LAB #: F000000-0000-0
PATIENT: Sample Patient
ID: P00000000
SEX: Female
AGE: 57

CLIENT #: 12345
DOCTOR:
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174

Toxigenic C. difficile DNA; stool

RESULTS

	Within	Outside	Reference Interval
Toxigenic *C. difficile*		**Positive**	Negative

INFORMATION

Clostridium difficile (C. difficile) is a major cause of antibiotic associated diarrhea and colitis and is the causative agent for virtually all cases of pseudomembranous colitis. Although about 3% of normal healthy adults are colonized with *C. difficile*, many patients acquire this organism through nosocomial infection. Exposure to most antibiotics is thought to allow proliferation of toxigenic *C. difficile* by disrupting the normal intestinal flora.

This molecular diagnostic assay utilizes DNA amplification technology to detect all known strains of toxigenic *C. difficile*. Toxin A and Toxin B, the primary virulence factors of *C. difficile,* are encoded by two separate genes, named *tcdA* and *tcdB*, respectively. Together, with three additional genes, they form a 19.6 kb pathogenicity locus called PaLoc. This PaLoc is a gene segment present in all known A+B+ and A-B+ toxinotypes. This assay detects the PaLoc by targeting a partial DNA fragment on the Toxin A gene.

SPECIMEN DATA

Comments: **C. difficile isolated from Comprehensive Clostridium Culture.**

Date Collected: **10/29/2011**
Date Received: **11/2/2011**
Date Completed: **12/5/2011**

V03.11

This test is for use with unformed stool samples. Performance characteristics using solid stool samples types have not been established.

Toxigenic Clostridium difficile was detected in this stool sample. This molecular diagnostic assay utilizes DNAamplification technology to detect the pathogenicity locus (PaLoc) of toxigenic C. difficile. The C. difficile PaLoc codes for both the Toxin A gene (tcdA) and the Toxin B gene (tcdB). This assay detects C. difficile by targeting a partial DNA fragment of the Toxin A gene. The tcdA target region is an intact region that remains on all known A+B+ and A-B+ toxinotypes. C. difficile is a gram-positive anaerobic bacterium causing15-25% of cases of antibiotic-associated diarrhea and 95-100% of cases of antibiotic-associated pseudomembranous colitis. C. difficile infection and its associated disease has increased significantly in the last decade, with the greatest increases observed among the elderly. In addition, the emergence of severe and fatal disease among otherwise healthy persons with minimal risk factors has also been reported. Risk of infection increases in individuals who have taken antibiotics, have inadequate levels of beneficial/commensal bacteria, and reside in places where C. difficile is prevalent such as hospitals and long-term care facilities. Cross-infection is common in these facilities due to patient-to-patient spread and environmental contamination. Disease occurs almost exclusively in presence of exposure to antibiotics, especially broad-spectrum, and the subsequent depletion of commensal bacteria (lactobacilli and bifidobacteria). C. difficile is ubiquitous in nature and has been isolated from soil, sand, animal feces, and water.

Mild cases of C. difficile infection may be associated with watery diarrhea with mucus, low-grade fever, and mild abdominal pain. Approximately 20% of patients with C. difficile associated disease (CDAD) will resolve within 2-3 days of discontinuing the antibiotic to which the patient was previously exposed. Additionally, reestablishment of expected intestinal flora can also aid in the resolution of symptoms. Symptoms of severe C. difficile infection may include watery diarrhea with blood, severe abdominal pain, high fever with chills, and a rapid heart beat. Complications of severe CDAD may include pseudomembranous colitis, arthritis, protein-losing enteropathy, increased morbidity and hospitalization. The infection can be treated with Metronidazole or Vancomycin (administered orally), 80% of patients respond well to this treatment. However, 20% of patients experience a relapse 3 to 28 days after discontinuation of antibiotics alone or discontinuation and treatment. Co-administration of Saccharomyces boulardii with standard antibiotic therapy significantly decreased incidence of relapse of CDAD in adults.

Carriage rates in healthy adults are 3% - 8%, and a positive result for these patients should be considered normal if CDAD is absent. Asymptomatic carriage may be associated with a decreased risk of CDAD. Asymptomatic carriage among hospitalized adults is 20%. Two distinct groups have been identified that can harbor C. difficile asymptomatically at very high rates. Colonization at rates up to 50% and higher have been reported in infants less than one year of age and rates up to 32% in cystic fibrosis patients. In these patients a positive result in the absence of CDAD can be considered normal and treatment should be considered accordingly on an individual patient basis.

Patient should be suspected to have C. difficile associated disease (CDAD) if:

- Presence of diarrhea and positive assay for toxigenic C. difficile DNA
- Sudden onset of diarrhea with no alternative explanation
- Pseudomembranous colitis on endoscopy or histology
- Nosocomial infection if
  - Diarrhea within 72 hrs or more after admission
  - CDAD within a month after a previous admission
  - New episode if occurred >8 weeks after previous diagnosis

Repeat testing following a positive test (test of cure) is not recommended since patients may carry toxigenic C. difficile for months after clinical cure. Repeat testing following a positive test is appropriate if the patient improves with therapy and relapses after the completion of a treatment regimen (clinical relapse). Repeat testing following a negative test is not recommended because nearly all positive patients will be detected (high sensitivity).

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3. Noren T, Alriksson I, Andersson J, Åkerlund T, and Unemo M. Rapid and Sensitive Loop-Mediated Isothermal Amplification (LAMP) Test for Clostridium difficile diagnosis challenges cytotoxin B cell test and culture as Gold standard. J Clin Micro:10.1128/JCM.01824-10. 2010, American Society for Microbiology.

4. McFarland LV, Mulligan ME, Kwok RY, et al. Nosocomial acquisition of Clostridium difficile infection. N Engl J Med 1989;320:204-210.

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6. Walter BAJ, Roberts R, Stafford R, et al. Recurrence of antibiotic-associated colitis: endogenous persistence C. difficile during Vancomycin therapy. Gut 1983;24:206-212.

7. McFarland LV, Surawicz CM, Greenberg RN. A randomized placebo-controlled trial of Saccharomyces boulardii in combination with standard antibiotic for C. difficile disease. JAMA 1994;271(24):1913-1918.

8. Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, Pepin J, Wilcox MH; Society for Healthcare Epidemiology of America; Infectious Diseases Society of America. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). Infect Control Hosp Epidemiol. 2010 May;31(5):431-55.