C. difficile GDH/Toxin With Reflex to PCR

Clostridium difficile GDH/Toxin EIA Testing
With Reflex to Nucleic Acid Amplification

Clinical Background

C. difficile is a Gram positive, spore-forming, anaerobic bacterium. The ability to produce (or even overproduce in the case of the NAP1 strain) toxins contributes to substantial morbidity and mortality. In the USA from 1999 to 2004, 20,642 deaths were attributed to C. difficile infection (CDI).This is about 7-fold the rate for all other intestinal infections combined. Mortality rates due to CDI have increased by approximately 35% each year during the same time period (i.e. 1999 to 2004). The rate of USA hospital discharges with CDI doubled from 1996 to 2003 (i.e. 31/100,000 to 61/100,000 population). This rate was also 7-fold higher for individuals >65 yrs. vs. the 45-64 yrs. old group. "This pathogen is now associated with a far higher incidence of hospitalizations than the more widely publicized methicillin-resistant Staphylococcus aureus."

The incidence and death from C. difficile infection (CDI) and the increase in health care costs in hospitalized patients has accelerated to an unprecedented high level over the past few years. CDI is also of growing concern in the nonhospital setting. Laboratory support is critical to both the diagnosis of CDI and prevention and control. Efficient and high performance laboratory tests with a quick turn-around-time are essential.

Test Performance Verification

In house test performance was conducted where specimens were tested using two EIA antigen tests and three molecular tests. Concordance between the molecular tests was considered the reference standard for the purpose of this test algorithm verification. Repeat, replicate testing was performed on all discordant results. The summary of test performance is shown on the next page with the algorithm.

Test Limitations

- This test is intended for use with non-formed stool.
- A negative test result does not rule out the presence of *C. difficile* below the test sensitivity.

Methodology

The C. DIFF QUIK CHEK COMPLETE test is a rapid membrane enzyme immunoassay for the simultaneous detection of *Clostridium difficile* glutamate dehydrogenase antigen (GDH) and toxins A and B. Test results revealing +/- or -/+ for GDH/Toxin will be reflexed to the Simplexa C difficile Universal Direct real-time PCR assay.

Test Ordering Information

Test Name	Test Code
C. difficile GDH/Toxin - Reflex to PCR	**7123**

Specimen Collection and Transport

Specimen Type: Raw, unpreserved stool (At least 1 gm)
Other specimen types: none

Specimen Stability

Ambient Stability: Unknown, send refrigerated only
Refrigerated (2-8°C): 2 days
Frozen Stability (-20°C or lower): Unknown
Local and Long Distance Transport: Refrigerated

