

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

K080931

B. Purpose for Submission:

To determine substantial equivalence of the device for the detection of *C. difficile* A & B in stool specimens. This an Intended Use claim extension to K072138

C. Measurand:

C. difficile toxins A & B

D. Type of Test:

Qualitative automated test on the VIDAS instrument using the enzyme linked fluorescent assay (ELFA) technique

E. Applicant:

bioMerieux Inc.

F. Proprietary and Established Names:

VIDAS *C. difficile* Toxin A & B (CDAB) assay

G. Regulatory Information:

1. Regulation section:

21 CFR 866.2660, reagents, *Clostridium difficile* toxin

2. Classification:

Class 1

3. Product code:

LLH

4. Panel:

H. Intended Use:1. Intended use:

The VIDAS C. difficile Toxin A & B (CDAB) assay is an automated test for use on the VIDAS instruments for the qualitative detection of Clostridium difficile toxin A and toxin B in stool specimens using the ELFA technique (Enzyme-Linked Fluorescent Assay). The VIDAS C. difficile toxin A & toxin B (CDAB) assay is an aid for diagnosing Clostridium difficile associated disease (CDAD).

2. Indication for use:

The VIDAS C. difficile Toxin A & B (CDAB) assay is an automated test for use on the VIDAS instruments for the qualitative detection of Clostridium difficile toxin A and toxin B in stool specimens using the ELFA technique (Enzyme-Linked Fluorescent Assay). The VIDAS C. difficile toxin A & toxin B (CDAB) assay is an aid for diagnosing Clostridium difficile associated disease (CDAD).

3. Special conditions for use statement:

For prescription use

4. Special instrument requirements:

The VIDAS Instruments

I. Device Description:

The VIDAS CDAB kit is now indicated for use as an aid for diagnosing Clostridium difficile associated disease (CDAD). No changes were made to the predicate device. The VIDAS CDAB kit consists of 60 ready to use reagent strips and 60 ready to use solid phase receptacles (SPRs) whose interiors are coated with C. difficile rabbit polyclonal anti-toxin A and mouse monoclonal anti-toxin B antibodies. It also contains one standard (S1), one positive control Toxin A (C1), one negative control (C2), one positive control Toxin B (C3), one sample diluent (R1) and one MLE card containing the factory master calibration data required to calibrate the test.

J. Substantial Equivalence Information:1. Predicate device name:

VIDAS CDAB Assay

2. Predicate K number:

K0721383. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For the qualitative detection of C.difficile toxins A & B	Same
Specimen	Stool	Same
Assay technique	Automated Enzyme-Linked Fluorescent Assay (ELFA)	Same
Capture and detection antibodies	Rabbit polyclonal and mouse monoclonal	Same
Conjugate	Mouse monoclonal antibodies conjugated with biotin	Same
Sample volume	200µl liquid stool 200 mg semi-solid stool	Same
Assay time	~ 75 mins	Same
Limit of detection	Toxin A ≥ 7.73 ng/ml Toxin B > 4.55 ng/ml	Same

Differences		
Item	Device	Predicate
Extended claim	As an aid in the diagnosis of CDAD	No claim for CDAD

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

1. "Review criteria for devices assisting in the diagnosis of C. difficile associated diseases" ODE guidance 5/31/1990
2. "Protocols for determination of limits of detection and limits of quantitation." Approved guideline CLSI EP 17-A, Vol. 24, No. 34

L. Test Principle:

The assay principle combines a two-step immunoassay sandwich method with a final fluorescent detection (ELFA). The SPR, a pipette tip-like device serves as the solid phase as well as the pipetting device for the assay. Assay reagents are ready to use and pre dispensed in the sealed reagent strips. Each of four reaction steps is

performed automatically by the VIDAS. The sample/conjugate mixture is cycled in and out of the SPR several times. Each step is followed by a wash cycle which eliminates unbound components. Step 1: Toxin A and/or B present in the sample binds with the anti-toxin A & B antibodies coated on the interior wall of the SPR. Step 2: Binding occurs between toxins and antibodies conjugated with biotin. Step 3: Presence of biotin is detected by incubation with streptavidin conjugated with alkaline phosphatase. Step 4: Two detection steps are performed successively. Alkaline phosphatase catalyzes hydrolysis of the substrate into a fluorescent product. Fluorescence is measured at 450 nm. Results are automatically calculated by the VIDAS. Test values as well as the qualitative result (positive, negative or equivocal) are provided on the result sheet for each sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Six pools of samples namely two negative, two equivocal, three positive (low, medium and high) were tested in duplicate in two runs per day over six days at each of three sites. Total precision was 7.4 – 37.6% C.V. intra- assay precision was 2.9 – 26.3% C.V. and inter-assay precision was 6.8 – 26.8% C.V.

b. Linearity/assay reportable range:

N/A

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

Stability studies were performed to determine the stability of the kit, specimen, standard, and control.

d. Detection limit:

The detection limit for Toxin A is $\geq 7.73\text{ng/ml}$ and for Toxin B $\geq 4.55\text{ng/ml}$

e. Analytical specificity:

Cross-reactivity and interference studies were performed in the original submission. No changes were made from the predicate device. An additional interference study was conducted to evaluate the potential interference of anti-diarrhea as well as therapeutic drugs. No interference was observed with vancomycin at 5mg/ml; metronidazole at 2mg/ml; Pepto-Bismol and Imodium liquid and tablets as well as their active ingredients Loperamide, bismuth subsalicylate and salicylate.

f. Assay cut-off:

The assay cut off is as follows:

Test value <0.13 is a negative result; test value ≥ 0.13 to <0.37 is equivocal and test value ≥ 0.37 is a positive result. The test value is equal to the patient relative fluorescence value/ standard relative fluorescence value.

