510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K132010

B. Purpose for Submission:

To obtain a substantial equivalence determination for a new device

C. Measurand:

Clostridium difficile antigen, glutamate dehydrogenase (GDH)

D. Type of Test:

Qualitative enzyme linked fluorescent assay (ELFA)

E. Applicant:

bioMérieux, SA

F. Proprietary and Established Names:

VIDAS® *C. difficile* GDH Assay

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.2660 - Microorganism Differentiation and Identification Device

2. Classification:

   Class I

3. Product code:

   MCB – Antigen, *C. difficile*

4. Panel:

   Microbiology (83)

H. Intended Use:

1. Intended use(s):

   VIDAS® *C. difficile* GDH (GDH) is an automated test based on the Enzyme Linked Fluorescent Assay technique (ELFA), for use on the VIDAS family instruments. The VIDAS *C. difficile* GDH *(*glutamate dehydrogenase*)* assay is a qualitative test that detects the *C. difficile* antigen, glutamate dehydrogenase, as a screen for the presence of *C. difficile* in fecal specimens from persons suspected of having *C. difficile* infection (CDI). 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* infection. As with other *C. difficile* tests, results should be considered in conjunction with the patient history.

2. Indication(s) for use:

   VIDAS® *C. difficile* GDH (GDH) is an automated test based on the Enzyme Linked Fluorescent Assay technique (ELFA), for use on the VIDAS family instruments. The VIDAS *C. difficile* GDH *(*glutamate dehydrogenase*)* assay is a qualitative test that detects the *C. difficile* antigen, glutamate dehydrogenase, as a screen for the presence of *C. difficile* in fecal specimens from persons suspected of having *C. difficile* infection (CDI). 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* infection. As with other *C. difficile* tests, results should be considered in conjunction with the patient history.

3. Special conditions for use statement(s):

   For prescription use

4. Special instrument requirements:

   VIDAS and mini-VIDAS instruments

I. Device Description:

Each VIDAS® *C. difficile* GDH kit contains 60 tests. The kit is comprised of the reagent strip (STR), the solid phase receptacle (SPR), the controls (C1 and C2), the standard (S1), the Pretreatment Reagent (R1), and the Master Lot Entry (MLE) card.

The interior of the SPR is coated during production with mouse monoclonal anti- *C. difficile* GDH antibody. Each SPR is identified by the code "GDH" code.

The reagent strip consists of 10 wells covered with a labeled, foil seal. The label contains a bar code which includes the assay code, kit lot number and expiration date. The foil of the first well is perforated to facilitate the introduction of the sample. The last well of each strip

is a cuvette in which the fluorometric reading is performed. The eight wells in the center section of the strip contain the various reagents required for the assay.

Description of the GDH reagent strip**:**

Wells	Reagents
1	Sample well.
2 - 3 - 4	Wash solution: Buffer 0.2 mol/L (pH 7.8) + detergent + preservatives (600 µL).
5	Conjugate: mouse monoclonal anti-*C. difficile* GDH antibody labeled with ALP + Protein stabilizer + preservative (400 µL).
6 - 7 - 8 - 9	Wash solution: Buffer 0.2 mol/L (pH 7.8) + detergent + preservatives (600 µL).
10	Reading cuvette with substrate: 4-Methyl-umbelliferyl phosphate (0.6 mmol/L) + diethanolamine DEA* (0.62 mol/L or 6.6%) pH 9.2 + sodium azide 1g/L (300 µL).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Techlab C. Diff QUIK CHECK®

2. Predicate 510(k) number(s):

   K053572

3. Comparison with predicate:

Similarities		
Item	Device VIDAS® *C. difficile* GDH Assay	Predicate C. DIFF QUIK CHEK® Assay (K053572)
Intended Use	VIDAS® *C. difficile* GDH (GDH) is an automated test based on the Enzyme Linked Fluorescent Assay technique (ELFA), for use on the VIDAS family instruments. The VIDAS *C. difficile* GDH *(*glutamate dehydrogenase*)* assay is a qualitative test that detects the *C. difficile* antigen, glutamate dehydrogenase, as a screen for the presence	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

Similarities		
Item	Device VIDAS® *C. difficile* GDH Assay	Predicate C. DIFF QUIK CHEK® Assay (K053572)
	of *C. difficile* in fecal specimens from persons suspected of having *C. difficile* infection (CDI). 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* infection. As with other *C. difficile* tests, results should be considered in conjunction with the patient history.	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.
Analyte	*C. difficile* glutamate dehydrogenase antigen	*C. difficile* glutamate dehydrogenase antigen
Interpretation	Qualitative	Qualitative

