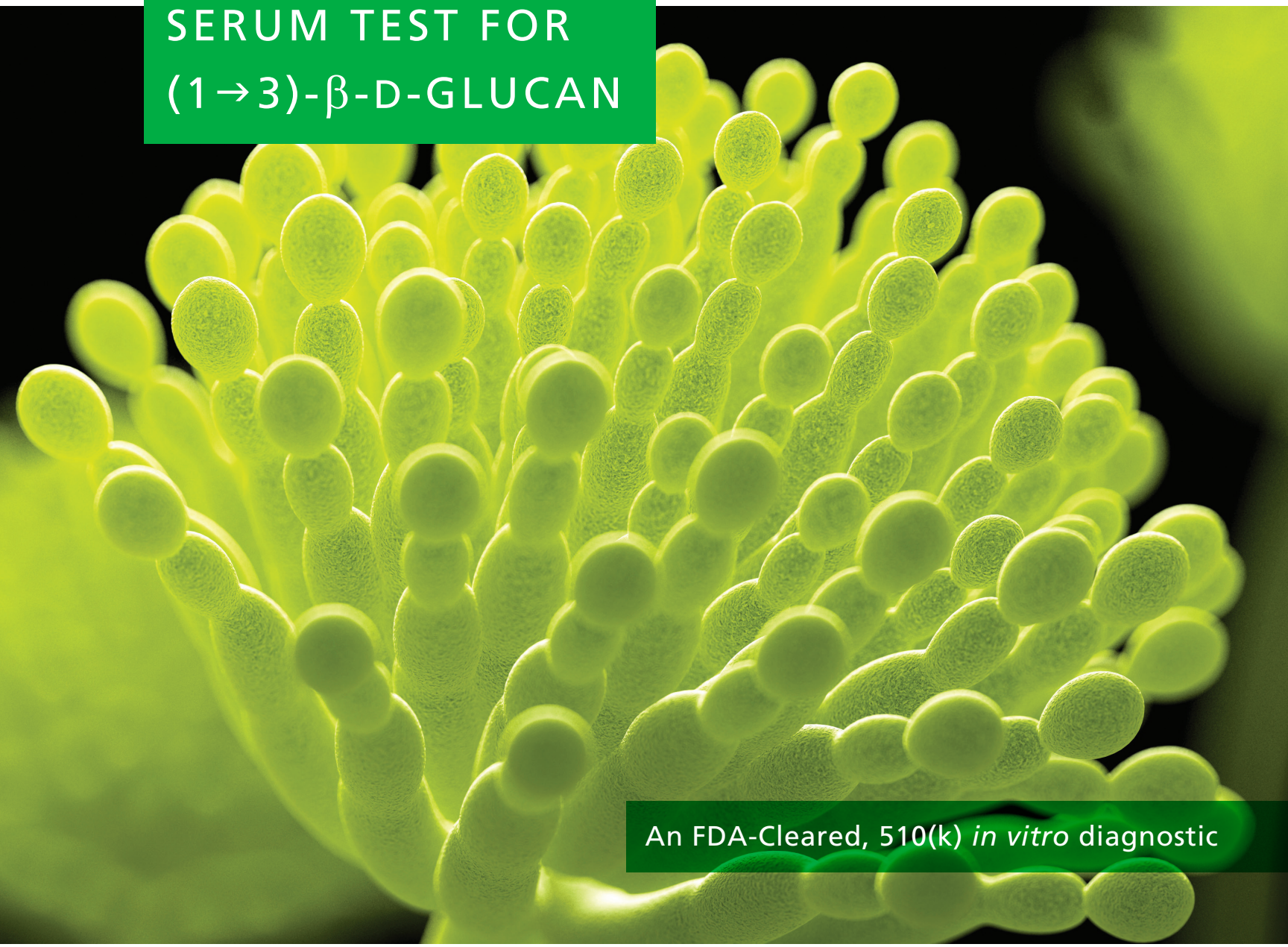
Fungitell®
(1→3)-β-D-Glucan Assay

FUNGITELL® ASSAY SERUM TEST FOR (1→3)-β-D-GLUCAN



An FDA-Cleared, 510(k) *in vitro* diagnostic

The Gold Standard in Rapid Screening For Invasive Fungal Infection (IFI)

Fungitell® is the first and the **only FDA-cleared and CE marked** rapid *in vitro* diagnostic screening test for IFI (including *Candida, Aspergillus* and *Pneumocystis*) that detects (1→3)-β-D-Glucan in serum.

