

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number:

K053572

B. Purpose of Submission:

For the detection of the *Clostridium difficile* common antigen glutamate dehydrogenase in human stool

C. Measurand:

glutamate dehydrogenase antigen

D. Type of Test:

Horizontal flow enzyme immunoassay

E. Applicant:

Tech Lab®, Inc.

F. Proprietary and Established Names:

C. DIFF QUIK CHEK™

G. Regulatory Information:

1. Regulation section:
21 CFR Part 866.2660 Microorganism Differentiation and Identification Device
2. Classification:
I
3. Product Code:
MCB – Antigen, *Clostridium difficile*.
4. Panel:
83 Microbiology

H. Intended Use:

1. Intended use(s):
The *C. DIFF QUIK CHEK™* test is a rapid membrane enzyme immunoassay for use as a screening test to detect *Clostridium difficile* antigen, glutamate dehydrogenase, in fecal specimens from persons suspected of having *C. difficile* disease. The test does not distinguish toxigenic from nontoxigenic strains of *C. difficile*. With the use of additional tests that detect *C. difficile* toxins, the test is to be used as an aid in the diagnosis of *C. difficile* disease. As with other *C. difficile* tests, results should be considered in conjunction with the patient history.
FOR IN VITRO DIAGNOSTIC USE.
2. Indication(s) for use:
The *C. DIFF QUIK CHEK™* test is a rapid membrane enzyme immunoassay for use as a screening test to detect *Clostridium difficile* antigen, glutamate dehydrogenase, in fecal specimens from persons suspected of having *C. difficile* disease. The test does not distinguish toxigenic from nontoxigenic strains of *C. difficile*. With the use of additional tests that detect *C. difficile* toxins, the test is to be used as an aid in the diagnosis of *C. difficile* disease. As with other *C. difficile* tests, results should be considered in conjunction with the patient history.

FOR *IN VITRO* DIAGNOSTIC USE.

3. Special condition for use statement(s):
For Prescription Use Only
4. Special instrument Requirements:
Not applicable

I. Device Description:

The *C. DIFF QUIK CHEK™* test is a rapid membrane enzyme immunoassay that utilizes antibodies specific for the antigen, glutamate dehydrogenase, of *C. difficile*. The device contains a *Reaction Window* with two vertical lines of immobilized antibodies. The test line contains antibodies against *C. difficile* glutamate dehydrogenase. The control line contains anti-IgG antibodies. The *Conjugate* consists of antibodies to glutamate dehydrogenase coupled to horseradish peroxidase.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Triage® *Clostridium difficile* Panel
2. Predicate K number(s):
K974881
3. Comparison with predicate(s):

Similarities		
Item	Device	Predicates
Intended use	an <i>in vitro</i> diagnostic product for the detection of <i>Clostridium difficile</i> in fecal specimens	same
Specimen type	fecal specimens	same
technology	Enzyme Immunoassay	same
Level of skill	Moderately complex	same
Differences		
Item	Device	Predicates
Limit of detection	0.8 ng/ml	2.0 ng/ml
Clinical sensitivity	92.8% CI (88.3% -95.7%)	91.1% CI (85.8-96.4%)
Clinical specificity	92.6% CI (90.4% - 94.3%)	93.0% CI (90.7-95.4%)

K. Standard/Guidance Document referenced (if applicable):

N/A

L. Test Principle:

The *C. DIFF QUIK CHEK™* test is a rapid membrane enzyme immunoassay that utilizes antibodies specific for the antigen, glutamate dehydrogenase, of *C. difficile*. The device contains a *Reaction Window* with two vertical lines of immobilized antibodies. The test line ("T") contains antibodies against *C. difficile* glutamate dehydrogenase. The control line ("C") contains anti-IgG antibodies. The *Conjugate* consists of antibodies to glutamate dehydrogenase coupled to horseradish peroxidase. To perform the test, the sample is added to a tube containing a mixture of *Diluent* and *Conjugate*. The diluted sample-conjugate mixture is added to the *Sample Well* and the device is allowed to incubate at room temperature for 15 minutes. During the incubation, any glutamate

dehydrogenase in the sample binds to the antibody-peroxidase conjugate. The antigen-antibody-conjugate complexes migrate through a filter pad to a membrane where they are captured by the immobilized glutamate dehydrogenase-specific antibodies in the line. The *Reaction Window* is subsequently washed with *Wash Buffer*, followed by the addition of *Substrate*. After a 10 minute incubation period, the “T” reaction is examined visually for the appearance of a vertical blue line on the “T” side of the *Reaction Window*. A blue line indicates a positive test. A positive “C” reaction, indicated by a vertical blue line on the “C” side of the *Reaction Window*, confirms that the test is working properly and the results are valid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A total of eight fecal specimens, 6 positive and 2 negative were coded to prevent identification and were sent to each of three independent laboratories for analysis using the *C. DIFF QUIK CHEK™* test. The results from each laboratory were compared with in-house results. The positive specimens were confirmed to be positive and the negative specimens were confirmed to be negative at each site.

b. Linearity/assay reportable range:

Not applicable

c. Traceability (controls, calibrators, or method):

Not applicable

d. Detection limit:

The limit of detection of the *C. DIFF QUIK CHEK™* test is 0.4 ng/mL.

e. Analytical specificity:

Fecal specimens inoculated with the following microorganisms to a final concentration of approximately 10^8 or higher organisms per mL did not react in the *C. DIFF QUIK CHEK™* test:

Bacteria: *Aeromonas hydrophila*, *Bacillus cereus*, *Bacillus subtilis*, *Bacteroides fragilis*, *Campylobacter coli*, *Campylobacter fetus*, *Campylobacter jejuni*, *Candida albicans*, *Clostridium bifermentans*, *Clostridium butyricum*, *Clostridium perfringens* Type A, *Clostridium septicum*, *Clostridium sordellii* (toxigenic and nontoxigenic), *Clostridium sporogenes*, *Enterococcus faecalis*, *Escherichia coli* EIEC, *Escherichia coli*, *Escherichia coli* 0157 H7, *Escherichia coli* ETEC, *Klebsiella pneumoniae*, *Peptostreptococcus anaerobius*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus aureus* (Cowans), *Staphylococcus epidermidis*, *Vibrio parahaemolyticus*, *Yersinia enterocolitica*.

The following viruses of $10^{3.3}$ to $10^{7.5}$ TCID units per 0.2mL did not react in the *C. DIFF QUIK CHEK™* test:

Viruses: Adenovirus types 1,2,3,5,40,41, Human coronavirus, Coxsackievirus B2,B3,B4,B5, Echovirus 9,11,18,22,33, Enterovirus type 68,69,70,71.

The following substances had no effect on test results when present in feces in the concentrations indicated: mucin (3.5% w/v), human blood (40% v/v), barium sulfate (5% w/v), Imodium[®] (5% w/v), Kaopectate[®] (5 mg/mL), Pepto-Bismol[®] (5% w/v), steric/palmitic acid (fecal fats, 40% w/v), Metronidazole (0.25% w/v), Vancomycin (0.25% w/v)

f. Assay cut-off

The assay cut-off of the *C. DIFF QUIK CHEK*[™] test is 0.8 ng/mL.

2. Comparison studies:

a. Method comparison with gold standard:

The *C. DIFF QUIK CHEK*[™] test was compared to the bacterial culture test at two clinical laboratories and in-house at TECHLAB[®], Inc. Specimens included in the evaluation were submitted to the clinical laboratories for routine testing. The presumptive bacterial culture test was performed according to the in-house procedures. The results are shown in Table 1.

Table 1. Summary of clinical performance comparing *C. DIFF QUIK CHEK*[™] test to presumptive bacterial culture

n=979	Presumptive Bacterial Culture positive	Presumptive Bacterial Culture negative
<i>C. DIFF QUIK CHEK</i> [™] positive	206	56
<i>C. DIFF QUIK CHEK</i> [™] negative	16	701

	95% Confidence Limits	
Sensitivity	92.8%	88.3% - 95.7%
Specificity	92.6%	90.4% - 94.3%
Predictive Positive Value	78.6%	73.1% - 83.3%
Predictive Negative Value	97.8%	96.3% - 98.7%
Correlation	92.6%	91.7% - 93.4%

Discrepant samples were resolved using commercial tests for *C. difficile* glutamate dehydrogenase in ELISA or membrane test formats, or by a research PCR assay for the detection of *C. difficile* GDH gene *gluD*. Twenty-nine of the 56 apparent false positive samples were positive by another GDH test, and were considered true positives. Twenty-seven remained false positive. Thirteen of the 16 apparent false negative samples were negative by another GDH test, and were considered true negatives. Three remained false negative.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical sensitivity:

The C. DIFF QUIK CHEK™ test was compared to the bacterial culture test at two clinical laboratories and in-house at TECHLAB®, Inc. Specimens included in the evaluation were submitted to the clinical laboratories for routine testing. The presumptive bacterial culture test was performed according to the in-house procedures. Of the 979 specimens analyzed by culture, 206 were positive for *Clostridium difficile*. Results are summarized in Tables 1. (See table above)

b. Clinical specificity:

Refer to (a.) above

c. Other clinical supportive data (when a and b is not applicable):

Not applicable

4. Clinical cut-off:

The clinical cut-off of this assay is approximately 0.4 ng/mL. This limit does not vary from solid to liquid/semi-solid stool.

5. Expected values/Reference range: (Interpretive Criteria)

Clostridium difficile disease is primarily a nosocomial disease of elderly patients, and the frequency of the disease is dependent on factors such as patient population, type of institution and epidemiology. The reported incidence of *C. difficile* disease in patients with antibiotic-associated diarrhea may range from 5 to 20%, and hospitals may experience rates lower or higher than this range. It is important to consider any test results in conjunction with clinical symptoms because some healthy adults and large numbers of healthy infants (up to 50%) will be positive for *C. difficile* toxin. In addition, *C. difficile* carriage rates of 22 to 32% have been reported in cystic fibrosis patients. Because the C. DIFF QUIK CHEK™ test detects both toxigenic and non-toxigenic strains of *C. difficile*, the expected values of this test are higher compared to that of any toxin test. A positive result in the C. DIFF QUIK CHEK™ test confirms the presence of *C. difficile* in a fecal specimen; a negative result indicates the absence of the organism. A positive result should be followed by a toxin-specific test to confirm the presence of toxigenic *C. difficile*. The prevalence of a positive C. DIFF QUIK CHEK™ test at an independent study site was 18.2% (N=578).

N. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.