Differences		
Item	Device VIDAS® *C. difficile* GDH Assay	Predicate C. DIFF QUIK CHEK® Assay (K053572)
Automated	Yes	No
Assay Technique	Enzyme-linked fluorescent assay (ELFA)	Rapid Membrane Enzyme Immunoassay
Assay time	Approximately 50 minutes	Approximately 25 minutes
Reading method	Automated	Visual
Specimen type	Human stool (unpreserved)	Human stool (unpreserved and preserved in Cary Blair or C&S transport media)
Specimen volume	200 µL	25 µL unpreserved stool, 100 µL Cary Blair or C&S transport media stool
Detection antibodies	Alkaline phosphatase labeled monoclonal anti-*C.difficile* GDH antibody	Horseradish peroxidase labeled monoclonal anti-*C.difficile* GDH antibody
Capture antibodies	Monoclonal anti-*C.difficile* GDH antibody	Polyclonal anti-*C.difficile* GDH antibody

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

CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods

CLSI EP07-A2: Interference Testing in Clinical Chemistry

CLSI EP12-A2: User Protocol for Evaluation of Qualitative Test Performance

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation

CLSI EP24-A2: Assessment of the Diagnostic Accuracy of Laboratory Tests Using ROC Curves

CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents

L. Test Principle:

The VIDAS® C. difficile GDH assay principle combines a two-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA).

The SPR serves as the solid phase as well as the pipetting device. Reagents for the assay are ready-to-use and are pre-dispensed in the sealed reagent strips. All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR several times. Each step is followed by a wash cycle which eliminates unbound components.

- Specific binding of GDH present in the sample with mouse monoclonal anti-GDH antibody coated on the interior of the SPR.

- Binding between GDH and mouse monoclonal anti-GDH antibody conjugated with alkaline phosphatase (ALP).

- Detection: alkaline phosphatase catalyzes the hydrolysis of the substrate (4-Methyl-umbelliferyl phosphate) into a fluorescent product (4-Methyl-umbelliferone) the fluorescence of which is measured at 450 nm.

The intensity of the fluorescence increases according to the quantity of GDH in the sample.

When the VIDAS C. difficile GDH test is completed, the results are analyzed automatically by the instrument, a test value is generated, and a result is printed for each sample.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   The within-laboratory precision was estimated at one site based on the recommendations of the CLSI EP5-A2. Three human samples, including two close to the clinical cut-off (one high negative and one low positive), were tested in triplicate

in two runs per day with two different operators, with two reagent lots for a total of 12 testing days (six days of test per lot) on one VIDAS instrument (N=72 test values for each sample). Two calibrations were used for each reagent lot (three days of test per calibration and lot) over the whole period of the study. Data from the study are summarized in the following table:

Sample	N	Mean test value	Repeatability		Total within-laboratory precision (total within-instrument, between-lot, between-calibration)	
			Standard deviation	CV (%)	Standard deviation	CV (%)
Sample 1 High negative	72	0.07	0.00	6.0	0.01	14.1
Sample 2 Low positive	72	0.12	0.01	5.2	0.01	11.9
Sample 3 Moderate positive	72	0.27	0.02	5.7	0.03	11.2

The within-laboratory precision of each panel member was also analyzed by determining the percentage of agreement between the test interpretation and the expected outcome (negative/positive interpretation). There was no change of interpretation for the 3 panel samples tested: all replicates of each panel member resulted in the expected interpretation. Data from the qualitative analysis are summarized in the following table:

Sample	Expected Result	N	Observed result Lot 1		Observed result Lot 2			
			Neg	Pos	Neg	Pos	Total Agreement	[CI_{95}] %
Sample 1 High negative	Negative	72	36	0	36	0	72/72 (100.0%)	[95.0 - 100.0]%
Sample 2 Low positive	Positive	72	0	36	0	36	72/72 (100.0%)	[95.0 - 100.0]%
Sample 3 Moderate positive	Positive	72	0	36	0	36	72/72 (100.0%)	[95.0 - 100.0]%

