510(K) Summary

DEC 5 2012

510(k) Number:

K123197: Verigene® *Clostridium difficile* Nucleic Acid Test (CDF)

Summary Preparation Date:

November 27, 2012

Submitted by:

Nanosphere, Inc.
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Contact:

Mark A. Del Vecchio
Vice President, Regulatory Affairs

Proprietary Names:

For the instrument:

Verigene® System

For the assay:

Verigene® *Clostridium difficile* Nucleic Acid Test (CDF)

Common Names:

For the instrument:

Bench-top molecular diagnostics workstation

For the assay:

Clostridium difficile Nucleic Acid Test
Clostridium difficile identification and differentiation system
C. difficile assay
C. diff test

Regulatory Information:

Regulation section:

866.3130

Classification:

Class II

Panel:

Microbiology (83)

Product Code(s):

OZN *Clostridium difficile* toxin gene amplification assay

Other codes used by predicate devices:

OMN *C. difficile* nucleic acid test assay
LLH Reagents, *Clostridium Difficile* toxin
OCC Respiratory Virus Panel Nucleic Acid System
NSU Instrumentation for clinical multiplex test systems

Predicate Devices:

Portrait Toxigenic C. *Difficile* Assay (K113358) (Great Basin Scientific)

Xpert *C. difficile/Epi* Assay (K110203) (Cepheid)

Verigene RVNAT$_{SP}$ Test (K092566) (Nanosphere)

Indications for Use:

The **Verigene® *Clostridium difficile* Nucleic Acid Test (CDF)** is a qualitative multiplexed *in vitro* diagnostic test for the rapid detection of toxin A (*tcdA*), toxin B (*tcdB*), and *tcdC* gene sequences of toxigenic *Clostridium difficile* and for presumptive identification of PCR ribotype 027 strains from unformed (liquid or soft) stool specimens collected from patients suspected of having *C. difficile* infection (CDI). Presumptive identification of the PCR ribotype 027 strain of *C. difficile* is by detection of the binary toxin (*cdt*) gene sequence and the single base pair deletion at nucleotide 117 in the *tcdC* gene. The *tcdC* gene encodes for a negative regulator in *C. difficile* toxin production. The test is performed on the Verigene System and utilizes automated specimen preparation and polymerase chain reaction (PCR) amplification, combined with a nanoparticle-based array hybridization assay to detect the toxin gene sequences associated with toxin-producing *C. difficile*.

The CDF Test is indicated for use as an aid in the diagnosis of CDI. Detection of PCR ribotype 027 strains of *C. difficile* by the CDF Test is solely for epidemiological purposes and is not intended to guide or monitor treatment for *C. difficile* infections. Concomitant culture is necessary only if further typing or organism recovery is required.

Technological Characteristics:

The Verigene *C. difficile* Nucleic Acid Test (CDF) is a molecular assay which relies on detection of specific nucleic acid targets in a microarray format. For each of the bacterial nucleic acid sequences detected by CDF, unique Capture and Mediator oligonucleotides are utilized, with gold nanoparticle probe-based endpoint detection. The Capture oligonucleotides are covalently bound to the microarray substrate and hybridize to a specific portion of the nucleic acid targets. The Mediator oligonucleotides have a region which bind to a different portion of the same nucleic acid targets and also have a sequence which allows binding of a gold nanoparticle probe. Specific silver enhancement of the bound gold nanoparticle probes at the capture sites results in gold-silver aggregates that scatter light with high efficiency and provide accurate detection of target capture.

The CDF Test is performed on the Verigene System, a "sample-to-result", fully automated, bench-top molecular diagnostics workstation. The System enables automated nucleic acid extraction from unformed stool specimens (liquid or soft) and detection of bacterial-specific target DNA. The Verigene System consists of two components: the Verigene Reader and the Verigene Processor *SP*.