CE nsai ISO 13485:2003 MEDICAL DEVICES

Invasive fungal infection: *More aggressive medical care, including immunosuppressive therapy and ICU care has greatly increased the population of patients at risk of invasive fungal infection (IFI). There are an estimated 40-60 thousand invasive fungal infections in the USA annually[1]. Candidemia represents the 4th leading cause of nosocomial blood stream infection and the 3rd most common ICU bloodstream infection[2].*

The low sensitivity and relatively long incubation times of microbial culture, the most widely used diagnostic technique, has resulted in a need for faster methods with greater sensitivity. With its high sensitivity and rapid availability of results, the demand for Fungitell® has increased steadily since its clearance by the FDA in 2004.

Early diagnosis and treatment have been shown to have increased survival rates in Candidal Shock[3]

Delay in Therapy

Administration (Hr):	*Survival*
0-2	*~ 82%*
2-6	*~ 65%*
6-12	*~ 17%*
12-24	*~ 9%*
24-72	*~ 8%*

FUNGAL TRENDS & STATISTICS

ASSAY
FOR INVASIVE FUNGAL INFECTION

Why Test For (1→3)-β-D-Glucan

Most pathogenic fungi* have (1→3)-β-D-Glucan in their cell walls and minute, but detectable quantities are released into the circulation during infection. Detection of elevated levels of (1→3)-β-D-Glucan is an aid to the presumptive diagnosis of invasive fungal infection (IFI) in at risk patients.

Multiple studies[4,5,6,7,8] have shown glucan to become elevated well in advance of conventional clinical signs and symptoms. The early diagnosis of and administration of therapy for invasive fungal infection is associated with improved clinical outcome; delayed diagnosis and therapy is associated with increased mortality[9]. Conversely, the elevated morbidity and mortality associated with invasive fungal infection drives potentially inappropriate systemic antifungal therapy. Research studies have demonstrated the utility of negative Fungitell® results to support decisions to withhold or withdraw antifungals with excellent patient safety.[10,11,12] Hence, there is significant utility in the application of the Fungitell® test in at risk patients.

At Risk Patients

Invasive Fungal Infection is increasing in at risk populations[13] such as:

- Aggressive Care (SICU/MICU/NICU)
- Mechanical Ventilation
- Stem Cell and Organ Transplants
- HIV
- Cancer Treatment
- Diabetes
- Central Venous Catheters
- Hemodialysis
- Gastrointestinal Surgery
- Total Parenteral Nutrition

Opportunities

Fungitell®, an FDA cleared and CE marked diagnostic test, is used for the detection of (1→3)-β-D-Glucan, which is frequently associated with the presence of fungal pathogens. The majority of these are *Candida* and *Aspergillus* species.

There are, potentially, clinical applications that could benefit from utilizing the (1→3)-β-D-Glucan test where pneumocystosis is suspected.

The Fungitell® Assay

Features and Benefits

- Provides earlier support for diagnosis of IFI
- Detects glucan from most fungi including *Candida* and *Aspergillus**
- Rapid results within an hour
- FDA Cleared
- CE Marked

FUNGITELL® ASSAY PRODUCT INFORMATION

Principle of the Fungitell® Reagent

Fungitell® is a (1→3)-β-D-Glucan specific Limulus amebocyte lysate (LAL) reagent containing a chromogenic peptide substrate. (1→3)-β-D-Glucan in the sample causes activation of serine proteases. An activated protease cleaves p-nitroaniline (*p*NA) from the peptide substrate and the free *p*NA is measured at 405 nm. The test is run in a standard incubating plate reader.

Materials Supplied with the Kit

- 2 vials Fungitell® Reagent
- 2 vials Pyrosol® Reconstitution Buffer[a]
- 2 vials Glucan Standard
- 2 bottles Reagent Grade Water,[a] 20 mL
- 2 vials Alkaline Pretreatment Solution [a]

Storage Conditions

Store all reagents at 2-8°C in the dark. Reconstituted Fungitell® reagent should be stored at 2-8°C and used within 2 hours. Alternatively, reconstituted Fungitell® reagent can be frozen at -20°C for 20 days, thawed once and used.