The reproducibility was estimated at three sites based on the recommendations of the CLSI EP5-A2. Three human samples, including two close to the clinical cut-off (one high negative and one low positive), were tested in triplicate in two runs per day with two different operators, using two reagent lots for a total of six testing days (three days of test for each lot) on three VIDAS instruments at three different sites (N=108 test values for each sample). One calibration was used for each reagent lot over the

whole period of the study. Data from the study are summarized in the following table:

Sample	N	Mean test value	Reproducibility (total between sample preparation/operator/run/day/lot/ instrument)	
			Standard deviation	CV (%)
Sample 1 High negative	108	0.06	0.01	19.1
Sample 2 Low positive	108	0.12	0.02	12.9
Sample 3 Moderate positive	108	0.26	0.03	13.0

The reproducibility of each panel member was also analyzed by determining the percentage of agreement between the test interpretation and the expected outcome (negative/positive interpretation). Data from the qualitative analysis for all sites combined are summarized in the following table:

Panel Sample	Expected Result	N	Observed result Site 1		Observed result Site 2		Observed result Site 3		Total Agreement	[CI_{95}] %
			Neg	Pos	Neg	Pos	Neg	Pos		
Sample 1 High negative	Negative	108	36	0	36	0	35	1	107/108 (99.1%)	[94.95 - 99.98]%
Sample 2 Low positive	Positive	108	0	36	1	35	3	33	104/108 (96.3%)	[90.79 - 98.98]%
Sample 3 Moderate positive	Positive	108	0	36	0	36	0	36	108/108 (100%)	[96.64 - 100]%

Out of the 108 results obtained for each precision sample, there were:

- 1 change of interpretation (0.9%) for the high negative sample (Sample 1),
- 4 changes of interpretation (3.7%) for the low positive sample (Sample 2),
- 0 change of interpretation (0%) for the moderate positive sample (Sample 3).

The percentages of change of interpretation observed for Sample 1 and Sample 2 were less than 5%, which was considered as normal and expected for these types of samples very close to the assay decision threshold (average test value for Sample 1 = 0.06 and average test value for Sample 2 = 0.12 for a decision threshold at 0.10.

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Controls:

One positive control (C1) and one negative control (C2) are included in each VIDAS C. difficile GDH kit. These controls must be performed each time a new lot of reagents is opened to ensure that reagent performance has not been altered. Each calibration must be checked using these controls. Results cannot be validated if the control values deviate from the expected values. The expected value range for each control is indicated on the Master Lot Entry (MLE) Card that is provided with the kit.

Calibrators:

Calibration, using the standard (S1) provided in the kit, must be performed each time a new lot of reagents is opened, after the master lot data have been entered. Calibration should then be performed every 28 days. The standard value must be within the set RFV "Relative Fluorescence Value" range as indicated on the MLE card. If this is not the case, recalibrate.

Sample stability:

Unpreserved stool specimens may be stored at 2-8°C for 3 days (from time of collection) prior to processing. If longer storage is required, freeze the specimens at -70°C+/- 10°C up to one month. Avoid repeated freezing and thawing cycles and storage at -19/-31°C.

Do not use containers which may contain detergents, preservatives or media that may interfere with the VIDAS *C. difficile* GDH assay results.

Samples stored in Cary Blair or C&S Transport media, or preserved 10% formalin, merthiolate formalin, sodium acetate formalin, or polyvinyl alcohol media have not been evaluated for use with the VIDAS *C. Difficile* GDH Assay.

Processed specimen supernatants, processed standard and reconstituted controls may be stored up to 8 hours at 18-25°C or 48 hours at 2-8°C before being tested with the VIDAS *C. difficile* GDH assay. Specimen supernatants and processed standard and control storage at -19/-31°C and -70°C +/-10°C was not validated and is therefore not recommended.

High dose hook effect:

No hook effect was observed up to purified native GDH antigen concentrations of 2 µg/mL.

d. Detection limit:

The limit of detection was evaluated using a range of dilutions of purified native *C.difficile* GDH *C. difficile* GDH in a pool of C. *difficile*-negative stool samples based on the recommendations of the CLSI EP17-A. The limit of detection of the VIDAS *C. difficile* GDH assay (at least 95% detection rate for positive samples) is 3.0 ng/mL for purified native GDH antigen.

e. Analytical specificity:

Cross reactivity:

To test for cross-reactivity, each micro-organism was diluted in a pool of *C. difficile*-negative stool samples, pretreated and a single replicate was tested using the VIDAS *C. difficile* GDH assay. To test for microbial interference, each micro-organism was diluted in a pool of *C. difficile*-positive stool samples, pretreated and a single replicate was tested using the VIDAS *C. difficile* GDH assay. The micro-organisms were tested at a concentration of $3x10^8$ CFU/mL (1 McFarland) for bacteria and $1x10^5$ PFU/mL for viruses.