The Reader is the Verigene System's user interface, which serves as the central control unit for all aspects of test processing, automated imaging, and result generation using a touch-screen control panel and a barcode scanner. The Verigene Processor *SP* executes the test procedure, automating the steps of (1) Sample Preparation and Target Amplification – cell lysis and magnetic bead-based bacterial DNA isolation and amplification, and (2) Hybridization–detection and identification of bacterial-specific DNA in a microarray format by using gold nanoparticle probe-based technology. Once the specimen is loaded by the operator, all other fluid transfer steps are performed by an automated pipette that transfers reagents between wells of the trays and finally loads the specimen into the Test Cartridge for hybridization. Single-use disposable test consumables and a self-contained Verigene Test Cartridge are utilized for each sample tested with the CDF assay.

To obtain the test results after test processing is complete, the user removes the Test Cartridge from the Processor *SP*, and inserts the substrate holder into the Reader for analysis. Light scatter from the capture spots is imaged by the Reader and intensities from the microarray spots are used to make a determination regarding the presence (Detected) or absence (Not Detected) of a bacterial nucleic acid sequence/analyte. This determination is made by means of software-based decision algorithm resident in the Reader.

Performance Data - Analytical Testing

Analytical Sensitivity / Limit of Detection (LoD)

Analytical sensitivity (LoD) of the CDF Test was determined for seven strains of *C. difficile*, representing all major toxinotypes found in North America and including two PCR Ribotype 027 strains. The LoD was defined as the concentration at which the test produces a positive result greater than 95% of the time. Serial dilutions of the strains were tested and the putative LoD confirmed with 20 replicates. The LoDs for the seven strains are shown in the table below and ranged from 63 to 1250 CFU/ml of stool. Thus, the study established the overall limit of detection of the CDF Test to be 1250 CFU/ml of organism present in stool.

Strain Designation (Source ID)	*Toxinotype*	*Calculated CFU/mL Stool at LoD*	*CFU per CDF Test at LoD*	*LoD Confirmation Results*
ATCC BAA-1805	III	250	5	20/20
ATCC 43255 (VPI 10463)	0	63	1.25	20/20
ATCC BAA-1875 (5325)	V	500	10	20/20
CDC 2007858	IX/XXIII	1250	25	20/20
CDC 2009087	0	1250	25	20/20
CDC 2009292	III	1250	25	20/20
ATCC 43598 (1470)	VIII	250	5	20/20

Analytical Reactivity (Inclusivity)

Analytical reactivity of the CDF Test was demonstrated with a comprehensive panel of sixty-three (63) independently-confirmed *C. difficile* strains, tested in triplicate at three times the LoD (i.e. 3,750 CFU/mL). The panel was comprised of a wide range of toxinotypes, including toxinotypes 0, I, IV, V, VIII, IX, X, XI, XII, XXI, XXII, IX/XXIII, XIV/XV, and six (6) PCR ribotype 027 strains (toxinotype III).

All tests correctly reported the expected results for the detection of gene sequences for toxigenic *C. difficile* and for presumptive PCR ribotype 027, with one exception. Strain CDC 2009048 strain, classified by the CDC as Toxinotype XIV/XV, is associated with non-027 strains (Ribotypes 111/122). However, the Verigene CDF Test reported detection of the *tcdA*, *tcdB*, binary and *tcdC*-MUT targets as would be expected for a PCR ribotype 027 strain. Subsequent sequencing of the *tcdC* gene verified the presence of the Δ117 deletion.

Analytical Specificity (Cross-reactivity)

Ninety-four (94) microorganisms, including two (2) non-toxigenic C. difficile strains and fourteen (14) non *C. difficile* Clostridium species, along with one human cell line, were tested with the CDF Test to determine analytical specificity. In addition, the cross-reactivity of *Clostridium botulinum* was evaluated by *in silico* analysis.

Each bacterial strain was prepared in Negative Stool Matrix and tested in triplicate in concentrations of 5×10^6 CFU/mL stool. Two (2) organisms, *Cryptosporidium parvum* and *Giardia lamblia*, were tested using genomic DNA at a concentration of 1×10^6 copies of gDNA. For the viruses, Echovirus 11 and Coxsackievirus were tested at 5×10^5 PFU/mL stool. Adenovirus, Enterovirus, Cytomegalovirus and Rotavirus were also tested using genomic DNA or RNA at a concentration of 1×10^6 copies per reaction. Noroviruses were tested as clinical samples.

Analytical specificity was observed to be 100%, including that determined by *in silico* analysis.

