

Overview

**Useful For**  
Diagnosis of infection with *Cryptococcus* species

Reflex Tests

| Test Id | Reporting Name                 | Available Separately | Always Performed |
|---------|--------------------------------|----------------------|------------------|
| PLFAT   | Cryptococcus Ag Titer, LFA, PF | No                   | No               |

**Testing Algorithm**  
If this screen is positive, the antigen titer will be performed at an additional charge.

**Highlights**  
This test can be used as an adjunct for diagnosis of pulmonary infection with *Cryptococcus* species. Positive results are indicative of infection; however, cryptococcal antigen may remain detectable for prolonged periods of time following disease resolution.

**Method Name**  
Lateral Flow Assay (LFA)

**NY State Available**  
Yes

Specimen

**Specimen Type**  
Pleural Fluid

**Additional Testing Requirements**  
Pleural fluid testing for cryptococcal antigen should also be submitted for routine fungal culture. Order FGEN / Fungal Culture, Routine.

**Specimen Required**  
**Container/Tube:** Sterile vial  
**Specimen Volume:** 0.5 mL

**Forms**  
If not ordering electronically, complete, print, and send [Infectious Disease Serology Test Request](#) (T916) with the

specimen.

Specimen Minimum Volume

0.25

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

| Specimen Type | Temperature              | Time    | Special Container |
|---------------|--------------------------|---------|-------------------|
| Pleural Fluid | Refrigerated (preferred) | 21 days |                   |
|               | Frozen                   | 30 days |                   |

Clinical & Interpretive

Clinical Information

Cryptococcosis is an invasive fungal infection caused by *Cryptococcus neoformans* or *Cryptococcus gattii*. *C neoformans* has been isolated from several sites in nature, particularly weathered pigeon droppings. *C gattii* was previously associated with tropical and subtropical regions only; however, more recently this organism has also been found to be endemic in British Columbia, along the Pacific Northwest, and in the Southeastern United States.

Infection is usually acquired via the pulmonary route. Patients are often unaware of any exposure history. Approximately half of the patients with symptomatic disease have a predisposing immunosuppressive condition such as AIDS, steroid therapy, lymphoma, or sarcoidosis. Symptoms may include fever, headache, dizziness, ataxia, somnolence, and cough. While the majority of *C neoformans* infections occur in immunocompromised patient populations, *C gattii* has a higher predilection for infection of healthy individuals.

In addition to the lungs, cryptococcal infections frequently involve the central nervous system (CNS), particularly in patients infected with HIV. Mortality among patients with CNS cryptococcosis may approach 25% despite antibiotic therapy. Untreated CNS cryptococcosis is invariably fatal. Disseminated disease may affect any organ system and usually occurs in immunosuppressed individuals.

Reference Values

Negative

Interpretation

The presence of cryptococcal antigen in pleural fluid is indicative of infection with *Cryptococcus* species.

Monitoring cryptococcal antigen levels as a means to determine response to therapy is discouraged, as antigen levels may persist despite adequate treatment and disease resolution.

A negative result indicates lack of infection; however, rare cases of false-negative results have been reported. Fungal

culture should always be ordered alongside antigen testing.

Cautions

A negative result does not preclude diagnosis of cryptococcal infection, particularly if the patient is at risk for cryptococcosis and shows symptoms consistent with this disease.

False-positive results may occur in patients with trichosporonosis or infection with *Capnocytophaga* species.

Supportive Data

Sixty pleural fluid samples, including 30 specimens collected from patients without microbiologic testing ordered and 30 specimens spiked at various dilutions with *Cryptococcus* antigen (CrAg)-positive specimens, were evaluated by both the IMMY CrAg lateral flow assay (LFA) and the Meridian *Cryptococcus* antigen latex agglutination (CALAS) assays. The results are summarized in Table 1.