None of the following micro-organisms, present in the stool samples, reacted with the VIDAS *C. difficile* GDH assay:

Abiotrophia defectiva, Acinetobacter baumannii, Acinetobacter lwoffii, Aeromonas hydrophila ssp hydrophila, Alcaligenes faecalis ssp faecalis, Anaerococcus tetradius, Bacillus cereus, Bacteroides caccae, Bacteroides merdae, Bacteroides stercoris, Bifidobacterium adolescentis, Bifidobacterium longum, Campylobacter jejuni ssp jejuni, Candida albicans, Candida catenulata, Cedecea davisae, Chlamydia trachomatis, Citrobacter amalonaticus, Citrobacter freundii, Citrobacter koseri, Citrobacter sedlakii, Clostridiuim nexile, Clostridium beijerinckii, Clostridium bifermentans, Clostridium bolteae, Clostridium butyricum, Clostridium chauvoei, Clostridium fallax, Clostridium haemolyticum, Clostridium histolyticum, Clostridium innocuum, Clostridium novyi, Clostridium paraputrificum, Clostridium perfringens, Clostridium ramosum, Clostridium scindens, Clostridium septicum, Clostridium sordellii, Clostridium sphenoides, Clostridium spiroforme, Clostridium sporogenes, Clostridium symbosum, Clostridium tertium, Clostridium tetani, Collinsella aerofaciens, Corynebacterium genitalium, Desulfovibrio piger, Edwardsiella tarda, Eggerthella lenta, Enterobacter aerogenes, Enterobacter cloacae, Enterococcus casseliflavus, Enterococcus cecorum, Enterococcus dispar, Enterococcus faecalis, Enterococcus faecium, Enterococcus gallinarum, Enterococcus hirae, Enterococcus raffinosus, Escherichia coli, Escherichia fergusonii, Escherichia hermannii, Flavonifractor plautii, Fusobacterium varium, Gardnerella vaginalis, Gemella morbillorum, Hafnia alvei, Helicobacter fenneliae, Helicobacter pylori, Klebsiella oxytoca, Klebsiella pneumoniae ssp pneumoniae, Lactobacillus acidophilus, Lactobacillus reuteri, Lactococcus lactis ssp lactis, Leminorella grimontii, Listeria grayi, Listeria innocua, Listeria monocytogenes, Peptoniphilus asaccharolyticus,

Peptostreptococcus anaerobius, Plesiomonas shigelloides, Porphyromonas asaccharolytica, Prevotella melaninogenica, Proteus mirabilis, Proteus penneri, Providencia alcalifaciens, Providencia rettgeri, Providencia stuartii, Pseudomonas aeruginosa, Pseudomonas putida, Salmonella enterica ssp arizonae, Salmonella ser.Choleraesuis, Salmonella ser.Typhimurium Serratia liquefaciens, Serratia marcescens, Shigella boydii, Shigella dysenteriae, Shigella sonnei, Staphylococcus aureus ssp aureus, Staphylococcus epidermidis, Stenotrophomonas maltophilia, Streptococcus agalactiae, Streptococcus dysgalactiae ssp dysgalactiae,Streptococcus intermedius, Streptococcus uberis, Trabulsiella guamensis, Veillonella parvula, Vibrio cholerae, Vibrio parahaemolyticus,Yersinia bercovieri, Yersinia rohdei, Adenovirus 40 et 41, Rotavirus RF, Norovirus, Enterovirus 70, Echovirus 12, Coxsackie virus, Cytomegalovirus AD169.

Interference study:

Potential interference by commonly used drugs and other substances was determined based on the recommendations of the CLSI® EP7-A2, at 2 levels of GDH (a low positive close to the clinical cut-off and a high positive).