Microbial Interference

Microorganisms that may be encountered in clinical stool samples, but not detected by the CDF Test, were tested in this study to evaluate the potential for microbial interference.
The CDF Test was tested against the same ninety-five (95) organisms/cell line that were used for analytical specificity, at the same medically relevant concentrations, using two strains of toxigenic *C. difficile* (ATCC BAA-1805 [toxinotype III] and ATCC 43255 [toxinotype 0]) at 1.5x LoD and 3x LoD, respectively.

No interference was observed with the CDF Test for any of the samples tested.

Interference

Thirty-four (34) products/exogenous substances (shown in the following table) that are possibly encountered in stool samples were evaluated for potential inhibitory effects with the CDF Test. Each interfering substance was evaluated at its "worst case" concentration, against two *C. difficile* strains (ATCC BAA-1805, ATCC 43255). Additionally, Cary-Blair media was tested. None of the thirty four (34) substances or the Cary-Blair media tested in this study showed any inhibitory effect on the detection of *C. difficile* using the CDF Test.

Stearic Acid	Preparation H® Hemorrhoidal Ointment	Aluminum Hydroxide, Reagent Grade
Palmitic Acid	Walgreens Enema Mineral Oil Laxative	Mesalazine
Whole Blood	Options Conceptrol® Vaginal Contraceptive Gel	Immodium® AD Anti-Diarrheal
Nasopharyngeal Swab Sample in Universal Transport Media (UTM)	Dulcolax® Laxative Suppositories	Pepto-Bismol Max Strength
Nystatin Suspension	Dimenhydrinate	Ex-lax® Maximum Strength Stimulant Laxative
Monistat® 3	Neosporin® First Aid Antibiotic Ointment	Vancomycin
Preparation H® Medicated Wipes	Wet Ones® Antibacterial Hand Wipes	Metronidazole Topical Cream (0.75%)
Vagisil Anti-Itch Crème Maximum Strength	K-Y® Personal Lubricant Jelly	Naproxen Sodium
Preparation H® Anti-Itch Hydrocortisone 1%	Vaseline Original 100% Pure Petroleum Jelly	Mucin from bovine submaxillary glands, Type I-S (Dehydrated)
Desitin Maximum Strength Original Paste	Sarna Anti-Itch Lotion, Sensitive	Barium Sulfate
Gaviscon® Extra Strength Liquid Antacid	Bile, bovine, dried, unfractioned	Cary-Blair Medium
Phillips'® Genuine Milk of Magnesia Saline Laxative	Tums® Antacid with Calcium Extra Strength 750	

Carry-over / Cross-contamination

The potential for carry-over and cross-contamination of the CDF Test on the Verigene system was assessed by alternately testing a high positive *C. difficile* sample (toxigenic & ribotype 027 *Clostridium difficile* strain BAA-1805) at $5x10^6$ CFU/mL, followed by testing a negative sample, comprising only of CDF-Negative Stool Matrix. The high-titer sample was alternated with the negative sample three times on three unique Verigene *SP* Processors, for a total of eighteen individual tests. No carry-over or cross-contamination was observed.

Cutoff Verification

Analytical testing of 59 strains of *C. difficile*, comprising a range of toxinotypes and non-toxinogenic strains, were performed in duplicate with the CDF Test to verify the cut off values of the two-tiered filter algorithm. Using the established cut-off levels for the assay, the CDF Test correctly detected the expected analytes for all the verification samples.

Performance Data - Clinical Testing

Precision

The precision study was conducted in-house by Nanosphere, during which a seven-member Precision Study Sample Panel was tested in duplicate twice daily by two operators for twelve non-consecutive days. This testing regime generated a total of 48 replicates per specimen and an overall total of 336 data points.

The seven sample panel was comprised of two different strains (ATCC 43255 and ATCC BAA-1805) at three different concentrations (six positive samples) and one negative sample. This panel included for each strain, a "High Negative" sample, which would be expected to produce a negative result approximately 20% to 80% of the time, a "Low Positive" sample, which would

be expected to produce a positive result approximately 95% of the time, and a "Moderate Positive" sample, which would be expected to yield a positive result approximately 100% of the time. Results are summarized below.

