



Contact: Barbara Kalavik
BD Public Relations
(201) 847-4209
Email: barbara_kalavik@bd.com

BD GeneOhm™ Cdiff Assay Backgrounder

What is *Clostridium difficile* Infection (CDI)?

- CDI, also known as *C. difficile*-associated disease, is caused by toxigenic *C. difficile*, a bacterium that produces diarrhea and more serious intestinal conditions, such as colitis, toxic megacolon, colon perforations, sepsis and even death.¹
- *C. difficile* is a spore-forming, gram-positive anaerobic bacillus that can produce two toxins: Toxin A and Toxin B. Most toxigenic *C. difficile* isolates (80 percent) produce both toxins, known as A+/B+ strains.²
- Only toxigenic *C. difficile* causes disease, accounting for 15 percent to 25 percent of antibiotic-associated diarrhea.¹
- Patients infected with *C. difficile* test positive for the organism and its toxin, and exhibit clinical symptoms, such as diarrhea, fever, loss of appetite, nausea and abdominal pain.¹

What is the BD GeneOhm™ Cdiff Assay?

- The BD GeneOhm™ Cdiff assay is a real-time polymerase chain reaction (PCR) test that detects toxigenic *C. difficile* directly in stool samples from patients suspected of having CDI. This sensitive molecular test identifies the toxin B gene associated with toxigenic *C. difficile* in less than two hours as compared to the 48 to 72 hours required to yield results from the highly sensitive tissue culture cytotoxicity test.

Technology Behind the Assay

- The assay is a qualitative *in vitro* test for the rapid detection of toxigenic, or disease-causing, *C. difficile* from a stool sample. PCR testing offers the required combination of sensitivity, specificity and turnaround time that traditional testing methods lack.
- Rapid molecular testing can potentially enable rapid and specific diagnosis of CDI patients. Prompt diagnosis allows for earlier administration of appropriate therapy and contact precautions, such as isolation, to prevent further spread of *C. difficile*.
- The BD GeneOhm Cdiff test involves a simple and efficient bacterial lysis procedure, which is followed by real-time PCR to detect the *C. difficile* toxin B gene. A commercially available instrument (thermocycler) is used to amplify low levels of the *C. difficile* toxin B gene, and fluorogenic, target-specific hybridization probes are used to detect the amplified DNA. Dedicated software interprets the data into a definitive assay result.

Why is a Rapid, Highly Sensitive *Clostridium difficile* Test Important?

- CDI is a concern to healthcare providers worldwide because it is a major source of morbidity and mortality. An urgent need exists for a single assay that is sensitive, specific, rapid and cost-effective for patients suspected of having CDI.



- Care of patients suspected of having CDI - an infection that can progress rapidly - depends on accurate and timely diagnosis. Recent exposure to antibiotics is a risk factor because it disrupts normal flora, which can increase patient susceptibility to CDI. Because there are many other causes of diarrhea in hospitalized patients, an accurate diagnosis is important for treatment and care decisions.
- Both positive and negative results from an accurate diagnostic test for *C. difficile* are important:
 - A positive result determines the need for appropriate CDI therapy and initiation of infection control protocols. In addition, patients are often on other antimicrobials, which may interfere with the response to CDI treatment. In such cases, healthcare providers may need to consider discontinuing these antimicrobials.
 - A negative result from a highly sensitive test means therapy is not needed for CDI, indicating a need to seek an alternative etiology for the patient's symptoms (diarrhea, fever, leukocytosis, etc.).
- Empiric therapy is not generally recommended, however, it may be necessary in seriously ill patients awaiting test results. When a patient is suspected of having CDI, diagnosis is usually made by either a tissue culture cytotoxicity assay and/or enzyme immunoassay (EIA).
- The BD GeneOhm Cdiff assay was designed to meet the combined need for specificity, sensitivity and speed -- offering the sensitivity of a tissue culture cytotoxicity assay with the speed of an EIA.
 - Clinical investigators have reported sensitivities ranging from 94 percent to 100 percent with the BD GeneOhm Cdiff assay compared to the cytotoxicity assay.^{3,4}
 - Negative predictive values (NPV) of 99 percent and greater have been reported by clinical investigators.^{3,4} High NPVs may allow the physician to rule out CDI,³ prompting determination of other causes for the patient's symptoms. This may also help avoid empiric treatment and unnecessary use of antibiotics, which increases the risk of CDI in negative patients.⁵

What are the Drawbacks to Traditional Methods for Diagnosing *C. difficile* Infection?

Diagnosing *C. difficile* with traditional methods remains a challenge. Since only toxigenic or toxin-producing *C. difficile* causes disease, methods (such as culture and the glutamate dehydrogenase assay (GDH)) that do not distinguish toxigenic from non-toxigenic strains must be followed by tests that detect Toxin A and/or Toxin B (EIA or tissue culture cytotoxicity). Virtually all disease-causing strains, including the epidemic BI/NAP1/027 strain, carry the gene for Toxin B.