Materials Required but not Supplied

All materials and glassware must be free of interfering glucan. Dry heat depyrogenation is effective in eliminating interfering levels of (1→3)-β-D-Glucan from glass surfaces.

Purchase supplies from a supplier that will certify the materials free of interfering glucan.

- 96-well microplate[b]
- Repeating Pipette and tips (250 mL; 1000 mL)[b]
- Test tubes for sample dilution (13 x 100 mm)[b]
- Glass pipettes – not plastic
- Parafilm®
- Incubating plate reader capable of reading at 405 and 490 nm with appropriate kinetic software for determination of V_{mean}[b]
- Vortex mixer

Order Information

FT001 Fungitell® Kit-110 test wells

The Fungitell® assay is a highly sensitive, microplate-based test that detects (1→3)-β-D-Glucan in serum. (1→3)-β-D-Glucan is a cell wall constituent of most medically important fungi including *Candida* and *Aspergillus*.* (1→3)-β-D-Glucan is normally found at low levels in the blood of healthy humans. In at risk patients, serum (1→3)-β-D-Glucan values of at least 80 pg/mL, are highly associated with invasive fungal infection. Conversely, low levels of (1→3)-β-D-Glucan have a high negative predictive value for invasive fungal infection.

(1→3)-β-D-Glucan detection is not subject to the usual interferences. It is not suppressed by anti-fungal therapy, nor is the test cross-reactive with other polysaccharides.

Diagnostic Performance

Multiple studies[4,5,6,7,8] in diverse patient groups have shown sensitivities from 70–100% and high negative predictive values. A variety of studies also demonstrate diagnostic utility in *Pneumocystis jirovecii* pneumonia[14,15].

Rapid Results

The Fungitell® assay is performed entirely within a microplate well without washing steps. The assay provides results within an hour.

Antimicrobial Stewardship

Studies have shown that early discontinuation of empirical therapy in high-risk ICU patients based on consecutive negative BDG tests may be a reasonable strategy, with great potential to reduce the overuse of antifungals[13].

Marketplace Longevity

Fungitell® has over a decade of proven clinical use and has been referenced in over 125 peer-reviewed clinical papers.

Warnings, Precautions and Limitations

(see instructions for use for details):

i. The tissue locations of fungal infection and encapsulation may affect the serum concentration of (1→3)-β-D-Glucan.

ii. Some individuals have elevated levels of (1→3)-β-D-Glucan that fall into the indeterminate zone of 60 – 79 pg/mL. In such cases, additional testing is recommended.

iii. Test levels were established in adult subjects. Infant and pediatric normal levels approach those of adults. Data for neonates, and infants less than six months, are lacking.

iv. Off-color or turbid samples such as those that are grossly hemolyzed, lipemic, or contain excessive bilirubin may cause interference.

v. Samples obtained by heel or finger stick methods are unacceptable as the alcohol-soaked gauze used to prepare the site and/or skin surface-pooling of blood may contaminate the specimens.

vi. Surgical gauzes and sponges can leach high levels of (1→3)-β-D-Glucan and may contribute to a transient positive result for the Fungitell® assay.

vii. The serum of hemodialysis patients may contain high levels of (1→3)-β-D-Glucan when certain cellulose dialysis membranes are used.

viii. In performing the test, great care must be taken to avoid contamination.

ix. The use of Fungitell® for purposes other than those described in the Intended Use section of instructions for use of the product is neither recommended nor supported by Associates of Cape Cod, Inc.

References:

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3. Kumar, A et al. Poster 2174 ICAAC 2007
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a.Products are free of interfering glucans

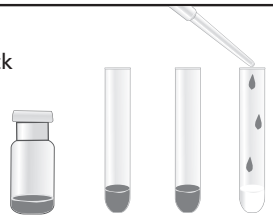
b.Available from Associates of Cape Cod, Inc.

*Cryptocuccus, Zygomycetes (such as Absidia, Mucor and Rhizopus) and Blastomyces dermatitidis (infective yeast form) are known to have little or no (1→3)-β-D-Glucan and thus, glucan is not detected during infection with these organisms.