Tested compound	**Highest concentration tested**	**Result**
Hemoglobin	3.2 mg/mL	No significant interference
Lipids	20 mg/mL	No significant interference
Mucin	3.33 mg/mL	No significant interference
Amoxicillin	206 µmol/L	No significant interference
Bismuth salicylate	8.2 mg/mL	No significant interference
Calcium carbonate	13.06 mg/mL	Potential interference*
Ceftriaxone	1.46 mmol/L	No significant interference
Benzalkonium chloride	2 µg/mL	No significant interference
Ciprofloxacin	30.2 µmol/L	No significant interference
Erythromycin	81.6 µmol/L	No significant interference
Ethanol	86.8 mmol/L	No significant interference
Fidaxomicin	4 mg/mL	No significant interference
Gentamicin	21 µmol/L	No significant interference
Mineral oil	0.27 v/v	Potential interference*
Hydrocortisone	0.6 mg/mL	No significant interference
Aluminium hydroxide	15.3 mg/mL	No significant interference
Magnesium	6.2 mg/mL	No significant interference

hydroxide		
Lidocaine	0.12 mg/mL	No significant interference
Loperamide	0.08 mg/mL	No significant interference
Mesalazine	19.2 mg/mL	No significant interference
Metronidazole	2 mg/mL	No significant interference
Naproxen	2170 µmol/L	No significant interference
Nystatin	600 UI/mL	No significant interference
Phenylephrine	0.225 mg/mL	No significant interference
Sennosides	0.24 mg/mL	No significant interference
Tergitol (nonoxynol-9)	0.5 v/v	Potential interference*
Tetracycline	34 µmol/L	No significant interference
Vancomycin	5 mg/mL	No significant interference

* Calcium carbonate at 9.80 mg/mL, Mineral oil at 0.20 v/v and Tergitol at 0.125 v/v did not cause interference.

Strain reactivity:

The VIDAS *C. difficile* GDH assay was evaluated using several strains of *C. difficile*. The VIDAS *C. difficile* GDH detects the following *C. difficile* strains at the tested concentrations of $9x10^8$ CFU/mL (3 McFarland) and $3x10^6$ CFU/mL:

Toxinogenic *C.difficile* strains :		Non toxinogenic *C.difficile* strains:
ATCC 43255 ™ ATCC9689 ™ ATCC 700792 ™ ATCC 17858 ™ ATCC BAA–1805 ™ ATCC BAA-1382 ™ ATCC 51695 ™	ATCC 43600 ™ ATCC 43599 ™ ATCC 43596 ™ ATCC 43594 ™ ATCC 17857 ™ ATCC 43598 ™ CCUG 20309	ATCC 700057 ™ ATCC 43593 ™ X1a IS58 X1b R1 1402 ATCC 43601 ™ ($3x10^8$ CFU/mL only)

The VIDAS *C. difficile* GDH detects the following *C.difficile* strains at the tested concentration of $9x10^8$ CFU/mL (3 McFarland):

Cardiff ECDC collection including the following ribotypes	001 (7 strains); 002; 003; 012; 014; 015; 017; 020; 023; 027; 029; 046; 053; 056; 070; 075; 077; 078; 081; 087; 095; 106; 126; 131; VPI 10463; 005; 010; 045; 048; 156; 174.
bioMerieux collection including the following ribotypes	001 (6 strains); 002 (9 strains); 005 (2 strains); 010 (1 strain); 012 (4 strains); 014 (10 strains); 015 (1 strain); 017 (20 strains); 020 (5 strains); 023 (1 strain); 027 (24 strains); 047 (1 strain); 050 (1 strain); 053 (4 strains); 054 (2 strains); 056 (2 strains); 057 (1 strain); 058 (1 strain); 075 (1 strain); 078 (3 strains); 096 (1 strain); 097 (1 strain); 103 (2 strains); 106 (16 strains); 110 (2 strains); 118 (1 strain); 153 (1 strain); 177 (1 strain).

f. Assay cut-off:

The clinical cut-off was established at a Test Value of 0.10. Interpretation according to the Test Value is as follows:

Test Value	Result	Interpretation
< 0.10	Negative	No detectable *C. difficile* GDH antigen.
≥ 0.10	Positive	Presumptive detection of *C. difficile* GDH antigen. The specimen must be tested with additional tests that detect *C. difficile* toxins.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison with a commercially available *C. difficile* GDH assay

One thousand nine hundred and four (1904, 1891 prospective and 13 retrospective) stool samples collected from patients suspected of having *C. difficile* infection (CDI) were tested at three sites (USA and Europe). A single replicate of each sample was tested using VIDAS *C. difficile* GDH on a VIDAS instrument and a commercially available *C. difficile* GDH assay. Data from the study are summarized in the following table:

Method comparison between the VIDAS C. difficile GDH assay and the commercially available C. difficile GDH assay on prospective samples