The following laboratory tests have been traditionally used to diagnose CDI:

- **Stool Culture for *C. difficile*:** This is the most sensitive test available, but can be associated with false-positive results due to the presence of non-toxigenic strains. Stool cultures for *C. difficile* are labor intensive, require expertise in anaerobic microbiology, as well as the appropriate equipment required to culture anaerobic microorganisms. Results are available within 48 to 96 hours. However, a stool culture does not differentiate between toxigenic and non-toxigenic *C. difficile* strains. Therefore, a toxin detection test must be performed on the *C. difficile* strain isolated via culture in order to detect the presence or absence of toxin; this adds additional time to obtaining the final result.



- **Common Antigen Detection for *C. difficile*:** This rapid test, with results available in less than one hour, detects the presence of *C. difficile* antigen by rapid membrane or microplate immunoassays. These assays must be combined with toxin testing to verify diagnosis.
 - **Glutamate Dehydrogenase Assay (GDH):** This test is a quick, easy-to-perform method for detecting the presence of *C. difficile*. However, it does not distinguish non-toxigenic from toxigenic strains, therefore, a second, confirmatory test for toxin detection is required.
- **Toxin Testing for *C. difficile*:** These tests vary in the specific toxin that is being identified: Toxin A only, Toxin B only, or Toxin A and B.
 - **Enzyme Immunoassay (EIA):** These tests detect Toxin A only or the production of Toxin A and B. This type of test is used most often because it is fast and is easy to perform. However, it is prone to false negatives, and typically has poor sensitivity. As a result, physicians often order repeat tests – sometimes as many as three or more over several days.
 - **Tissue Culture Cytotoxicity:** This test detects Toxin B production only and is labor-intensive, can lack specificity and sensitivity, and time consuming in nature, requiring 48 to 72 hours for a test result. Results also may vary with technician experience and not all labs are equipped to conduct this type of test.

BD GeneOhm Product Line

The BD GeneOhm line of products is developed to help improve patient outcomes by delivering cost-effective, rapid molecular solutions for the prevention and identification of HAIs.

BD GeneOhm™ StaphSR Assay: The new BD GeneOhm™ StaphSR assay is the first test available to rapidly and simultaneously identify within two hours the deadly healthcare-associated infections (HAIs) – *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* – directly from a positive blood culture. It is easy to perform and requires less technologist time than traditional microbiology algorithms, which can take up to 48 hours to generate results.

BD GeneOhm™ MRSA Assay: This is a qualitative *in vitro* diagnostic test for the direct detection of MRSA from a nasal specimen. Compared to culture methods requiring two to five days, this two hour turn-around time can be used to enhance any infection control program. The BD GeneOhm™ MRSA assay rapidly identifies patients who are colonized with MRSA and allows infection control professionals to break the chain of MRSA transmission.

BD GeneOhm™ VanR Assay: This two-hour molecular test is currently available in Europe as a CE-marked test for the identification of vancomycin-resistant genes associated with vancomycin-resistant enterococci (VRE). This test, using rectal swab specimens, enables rapid identification of patients potentially colonized with VRE, allowing earlier implementation of effective interventions aimed at controlling its spread, preventing infection, and reducing healthcare costs, with the goal of improving overall patient outcomes. This test is not available for sale in the United States; it is currently under review by the U.S. Food and Drug Administration.

¹ Centers for Disease Control and Prevention. (2005, July, 22). Information for healthcare providers. Retrieved June 27, 2008 from http://www.cdc.gov/ncidod/dhqp/id_CdiffFAQ_HCP.html



² McFarland, L.V., Beneda, H.W., Clarridge, J.E., & Raugi, G.J. (2007). Implications of the changing face of *Clostridium difficile* disease for health care practitioners. *American Journal of Infection Control*, 35(4), 237-253.

³ Alcabasa, R., Aird, D., Wehrin, J., Babiker, W., Ikpeama, I., Stamper, P.D., et al. (2008). Comparison of the BD GeneOhm Cdiff Assay (BD GeneOhm™, San Diego, CA) to the Wampole *Clostridium difficile* Toxin B Test (TechLab, Blacksburg, VA). Poster session presented at the annual American Society for Microbiology, Boston, Massachusetts.

⁴ Fuller, D., Buckner, R., Newcomer, K., Davis, E., Davis, T., Lineback, P. et al. (2008). Clinical Comparison of the Molecular-Based BD GeneOhm™ Cdiff Assay to the Cytotoxicity Tissue Culture Assay for the Direct Detection of Toxin B gene from Toxigenic *Clostridium difficile* Strains in Fecal Specimens. Poster session presented at the annual meeting of the Anaerobe Society of the Americas. Long Beach, California.

⁵ Sunenshine, R.H., & McDonald, L.C. (2006). *Clostridium difficile*-associated disease: New challenges from an established pathogen. *Cleveland Clinic Journal of Medicine*, 73(2), 187-197.