Panel Member	***Strain***	***Level***	***Expected Occurrence***	***Total Agreement with Expected Result****
1	CDF Negative Stool Matrix	Negative	~100% Negative	100% 48/48 (92.6–100%)
2	Toxigenic Wild Type *C. difficile*	Moderate Positive (MP)	~100% Positive	100% 48/48 (92.6–100%)
3	Toxigenic Wild Type *C. difficile*	Low Positive (LP)	~95% Positive	97.9% 47/48 (88.9–100%)
4	Toxigenic Wild Type *C. difficile*	High Negative (HN)	~20-80% Negative	12.5% 6/48 (4.7–25.3%)
5	Toxigenic Hypervirulent *C. difficile*	Moderate Positive (MP)	~100% Positive	100% 48/48 (92.6–100%)
6	Toxigenic Hypervirulent *C. difficile* '	Low Positive (LP)	~95% Positive	95.8% 46/48 (85.6–99.5%)
7	Toxigenic Hypervirulent *C. difficile*	High Negative (HN)	~20-80% Negative	20.8% 10/48 (10.5–35.0%)

Reproducibility

The inter-laboratory reproducibility of the CDF was determined by conducting a reproducibility study at three external sites. Seven samples were tested daily in triplicate by two (2) operators for five (5) non-consecutive days at three (3) sites for a total of ninety (90) tests per sample (3 sites x 2 operators / site x 3 replicates / operator x 5 days = 90 tests per sample). The study tested a total of 630 samples.

The seven (7) sample panel for the reproducibility study was the same panel described previously for the precision study, comprised of two (2) different strains at three (3) different concentrations (six positive samples) and one (1) negative sample. The results of the Reproducibility Study are provided in the table below.

Panel Member	*Strain*	*Level*	*Expected Occurrence*	*Total Agreement with Expected Result* (95% CI)*			
				Site 1	*Site 2*	*Site 3*	*Total*
1	CDF Negative Stool Matrix	Negative	~100% Negative	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 90/90 (96.0–100)
2	Toxigenic Wild Type *C. difficile*	Moderate Positive (MP)	~100% Positive	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 90/90 (96.0–100)
3	Toxigenic Wild Type *C. difficile*	Low Positive (LP)	~95% Positive	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 90/90 (96.0–100)
4	Toxigenic Wild Type *C. difficile*	High Negative (HN)	~20-80% Negative	30% 9/30 (14.7–49.4)	33.30% 10/30 (17.3–52.8)	16.70% 5/30 (5.6–34.7)	26.70% 24/90 (17.9–37.0)
5	Toxigenic Hypervirulent *C. difficile*	Moderate Positive (MP)	~100% Positive	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 30/30 (88.4–100)	100% 90/90 (96.0–100)
6	Toxigenic Hypervirulent *C. difficile*	Low Positive (LP)	~95% Positive	96.70% 29/30 (82.8–99.9)	96.70% 29/30 (82.8–99.9)	100% 30/30 (88.4–100)	97.80% 88/90 (92.2–99.7)
7	Toxigenic Hypervirulent *C. difficile*	High Negative (HN)	~20-80% Negative	36.70% 11/30 (19.9–56.1)	40.00% 12/30 (22.7–59.4)	30.00% 9/30 (14.7–49.4)	35.60% 32/90 (25.7–46.4)

Method Comparison

The performance characteristics of the CDF Test were determined in a multi-site prospective investigation study at five U.S. institutions by comparing the Verigene CDF Test results to reference culture followed by cell cytotoxicity testing on the isolates and strain typing on the toxigenic strains by PCR Ribotyping and Bi-Directional Sequencing methods.

Subjects included individuals whose routine care called for *C. difficile* testing. A portion of each leftover unformed stool specimen was obtained for testing with the CDF Test. In parallel to Verigene CDF Testing, an aliquot of the same specimen was sent to a central laboratory for reference culture and cytotoxin B isolate testing. Each stool specimen was inoculated onto pre-reduced CCFA-D (cycloserine-cefoxitin-fructose agar-direct plate) and CCMB-Tal (cycloserine cefoxitin mannitol broth with taurocholate lysozyme cysteine). After 24 hours the CCMB-TAL was subcultured onto a second CCFA-E plate (CCFA-Enriched). The direct culture method is referred to hereafter as the "direct culture" and the enriched culture method is referred to hereafter as the "enriched culture".