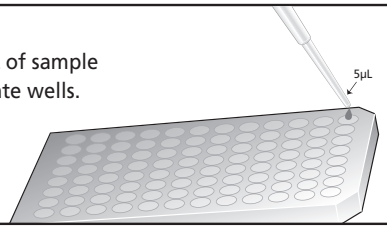
FUNGITELL® ASSAY
TEST PROCEDURE OUTLINE

SET-UP

1 Reconstitute glucan stock and make standards.

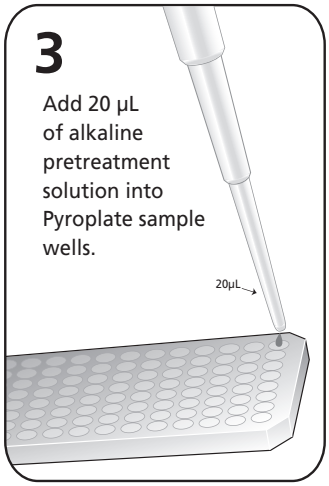


2 Pipette 5 µL of sample into Pyroplate wells.

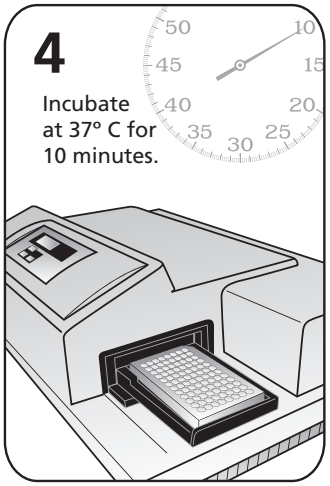


TEST SAMPLES

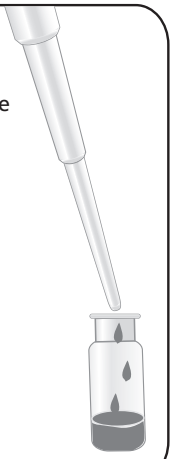
3 Add 20 µL of alkaline pretreatment solution into Pyroplate sample wells.



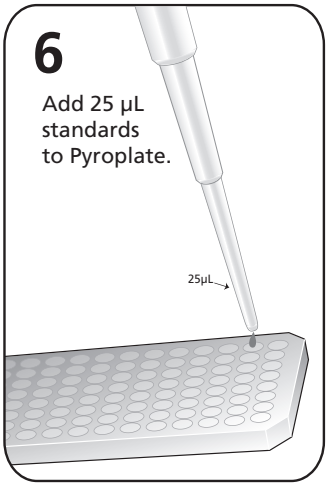
4 Incubate at 37° C for 10 minutes.



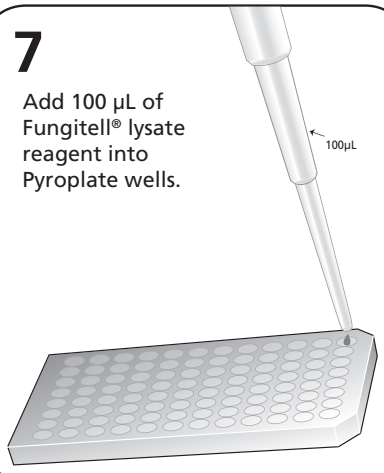
5 Reconstitute Fungitell® Reagent.



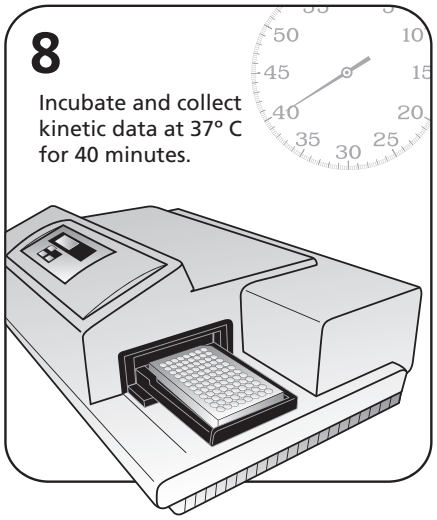
6 Add 25 µL standards to Pyroplate.