Table 1. Comparison of the IMMY CrAg LFA and the Meridian CALAS assays

|                       |              | Meridian<br>CALAS<br>result |              | Positive<br>agreement<br>(95% CI) | Negativ<br>e<br>agreement<br>(95% CI) | Overall<br>agreement<br>(95%<br>CI) |
|-----------------------|--------------|-----------------------------|--------------|-----------------------------------|---------------------------------------|-------------------------------------|
|                       |              | Posi<br>tive                | Neg<br>ative | 81%<br>(65.4-90.8)                | 100%<br>(86.5-100)                    | 89.5%<br>(79.6-95.1)                |
| IMMY<br>LFA<br>result | Posi<br>tive | 23                          | 7(a)         |                                   |                                       |                                     |
|                       | Neg<br>ative | 0                           | 30           |                                   |                                       |                                     |

(a)Details for these 7 discordant samples are provided in Table 2. All 7 specimens were pleural fluid spiked with CrAg-positive material and were expected to be positive by both assays.

Table 2. Comparison of discordant specimens between the IMMY CrAg LFA and Meridian CALAS Assays

| Sa<br>mpl<br>e | Meridian<br>qualitative<br>result | LFA<br>qualitativ<br>e result | LFA<br>quantitativ<br>e result |
|----------------|-----------------------------------|-------------------------------|--------------------------------|
| 1              | Negative                          | Positive                      | 1:10                           |
| 2              | Negative                          | Positive                      | 1:2                            |
| 3              | Negative                          | Positive                      | 1:10                           |
| 4              | Negative                          | Positive                      | 1:2                            |
| 5              | Negative                          | Positive                      | 1:5                            |
| 6              | Negative                          | Positive                      | 1:160                          |
| 7              | Negative                          | Positive                      | 1:80                           |

The IMMY CrAg LFA has been shown to be significantly more sensitive in both serum and CSF specimens in prior studies.(1) Our findings in pleural fluid are consistent with these previous studies.

The reportable range for this assay is 1:2 to 1:2560 and the reference range is negative. Cross-reactivity was not

observed with specimens positive for *Histoplasma capsulatum* or *Aspergillus* species antigens.

### Clinical Reference

1. Binnicker MJ, Jespersen DJ, Bestrom JE, Rollins LO: Comparison of four assays for the detection of cryptococcal antigen. Clin Vaccine Immunol. 2012 Dec;19(12):1988-1990
2. Howell SA, Hazen KC, Brandt ME: *Candida, cryptococcus*, and other yeast of medical importance. In: Manual of Clinical Microbiology. 11th ed. ASM Press; 2015:1984-2014

### Performance

### Method Description

The *Cryptococcus* antigen (CrAg) lateral flow assay is a sandwich immunochromatographic assay. Specimens and diluent are added to a test tube and the lateral flow device is added. The test uses specimen wicking to capture gold-conjugated, anti-cryptococcal antigen monoclonal antibodies and gold-conjugated control antibodies deposited on the test membrane. If cryptococcal antigen is present in the specimen, it binds to the gold-conjugated anti-cryptococcal antigen antibodies. This complex wicks up the membrane and interacts with the test line, which has immobilized anti-cryptococcal antigen monoclonal antibodies. The antigen-antibody complex forms a sandwich at the test line causing a visible line to form. A valid test shows a visible line at the control line. Positive test results create 2 lines (control and specimen), while negative results form only the control line.(Package insert: CrAg Lateral Flow Assay. IMMY; Rev 06/27/2019)

### PDF Report

No

### Day(s) Performed

Monday through Sunday

### Report Available

Same day/1 to 2 days

### Specimen Retention Time

7 days

### Performing Laboratory Location

Rochester

### Fees & Codes

#### Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.

- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

Test Classification

This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

87899-Cryptococcus Ag Screen, LFA, PF  
87899-Cryptococcus Ag Titer, LFA, PF (if appropriate)

LOINC® Information

| Test ID | Test Order Name                 | Order LOINC® Value |
|---------|---------------------------------|--------------------|
| PLFA    | Cryptococcus Ag Screen, LFA, PF | 29533-7            |

| Result ID | Test Result Name                | Result LOINC® Value |
|-----------|---------------------------------|---------------------|
| 42396     | Cryptococcus Ag Screen, LFA, PF | 29533-7             |