If *C. difficile* was isolated from the CCFA-D plate and the isolate was positive by the cell cytotoxicity assay, the specimen was classified as "toxigenic *C. difficile* positive" and the CCFA-E plate was not further analyzed. If no *C. difficile* was isolated from the CCFA-D plate or if the isolate was negative by the cell cytoxicity assay, the CCFA-E plate was further analyzed.

If CCFA-E was positive for *C. difficile* and the isolate was positive for cell cytotoxicity assay, the specimen was classified as "toxigenic *C. difficile* positive". The specimen was reported as "negative" if CCFA-E was negative for *C. difficile* or the isolate was tested negative by the cell cytotoxicity assay.

Following central site culture testing, the toxigenic *C. difficile* positive isolates were sent for strain identification by PCR Ribotyping at an external third-party site. In addition to conventional agarose-gel electrophoresis, for added discrimination, PCR products were analyzed using the Agilent 2100 Bioanalyzer with the strain type assignment based on a comparison of isolate sizing profiles with known *C. difficile* reference strains. The strains were designated into two PCR Ribotyping categories, 027 and non-027.

In parallel, following central culture testing, CDF Test extracted DNA from the culture-confirmed *C. difficile* positive isolates or the DNA extracted during the PCR Ribotyping were sent for *tcdC* Bi-Directional Sequencing. Sequencing templates were prepared by PCR amplification of the stored DNA using sequencing primers. The same set of primers was also used for sequencing the amplified material. The PCR primers were designed from conserved regions based on multiple sequence alignments of all available sequence entries for each target in GenBank at the time of this study.

The clinical performance of the CDF Test was evaluated against four basic metrics, consisting of the combination of two reference methods for the detection of toxigenic *C. difficile* and two reference methods for the detection of the 027 (hypervirulent) strain of *C. difficile*: 1) Direct Culture and PCR Ribotyping, 2) Enriched Culture and PCR Ribotyping, and 3) Direct Culture

and Bidirectional Sequencing, and 4) Enriched Culture and Bidirectional Sequencing. The overall performance of the CDF Test evaluated against these metrics is summarized in **Table 1**.

Table 1: Summary of Overall CDF Test Clinical Performance n=1875

	Toxigenic C. difficile					*Toxigenic C. difficile / 027 Strain*				
						Agreement				
	Sensitivity (95% CI)	*Specificity* (95% CI)	*Accuracy* (95% CI)	*PPV* (95% CI)	*NPV* (95% CI)	*POS* (95% CI)	*NEG* (95% CI)	*Total* (95% CI)	*PPV* (95% CI)	*NPV* (95% CI)
Direct Culture & PCR Ribotyping[a]	98.7% 154/156 (95.5-99.8)	87.6% 1500/1713 (85.9-89.1)	88.5% 1654/1869 (87.0-89.9)	42.0% 154/367 (36.9-47.2)	99.9% 1500/1502 (99.5-99.9)	97.5% 39/40 (86.8-99.9)	97.8% 1787/1828 (97.0-98.4)	97.7% 1826/1869 (96.9-98.3)	48.2% 39/81 (36.9-59.5)	99.9% 1787/1788 (99.7-100)
Enriched Culture & PCR Ribotyping[a]	91.8% 247/269 (87.9-94.8)	92.5% 1480/1600 (91.1-93.7)	92.4% 1727/1869 (91.1-93.6)	67.3% 247/367 (62.2-72.1)	98.5% 1480/1502 (97.8-99.1)	91.4% 53/58 (81.0-97.1)	98.5% 1783/1811 (97.8-99.0)	98.2% 1836/1869 (97.5-98.8)	65.4% 53/81 (54.0-75.7)	99.7% 1783/1788 (99.4-99.9)
Direct Culture & BDS[b]	98.7% 156/158 (95.5-99.9)	87.5% 1500/1715 (85.8-89.0)	88.4% 1656/1873 (86.9-89.8)	42.1% 156/371 (37.0-47.3)	99.9% 1500/1502 (99.5-100)	97.7% 42/43 (87.7-99.9)	97.8% 1790/1830 (97.0-98.4)	97.8% 1832/1873 (97.0-98.4)	51.2% 42/82 (39.9-62.4)	99.9% 1790/1791 (99.7-100)
Enriched Culture & BDS[b]	91.9% 251/273 (88.1-94.9)	92.5% 1480/1600 (91.1-93.7)	92.4% 1731/1873 (91.1-93.6)	67.7% 251/371 (62.6-72.4)	98.5% 1480/1502 (97.8-99.1)	93.7% 59/63 (84.5-98.2)	98.7% 1787/1810 (98.1-99.2)	98.6% 1846/1873 (97.9-99.1)	72.0% 59/82 (60.9-81.3)	99.8% 1787/1791 (99.4-99.9)

