

## Overview

### Useful For

Diagnosis of coccidioidomycosis using serum specimens

### Method Name

Complement Fixation (CF)/Immunodiffusion (ID)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Ordering Guidance

This test is a confirmatory assay for positive screening tests (ie, enzyme immunoassay).

The recommended test to evaluate for possible *Coccidioides* infection is COXIS / *Coccidioides* Antibody Screen with Reflex, Serum.

### Specimen Required

**Supplies:** Sarstedt Aliquot Tube 5 mL (T914)

**Collection Container/Tube:**

**Preferred:** Serum gel

**Acceptable:** Red top

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 1.8 mL

**Collection Instructions:** Centrifuge and aliquot serum into plastic vial.

### Forms

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

### Specimen Minimum Volume

1.2 mL

### Reject Due To

Gross	Reject
-------	--------

hemolysis	
Gross lipemia	Reject

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	14 days	

### Clinical & Interpretive

#### Clinical Information

Coccidioidomycosis (valley fever, San Joaquin Valley fever) is a fungal infection found in the Southwestern US, Central America, and South America. It is acquired by inhalation of arthroconidia of *Coccidioides immitis/posadasii*. Usually, it is a mild, self-limiting pulmonary infection. Less commonly, chronic pneumonia may occur, progressing to fibronodular, cavitary disease. A rash often develops within a day or 2, followed by erythema nodosum or multiforme and accompanying arthralgias. About 2 weeks after exposure, symptomatic patients develop fever, cough, malaise, and anorexia; chest pain is often severe. Coccidioidomycosis may disseminate beyond the lungs to involve multiple organs, including the meninges.

IgG antibody is detected by the complement-fixation tests. Precipitating antibodies (IgM and IgG) are detected by immunodiffusion. They are rarely found in cerebrospinal fluid; however, their presence is associated with meningitis. Chronic coccidioidal pulmonary cavities are often accompanied by IgG and IgM precipitating antibodies.

Serologic testing for coccidioidomycosis should be considered when patients exhibit symptoms of pulmonary or meningeal infection and have lived or traveled in areas where *C immitis/posadasii* is endemic. Any history of exposure to the organism or travel cannot be overemphasized when a diagnosis of coccidioidomycosis is being considered.

#### Reference Values

Complement Fixation: Negative

If positive, results are titered.

Immunodiffusion: Negative

Results are reported as positive, negative, or equivocal.

#### Interpretation

Complement Fixation:

Titer results of 1:2 or higher may suggest active disease; however, titers may persist for months after infection has resolved. Increasing complement fixation (CF) titer results in serial specimens are considered diagnostic of active disease.

Immunodiffusion:

The presence of IgM antibodies may be detectable within 2 weeks after the onset of symptoms; however, the antibody

---

may be detected longer than 6 months after infection.

The presence of IgG antibodies parallels the CF antibodies and may suggest an active or a recent asymptomatic infection with *Coccidioides immitis/posadasii*; however, antibodies may persist after the infection has resolved.

An equivocal result (a band of nonidentity) cannot be interpreted as significant for a specific diagnosis. However, this may be an indication that a patient should be followed serologically.

Over 90% of primary symptomatic cases will be detected by combined immunodiffusion and CF testing.

### **Cautions**

Antibodies (both IgM and IgG) may be present after the infection has resolved.

### **Clinical Reference**

1. McHardy IH, Barker B, Thompson GR 3rd. Review of clinical and laboratory diagnostics for coccidioidomycosis. *J Clin Microbiol.* 2023;61(5):e0158122. doi:10.1128/jcm.01581-22
2. Ramanan P, Wengenack NL, Theel ES. Laboratory diagnosis for fungal infections: a review of current and future diagnostic assays. *Clin Chest Med.* 2017;38(3):535-554. doi:10.1016/j.ccm.2017.04.013

## **Performance**

### **Method Description**

#### Complement Fixation:

Antibody to coccidioidin in the patient's serum is quantitated by complement fixation (CF). The CF test is a 2-stage test based on the ability of antigen-antibody complexes to bind complement (C'). In the first stage, antigen and antibody combine and fix C'. The second stage is an indicator system in which sheep erythrocytes, sensitized by rabbit anti-sheep red cell antibody (hemolysin), are used to demonstrate the presence of unfixed C'. If the patient's serum contains C'-fixing antibody that reacts with the specific antigen (a positive reaction), C' will be fixed and excess C' will not be available to react with and lyse the sensitized sheep erythrocytes. If no antigen-antibody reaction occurs (a negative reaction), C' will be available to lyse the sheep erythrocytes. The CF titer is determined by the greatest dilution of serum (antibody) in which the sheep erythrocytes are not lysed. (Kaufman L, Kovacs JA, Reiss E. *Immunomycology*. In: Rose NR, de Macario ED, Folds JD, Lane HC, Nakamura RM, eds. *Manual of Clinical Laboratory Immunology*. 5th ed. ASM Press; 1997:591-592; Pappagianis D, Zimmer BL. *Serology of coccidioidomycosis*. *Clin Microbiol Rev.* 1990;3:247-268; Ramanan P, Wengenack NL, Theel ES. *Laboratory diagnosis for fungal infections. A review of current and future diagnostic assays*. *Clin Chest Med.* 2017;38[3]:535-554. doi:10.1016/j.ccm.2017.04.013)

#### Immunodiffusion:

Immunodiffusion (ID) is a qualitative test employed for the detection of precipitating antibodies present in the serum. Soluble antigens of the fungus are placed in wells of an agarose gel filled Petri dish and the patient's serum and a control (positive) serum are placed in adjoining wells. If present, specific precipitate antibody will form precipitin lines between the wells. Their comparison to the control serum establishes the results. When performing the ID test, only precipitin bands of identity with the reference bands are significant. (Kaufman L, Kovacs JA, Reiss E. *Immunomycology*. In: Rose NR,

Macario ED, Folds JD, Lane HC, Nakamura RM, eds. Manual of Clinical Laboratory Immunology. 5th ed. ASM Press; 1997:591-593; Pappagianis D, Zimmer BL. Serology of coccidioidomycosis. Clin Microbiol Rev. 1990;3[3]:247-268. doi:10.1128/CMR.3.3.247; Ramanan P, Wengenack NL, Theel ES. Laboratory diagnosis for fungal infections. A review of current and future diagnostic assays. Clin Chest Med. 2017;38[3]:535-554)

**PDF Report**

No

**Day(s) Performed**

Monday through Friday

**Report Available**

4 to 7 days

**Specimen Retention Time**

14 days

**Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Superior Drive

**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 cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

**CPT Code Information**

86635 x 3

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
SCOC	Coccidioides Ab, CompF/ImmDiff, S	87435-4
Result ID	Test Result Name	Result LOINC® Value
8295	Coccidioides Ab, CompF, S	In Process
21649	Coccidioides, IgG, ImmDiff, S	62459-3

21648

Coccidioides, IgM, ImmDiff, S

62458-5