsular polysaccharide antigen of 50 000 ng/mL.

Fast Cryptococcus neoformans Ag Lateral Flow Assay

Assay Procedure – Quick Guide

Bring samples and components to room temperature (20-25°C) for 30 min and prepare the FIC-Q100N according to the Operational Guide.
Mix the samples well.

Test Procedure:



Please read Kit instruction before using the Quick Guide