

## Overview

### Useful For

Diagnosis of infection with *Cryptococcus* species

### 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.

### 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.

### 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 a [Microbiology Test Request](#) (T244) 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 and 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 CALAS result		Positive agreement (95% CI)	Negative agreement (95% CI)	Overall agreement (95% CI)
		Positive	Negative			
IMMY LFA Result	Positive	23	7(a)	81% (65.4-90.8)	100% (86.5-100)	89.5% (79.6-95.1)
	Negative	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

Sample	Meridian qualitative result	LFA qualitative result	LFA quantitative 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. J Clin Micro. 2012;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 2012)

**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 and 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 Regional Manager. 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 U.S. 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