		Commercially available *C. difficile* GDH assay							
		Site 1 (EU)		Site 2 (US)		Site 3 (US)		Total (All Sites)	
		Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg
VIDAS *C. difficile* GDH	Pos	56	10	92	7	207	69	355	86
	Neg	4	454	2	365	4	621	10	1440
Total		60	464	94	372	211	690	365	1526
Performance		%	**[$CI_{95\%}$]**	%	**[$CI_{95\%}$]**	%	**[$CI_{95\%}$]**	%	**[$CI_{95\%}$]**
Positive Percent Agreement		93.3%	[83.8 – 98.2]%	97.9%	[92.5 – 99.7]%	98.1%	[95.2 – 99.5]%	97.3%	[95.0 – 98.7]%
Negative Percent Agreement		97.8%	[96.1 – 99.0]%	98.1%	[96.2 – 99.2]%	90.0%	[87.5 – 92.1]%	94.4%	[93.1 – 95.5]%

In order to better estimate the performance of the VIDAS *C. difficile* GDH assay in specimens from pediatric patients (2-12 years), thirteen (13) *C. difficile* retrospectively collected samples were tested according to the same protocol. For all 1904 specimens and all sites combined, the VIDAS C. difficile GDH assay demonstrated a positive percent agreement of 97.3% (367/377) with 95%CI: 95.2 – 98.7%, and a negative percent agreement of 94.4% (1441/1527) with 95%CI: 93.1 – 95.5%.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

One thousand nine hundred and four (1904, 1891 prospective and 13 retrospective) stool samples collected from patients suspected of having *C. difficile* infection (CDI) were tested at three sites (USA and Europe). The age groups of the patients range from one year to 100 years. A single replicate of each sample was tested using VIDAS *C. difficile* GDH on a VIDAS instrument. A bacterial culture test was performed for each sample on a CCFA medium according to the instructions for use. Data from the study are summarized in the following tables:

Performance of the VIDAS *C. difficile* GDH assay versus CCFA bacterial culture on prospective samples

		CCFA bacterial culture test							
		Site 1 (EU)		Site 2 (US)		Site 3 (US)		Total (All Sites)	
		Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg
VIDAS *C. difficile* GDH	Pos	42	24	78	21	163	113	283	158*
	Neg	7	451	4	363	2	623	13**	1437
Total		49	475	82	384	165	736	296	1595
Performance		%	**[$CI_{95\%}$]**	%	**[$CI_{95\%}$]**	%	**[$CI_{95\%}$]**	%	**[$CI_{95\%}$]**
Sensitivity		85.7%	[72.8 - 94.1]%	95.1%	[88.0 - 98.7]%	98.8%	[95.7 - 99.9]%	95.6%	[92.6 - 97.6]%
Specificity		94.9%	[92.6 - 96.7]%	94.5%	[91.8 - 96.6]%	84.6%	[81.8 - 87.2]%	90.1%	[88.5 - 91.5]%
Negative Predictive Value (NPV)		98.5%	[96.9 - 99.4]%	98.9%	[97.2 - 99.7]%	99.7%	[98.8 - 99.9]%	99.1%	[98.5 - 99.5]%

* 158 samples were found positive with the VIDAS *C. difficile* GDH assay and negative with the CCFA bacterial culture test, 73 of which were found positive and 85 negative with the commercially available *C. difficile* GDH assay.

**13 samples were found negative with the VIDAS *C. difficile* GDH assay and positive with the CCFA bacterial culture test, 9 of which were found negative and 4 positive with the commercially available *C. difficile* GDH assay.

Out of 2038 patient samples tested with the VIDAS *C. difficile* GDH assay, 21 (1.0%) were reported as invalid.

Testing on retrospective samples

Thirteen (13) retrospectively collected samples from pediatric patients submitted for routine *C. difficile* testing (2-12 years) were assayed for *C. difficile* according to the same protocol. For these 13 retrospective samples alone, the VIDAS *C. difficile* GDH assay demonstrated a sensitivity of 100.0% (10/10) and a specificity of 33.3% (1/3).

Performance of the VIDAS *C. difficile* GDH assay versus CCFA bacterial culture on all prospective and retrospective samples

For all 1904 specimens and all sites combined, the VIDAS *C. difficile* GDH assay demonstrated a sensitivity of 95.8% (293/306) with 95%CI: 92.8 – 97.7%, a specificity of 90.0% (1438/1598) with 95%CI: 88.4 – 91.4%, and a negative predictive value of 99.1% with 95%CI: 98.5 – 99.5%.