2. Comparison studies:

a. Method comparison with predicate device:

The VIDAS CDAB assay was compared to a commercial EIA at two clinical testing sites. At site one, 623 samples were tested and at site two, 388 samples were tested. Results from both sites were as follows:

Positive agreement 81.3% (73.4 – 87.6 % C.I.)

Negative agreement 99.5% (98.8 – 99.9% C.I.)

Overall agreement 97.1% (95.9 – 98.1% C.I.)

Forty-two samples were found equivocal and calculations were done with the equivocal samples considered first as negative and then as positive. Results from both sites were as follows:

When equivocal samples were considered as negative, positive agreement was 75.9% (67.9 – 82.8% C.I.) and negative agreement was 99.5% (98.8 - 99.9 % C.I.). Overall agreement was 96.3% (95.0 – 97.4 % C.I.). When equivocal samples were considered as positive, positive agreement was 82.5% (75.1 – 88.4 % C.I.) and negative agreement was 95.8% (94.2 – 97.0 % C.I.). Overall agreement was 94.0% (92.3 – 95.4% C.I.).

b. Matrix comparison:

N/A

3. Clinical studies:

a. Clinical Sensitivity:

There were 1011 fresh stool specimens collected from two sites (USA and Europe) and tested in house by both cellular cytotoxicity assay (CTA) and the VIDAS CDAB Assay. Results were as follows: Sensitivity 88.3% (81.2-93.5 % C.I.); Specificity 99.8% (99.2 99.9% C.I.); PPV 98.1% (93.5-99.8% C.I.); NPV 98.4% (97.3 – 99.1% C.I.). An additional clinical study was performed

to compare the VIDAS CDAB assay to CTA testing at an outside reference lab. The samples were 90 frozen stool specimens and the results were as follows: Sensitivity 88.0% (68.8 – 97.5% C.I.); Specificity 95.1% (86.3 – 99.0% C.I.

b. Clinical Specificity:

Specificity 99.8% (99.2-99.9% C.I.); PPV 98.1% (93.5-99.8% C.I.); NPV 98.4% (97.3 – 99.1% C.I.). See 3(a)

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

N/A

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

Data provided from the literature showed that the frequency of stools with positive toxins was 9.5% from 136 hospitals in North America and 13.2 – 17.2 % from 380 hospitals in Canada. The Society for HealthCare Epidemiology of America (SHEA) reported rates of 17 to 60 cases per 100,000 bed-days.

N. Instrument Name:

The VIDAS PC and the miniVIDAS

O. System Descriptions:

1. Modes of Operation:

The VIDAS PC instrument cleared in 1989 under K891385 is attached to a computer and a printer. Each instrument has 5 independent sections allowing 5 different assays to be run simultaneously. Each section can process up to six samples. When fully loaded it can process 30 samples. The miniVIDAS is a smaller compact version of the VIDAS PC and was cleared under K923579 in 1993. It has a built in computer, keyboard and printer and is popular in POL's. Two independent sections each accept six tests so twelve samples can be processed simultaneously. The VIDAS assay can be run on either instrument.

2. Software:

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

Yes _____ or No X

3. Specimen Identification:

All assay steps are controlled automatically by the instrument. The sample is transferred into the wells. The CDAB 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 1st well is perforated to allow introduction of the sample into well 1. The last well (well 10) 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 standard S1. It is a dilution of recombinant toxin A from *C. difficile* in TRIS buffered saline and BSA 5% and preservatives. It also contains 3 controls. C1 is positive control Toxin A, C2 is the negative control and C3 is positive control Toxin B.

6. Quality Control:

The Master curve is established at time of manufacture for each lot of reagents. It is provided with each test kit and is entered into the VIDAS instrument using the Master Lot Entry card (MLE) included in the kit. Data from the MLE card is entered once for each lot of reagents. Each lab establishes its own calibration curve (recalibration) based on the mathematical master curve data and the test results of two calibrators tested in duplicate by the lab. Recalibration serves to control for minor variations in assay signal from one VIDAS instrument to another and is therefore specific for each instrument.

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

For the VIDAS CDAB assay, validation tests were performed on both the miniVIDAS and VIDAS PC instruments and no anomalies were detected. Defined acceptance criteria were met as a result of the validation studies demonstrating conformance and satisfactory performance with the miniVIDAS instrument.

Q. Proposed Labeling:

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

R. Conclusion:

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