[a] Of the 1,875 specimens evaluated, six specimens were culture positive but were not PCR-ribotyped because the isolate was either not sent or the result was inconclusive. These six specimens were not included in the performance characteristics above.

[b] Of the 1,875 specimens evaluated, two specimens were culture positive but were not sequenced because the isolate was either not sent or the result was inconclusive. These two specimens were not included in the performance characteristics above.

Substantial Equivalence

The Verigene *C. difficile* Nucleic Acid Test (CDF) is as safe and effective as the combination predicate consisting of the Cepheid Xpert *C. difficile/Epi* Assay, the Great Basin Scientific Portrait *C. difficile* assay and the Nanosphere Verigene RVNAT$_{SP}$. CDF has similar intended use and indications, performance characteristics and principles of operation as Cepheid's Xpert *C. difficile/Epi* Assay and Great Basin Scientific's Portrait *C. difficile* assay. CDF has similar technological characteristics as Nanosphere's Verigene RVNAT$_{SP}$. The minor differences between CDF and its predicate devices raise no new issues of safety or effectiveness. Performance data demonstrate that the CDF is as safe and effective as the predicate devices. Thus, CDF is substantially equivalent.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

DEC 5 2012

Nanosphere, Inc.
Mr. Mark A. Del Vecchio
4088 Commercial Avenue
Northbrook, IL 60062

Re: K123197

Trade/Device Name:	Verigene® *Clostridium difficile* Nucleic Acid Test (CDF)
Regulation Number:	21 CFR 866.3130
Regulation Name:	*C. Difficile* Nucleic Acid Amplification Test Assay
Regulatory Class:	Class II
Product Code:	OZN
Dated:	October 10, 2012
Received:	October 11, 2012

Dear Mr. Del Vecchio:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

4. Indications for Use Statement

510(k) Number (if known): K123197

Device Name: Verigene® *Clostridium difficile* Nucleic Acid Test (CDF) on the Verigene® System

The **Verigene® *Clostridium difficile* Nucleic Acid Test (CDF)** is a qualitative multiplexed *in vitro* diagnostic test for the rapid detection of toxin A (*tcdA*), toxin B (*tcdB*), and *tcdC* gene sequences of toxigenic *Clostridium difficile* and for presumptive identification of PCR ribotype 027 strains from unformed (liquid or soft) stool specimens collected from patients suspected of having *C. difficile* infection (CDI). Presumptive identification of the PCR ribotype 027 strain of *C. difficile* is by detection of the binary toxin (*cdt*) gene sequence and the single base pair deletion at nucleotide 117 in the *tcdC* gene. The *tcdC* gene encodes for a negative regulator in *C. difficile* toxin production. The test is performed on the Verigene System and utilizes automated specimen preparation and polymerase chain reaction (PCR) amplification, combined with a nanoparticle-based array hybridization assay to detect the toxin gene sequences associated with toxin-producing *C. difficile*.

The CDF Test is indicated for use as an aid in the diagnosis of CDI. Detection of PCR ribotype 027 strains of *C. difficile* by the CDF Test is solely for epidemiological purposes and is not intended to guide or monitor treatment for *C. difficile* infections. Concomitant culture is necessary only if further typing or organism recovery is required.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) and/or Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K123197