MAYO CLINIC LABORATORIES

# Test Definition: SFUNG

1,3-Beta-D-Glucan (Fungitell), Serum

## Overview

### Useful For

Aiding in the diagnosis of invasive fungal infections caused by various fungi, including *Aspergillus* species, *Fusarium* species, *Candida* species, and *Pneumocystis jirovecii*, among others

### Highlights

The Fungitell assay may aid in identifying deep-seated fungal infections or fungemia in patients with symptoms of, or with a medical condition predisposing the patient to, an invasive fungal infection.

The Fungitell assay detects circulating (1,3)-beta-D-glucan in serum. This antigen is released from many invasive fungal organisms (eg, *Candida* species, *Aspergillus* species, *Fusarium* species, and *Pneumocystis jirovecii*).

### Method Name

Protease Zymogen-Based Colorimetric Assay

### NY State Available

Yes

## Specimen

### Specimen Type

Serum SST

### Specimen Required

**Container/Tube:** Serum gel (red top tube is **not acceptable**)

**Specimen Volume:** 1 mL

**Collection Instructions:**

1. Avoid exposure of specimen to atmosphere to prevent environmental contamination of the sample.
2. Centrifuge and send entire specimen in original collection tube. **Do not aliquot or open tube**.

### Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-General Request (T239)

-Microbiology Test Request (T244)

-Kidney Transplant Test Request

### Specimen Minimum Volume

0.5 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | Reject |
| Gross icterus | Reject |
| Finger/heel sticks | Reject |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Serum SST | Refrigerated (preferred) | 14 days | SERUM GEL TUBE |
| | Frozen | 30 days | SERUM GEL TUBE |

## Clinical & Interpretive

### Clinical Information

Invasive fungal infections (IFI) due to opportunistic fungal pathogens are a significant cause of morbidity and mortality, particularly among patients who are significantly immunosuppressed, including hematopoietic stem cell transplant recipients, solid organ transplant recipients, and those with hematologic or immune deficiencies. Patient recovery and survival following an IFI are directly related to the timely clinical recognition and prompt administration of antifungal therapy. Laboratory diagnosis of IFI is largely based on direct microscopic examination of patient specimens, histopathologic examination of tissue biopsies, isolation of fungi via culture, and, more recently, through molecular methods. However, these techniques commonly require invasive sample collection methods (eg, biopsy, bronchoalveolar lavage), which may be contraindicated in certain patients. Additionally, both microscopy and culture are frequently insensitive, with prior studies showing the sensitivity of culture for invasive *Aspergillus* infections ranges from 40% to 85%, and some fungi require prolonged incubation times, limiting the utility of culture in the acute patient setting. Due to these limitations, use of fungal biomarkers, including detection of (1,3)-beta-D-glucan (BDG), have emerged as useful adjunct tests available for detection of IFI.

(1,3)-beta-D-glucan is found in the cell walls of most fungi (eg, *Candida, Aspergillus, Fusarium, Pneumocystis jirovecii*) with the notable exception of *Cryptococcus* species, *Blastomyces* species, and the Mucorales (eg, *Lichtheimia, Mucor, Rhizopus*), which either lack BDG entirely or produce it in very low amounts. Elevated serum BDG levels have been associated with the presence of a fungal infection. The BDG levels may be detected prior to the development of clinical symptoms and before isolation or identification of the fungal organism via routine methods. The sensitivity and specificity of BDG detection in patients with proven or probable IFI range from 64% to 93% and 87% to 100%, respectively, among different studies.

Importantly, the BDG assay should not be used alone to diagnose an IFI but rather in conjunction with careful evaluation of patient risk factors for infection, other laboratory testing, and radiologic findings.

### Reference Values

Fungitell quantitative value:
<60 pg/mL

Fungitell qualitative result:
Negative

Reference values apply to all ages.

## Interpretation

The Fungitell assay should be used in conjunction with other diagnostic procedures, such as routine bacterial/fungal cultures, histologic examination of biopsy material, and radiologic studies.