CPT Code

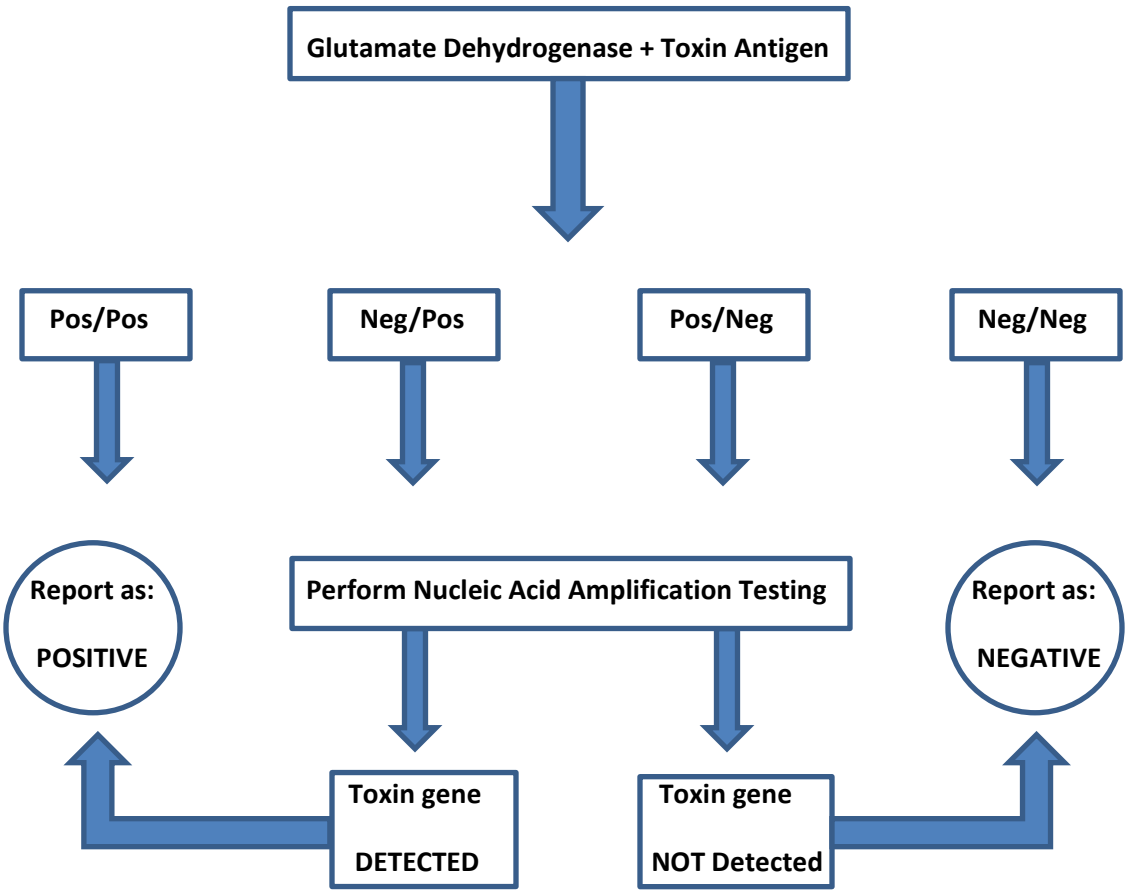
87324	EIA – Clostridium difficile toxin
87449	EIA – Infectious agent, not otherwise specified
87493	C. difficile, toxin gene(s), amplified probe

References

1. Centers for Disease, C., and Prevention. 2012. Vital signs: preventing Clostridium difficile infections. MMWR Morb Mortal Wkly Rep 61:157-162.
2. Freeman, J., M. P. Bauer, S. D. Baines, J. Corver, W. N. Fawley, B. Goorhuis, E. J. Kuijper, and M. H. Wilcox. 2010. The changing epidemiology of Clostridium difficile infections. Clin Microbiol Rev 23:529-549.
3. Martinez, F. J., D. A. Leffler, and C. P. Kelly. 2012. Clostridium difficile outbreaks: prevention and treatment strategies. Risk management and healthcare policy 5:55-64.
4. O'Horo, J. C., A. Jones, M. Sternke, C. Harper, and N. Safdar. 2012. Molecular Techniques for Diagnosis of Clostridium difficile Infection: Systematic Review and Meta-analysis. Mayo Clin Proc 87:643-651.
5. Tenover, F. C., E. J. Baron, L. R. Peterson, and D. H. Persing. 2011. Laboratory diagnosis of Clostridium difficile infection can molecular amplification methods move us out of uncertainty? J Mol Diagn 13:573-582.

Diagnostic Laboratory Services Inc.
99-859 Iwaiwa Street· Aiea, HI·96701 (808) 589-5100 · www.dlslab.com

Clostridium difficile Clinical Diagnostic Testing Algorithm



Test Type	Result	Sensitivity	Specificity	PPV	NPV
GDH + Toxin	Pos/Pos	100	100	100	100
GDH + Toxin	Neg/Pos or Pos/Neg	45.5	92.2	83.3	66.2
GDH + Toxin	Neg/Neg	100	100	100	100
NAAT	Detected	97.7-100	100	100	98.1-100
NAAT	Not Detected	100	100	100	100

Notes: -The test performance is based upon a study consisting of two EIA-based tests and three NAAT.
-The testing algorithm will consist of a screening test using GDH/Toxin with a reflex to NAAT.
-The reflex to NAAT occurs when the GDH/Toxin test result is Neg/Pos or Pos/Neg.
-It is anticipated that approximately 30% of the specimens screened will result in a reflex to NAAT.

Diagnostic Laboratory Services Inc.
99-859 Iwaiwa Street· Aiea, HI·96701 (808) 589-5100 · www.dlslab.com