Sensitivity and Specificity performances versus CCFA medium by age group on prospective samples

Age Group	VIDAS Positive /CCFA Positive	Sensitivity [CI_{95}] %	VIDAS Negative /CCFA Negative	Specificity [CI_{95}] %
< 2 years	1/1	100.0% [2.5 – 100.0]%	2/2	100.0% [15.8 – 100.0]%
2-12 years	12/12	100.0% [73.5 – 100.0]%	39/44	88.6% [75.4 - 96.2]%
13-21 years	13/13	100.0% [75.3 – 100.0]%	40/45	88.9% [75.9 - 96.3]%
22-59 years	122/125	97.6% [93.1 - 99.5]%	562/632	88.9% [86.2 - 91.3]%
≥ 60 years	135/145	93.1% [87.7 - 96.6]%	794/872	91.1% [89.0 - 92.9]%

For all 69 (56 prospective and 13 retrospective) samples from the 2-12 years pediatric population, the VIDAS *C. difficile* GDH assay demonstrated a sensitivity of 100.0% (22/22) with 95%CI: 84.6 – 100.0%, and a specificity 85.1% (40/47) with 95%CI: 71.7 – 93.8%.

*b. Clinical specificity**:***

See section M3a above.

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

Not applicable.

4. Clinical cut-off**:**

Not applicable

5. Expected values/Reference range:

The following table summarizes the expected (observed) values for the studies performed with the VIDAS GDH Assay using a population of 1891 prospectively collected specimens submitted to the laboratory on suspicion of CDI. This population was 41.2% male, 58.8% female with a mean age of 58 years. The VIDAS GDH test values ranged from 0.00 to 7.98 with overall positivity rate of 23.3% and overall negativity rate 76.7%.

Age Group	N	Age (Mean)	Male (%)	Female (%)	Test Values Range	Positive Results (%)	Negative Results (%)
<2 years	3	1	66.7	33.3	(0.00 – 5.55)	33.3%	66.7%
2-12 years	56	6	48.2	51.8	(0.00 – 7.77)	30.4%	69.6%
13-21 years	58	17	48.3	51.7	(0.00 – 6.91)	31.0%	69.0%
22-59 years	757	44	41.6	58.4	(0.00 – 7.98)	25.4%	74.6%
≥ 60 years	1017	73	40.0	60.0	(0.00 – 7.63)	20.9%	79.1%
All	1891	58	41.2	58.8	(0.00 – 7.98)	23.3%	76.7%

N. Instrument Name:

The VIDAS and miniVIDAS instruments.

O. System Descriptions:

1. Modes of Operation:

   The VIDAS instrument (K891385) was cleared in 1989. The VIDAS instrument is attached to a computer and printer. Each instrument has five independent sections allowing five different assays to be run simultaneously. Each section can process up to six samples. Therefore, a fully loaded VIDAS can process thirty samples. A smaller compact version of the VIDAS instrument, appropriately called the miniVIDAS, was cleared under K923579 in 1993. The miniVIDAS instrument has a built-in computer, keyboard and printer. Two independent sections each accept six tests and can process up to twelve samples simultaneously. Each FDA cleared VIDAS assay can be run on either the VIDAS or the miniVIDAS instrument.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes X or No _____

3. Specimen Identification:

   All assay steps are controlled automatically by the instrument. The sample is transferred into the wells. The STR strip consists of ten wells covered with labeled foil seal. The label comprises a bar code which indicates the assay code, kit lot number and expiration date.

4. Specimen Sampling and Handling:

   The solid phase receptor (SPR) serves as both the solid phase and the pipetting device. The foil of the first well is perforated to allow introduction of the sample. The last well (well ten) of each strip is a cuvette in which the fluorometric reading is performed. The center wells of the strip contain the various reagents required for the assay.

5. Calibration:

   The kit contains a GDH standard (S1), a positive control (C1) and a negative control (C2). Each calibration must be checked using these controls. Calibration should be performed with each new lot of reagents and then every 28 days.

6. Quality Control:

   The kit contains a Master Lot Entry card (MLE) which contains specifications for the factory master data required to calibrate the test. Data from the MLE card is entered into the instrument before each new lot of reagents is used. Calibration provides instrument-specific information and compensates for possible minor variations in assay signal throughout the shelf-life of the kit.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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