Positive:
(1,3)-Beta-D-glucan detected. A single positive result should be interpreted with caution and correlated alongside consideration of patient risk for invasive fungal disease, results of routine laboratory tests (eg, bacterial and fungal culture, histopathologic evaluation), and radiologic findings. Repeat testing on a new sample (collected in 3-4 days) is recommended as serially positive samples are associated with a higher diagnostic odds ratio for invasive fungal infection compared to a single positive result.

False-positive results may occur in patients who have recently (in the past 3-4 days) undergone hemodialysis, treatment with certain fractionated blood products (eg, serum albumin, immunoglobulins), or those who have had significant exposure to glucan-containing gauze during surgery.

Indeterminate:
Repeat testing on a new sample is recommended in patients at risk for an invasive fungal infection.

Negative:
No (1,3)-Beta-D-glucan detected.

This assay does not detect certain fungi, including *Cryptococcus* species, which produce very low levels of (1,3)-beta-D-glucan (BDG) and the Mucorales (eg, *Lichtheimia, Mucor*, and *Rhizopus*), which are not known to produce BDG. Additionally, the yeast phase of *Blastomyces dermatitidis* produces little BDG and may not be detected by this assay.

## Cautions

(1, 3)-Beta-D-glucan (BDG) is not present in the Mucorales (eg, *Lichtheimia*, *Mucor*, *Rhizopus*), *Cryptococcus* species, or *Blastomyces* species. Therefore, invasive fungal infection with any of these agents will lead to a negative BDG result.

BDG results should be interpreted alongside other diagnostic testing results, including culture, molecular assays, or serology.

False-positive BDG results have been documented in patients having undergone recent hemodialysis, those that have received certain fractionated blood products (eg, albumin, immunoglobulins), and those who have had exposure to high amounts of glucan-containing gauze during surgery. BDG levels normalize approximately 3 to 4 days following these events.

Single time-point testing with the BDG assay is associated with limited clinical sensitivity and specificity. Serial testing, at least 2 times per week, is associated with higher diagnostic odds ratio (DOR 112) for the presence of an invasive fungal infection in an at-risk patient compared to single time-point positive result (DOR 16).

The BDG assay does not identify or indicate the presence of a specific fungal organism.

Serial testing to document BDG levels may be used to monitor disease progression and response to therapy; however, data on the clinical utility and accuracy of this practice is limited.

### Clinical Reference

Ramanan P, Wengenack NL, Theel ES. Laboratory diagnostics for fungal infections: a review of current and future diagnostic assays. Clin Chest Med. 2017;38(3):535-554

## Performance

### Method Description

The Fungitell assay measures levels of (1,3)-beta-D-glucan (BDG). The assay is based upon a modification of the limulus amebocyte lysate pathway. The Fungitell reagent is modified to eliminate factor C and, thus, to only react to BDG through the factor G-mediated side of the pathway. BDG activates factor G, a serine protease zymogen. The activated factor G converts the inactive proclotting enzyme to the active clotting enzyme, which in turn cleaves pNA from the chromogenic peptide substrate, Boc-Leu-Gly-Arg-pNA, creating a chromophore that absorbs at 405 nm. The Fungitell kinetic assay is based upon the determination of the rate of optical density increase produced by a sample. This rate is interpreted against a standard curve to produce estimates of BDG concentration in the sample.(Package insert: Assay for [(1,3]-Beta-D-Glucan in Serum. Associates of Cape Cod Inc; 06/13/2023)

### PDF Report

No

### Day(s) Performed

Monday through Friday, Sunday

### Report Available

1 to 2 days

### Specimen Retention Time

2 weeks

### 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

87449

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| SFUNG | (1, 3) Beta-D-Glucan (Fungitell), S | 42176-8 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 603615 | Fungitell Quantitative Value | 42176-8 |
| 603616 | Fungitell Qualitative Result | 93812-6 |