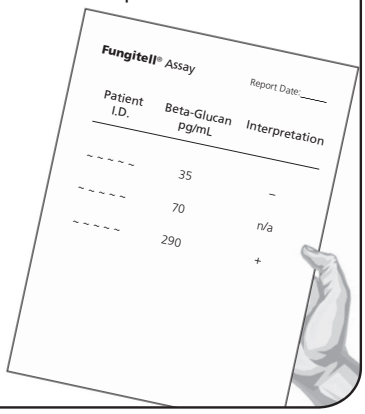
7 Add 100 µL of Fungitell® lysate reagent into Pyroplate wells.



8 Incubate and collect kinetic data at 37° C for 40 minutes.



9 Read report data.



NOTE: For complete test procedure refer to Fungitell® Instructions For Use (IFU).

About Beacon

The Beacon Diagnostics® Laboratory is a fully CLIA-certified reference laboratory specializing in (1→3)-β-D-Glucan analysis services to support the diagnosis of Invasive Fungal Infection (IFI). Serving clinical and reference laboratories, we offer a rapid, cost-effective alternative to in-house testing.

The laboratory is a division of Associates of Cape Cod, Inc. The expert staff at Beacon Diagnostics® Laboratory provides clients with rapid diagnostic and analytical service, to assist in the medical evaluation of patients suspected of having invasive fungal infection. Our laboratory also tests veterinary samples. We currently hold certifications and licenses in Massachusetts, California, Florida, Maryland, New York, Pennsylvania and Rhode Island. An updated list can be found on our website at www.BeaconDiagnostics.com.

Additional information concerning the applications and latest findings of (1→3)-β-D-Glucan testing in patients can also be found on our website.

Hours of Operation

Testing: Mon.-Fri., 8:00 a.m. to 6:00 p.m. EST
Sample Receiving: Mon.-Sat., 8:00 a.m. to 7:00 p.m. EST
CLIA License Number: 22D1021258

Test Information and Sample Requirements

Pricing and Current Procedure Terminology (CPT) Coding

- Call for Pricing
- The Fungitell® assay does not have an assigned CPT code. Commonly accepted laboratory practice for coding a diagnostic test is to seek an existing CPT code that exactly describes the test; i.e. the organism, methodology, analyte and sample, as appropriate. If there is no exact match, then a code is chosen that most closely describes the laboratory procedure on the basis of methodology. Based on comparison of the test characteristics to the CPT code description, commonly accepted coding practice may allow coding for Fungitell® using 87449. The coding preferred by individual payers may vary. Please check with your payer for specific billing instructions.

Testing and Turn-around Time

Testing is performed Monday through Friday. Typical turnaround time is about 48 hours from receipt of sample at our facility, but most results are available the same day they are received.

Specimen Requirements

Each sample sent to Beacon Diagnostics® Laboratory for testing must be accompanied by a completed Sample Submission Form. Forms can be obtained by calling (800) 568–0058 or by visiting our website at www.BeaconDiagnostics.com.

- Please provide at least 0.5 mL of serum separated from the clot and shipped cold or frozen on ice packs or dry ice. Secure the vial closure with Parafilm® or tape. Next day shipping is required.
- Serum should be shipped in a sterile, clean, screw-cap plastic vial (most cryogenic vials certified DNAse and RNAse free are typically suitable for use). Do not send serum in glass tubes. Samples not separated from the clot prior to shipment may incur an additional handling and preparation fee.
- Avoid contact between the serum and potential sources of (1→3)-β-D-Glucan contamination including cellulosic filters, gauze, and cotton swabs.
- Hemolyzed, lipemic, and icteric samples are not suitable for testing.
- Samples must be shipped in accordance with federal shipping requirements for Clinical Diagnostic Specimens.
- Use Red Top Tubes
- Heel and finger stick samples are inappropriate
- Our laboratory also tests veterinary samples.

Note: To maintain optimal sample temperatures during transit, especially during the warm summer months, it is advisable to use insulated shipping containers (e.g. Styrofoam liners) and extra cold packs or dry ice when shipping samples.

Contact Information

Beacon Diagnostics® Laboratory
124 Bernard E. Saint Jean Dr., E. Falmouth, MA 02536

Technical information and sample submission:
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