November 22, 2017

GenePOC Inc.
Guy Sevigny
Senior Regulatory Affairs Specialist
360 rue Franquet
Quebec, G1P 4N3 Ca

Re: K172569
Trade/Device Name: GenePOC CDiff
Regulation Number: 21 CFR 866.3130
Regulation Name: *Clostridium difficile* toxin gene amplification assay
Regulatory Class: Class II
Product Code: OZN
Dated: August 25, 2017
Received: August 25, 2017

Dear Guy Sevigny:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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 and Part 809); 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.

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.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Steven R. Gitterman -S for

Uwe Scherf, Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K172569

Device Name
GenePOC CDiff

Indications for Use *(Describe)*

The GenePOC CDiff assay performed on the revogene instrument is a qualitative *in vitro* diagnostic test that utilizes automated sample processing and real-time polymerase chain reaction (PCR) to detect the toxin B (tcdB) gene of toxigenic *Clostridium difficile* (*C. difficile*) in unformed (liquid or soft) stool specimens obtained from patients suspected of having *C. difficile* infection (CDI). The GenePOC CDiff assay is intended to aid in the diagnosis of CDI.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) SUMMARY

A. GENERAL INFORMATION

Submission Date: November 17, 2017

Submitter Information:

Submitted By: GenePOC Inc.
360 rue Franquet
Québec (Québec) G1P 4N3 Canada

Contact Person: Guy Sevigny
Sr. Regulatory Affairs Specialist
GenePOC Inc.
Telephone: +1 418 650-3535 ext. 261
Email: guy.sevigny@genepoc.ca

B. PURPOSE FOR SUBMISSION:

To obtain a substantial equivalence determination for the GenePOC™ CDiff assay

C. MEASURAND:

tcdB gene of toxigenic *Clostridium difficile* (*C. difficile*)

D. TYPE OF TEST:

Real-time Polymerase chain reaction (rtPCR)

E. DEVICE INFORMATION:

1. Trade Name:
   GenePOC™ CDiff

2. Regulation:
   21 CFR 866.3130 - *Clostridium difficile* toxin gene amplification assay

3. Classification:
   Class II

4. Product Code:
   OZN

5. Panel:
   83, Microbiology

F. INTENDED USE:

1. Intended Use and Indications for Use:
   The GenePOC™ CDiff assay performed on the revogene™ instrument is a qualitative in vitro diagnostic test that utilizes automated sample processing and real-time polymerase chain reaction (PCR) to detect the toxin B (*tcdB*) gene of toxigenic *Clostridium difficile* (*C. difficile*) in unformed (liquid or soft) stool specimens obtained from patients suspected of having *C. difficile* infection (CDI). The GenePOC™ CDiff assay is intended to aid in the diagnosis of CDI.

2. Special conditions for use statement(s):
   Prescription Use Only

3. Special instrument requirements:
   revogene™

G. DEVICE DESCRIPTION:

The GenePOC™ CDiff assay is a single-use test for the qualitative detection of the toxin B (*tcdB*) gene of toxigenic *Clostridium difficile* (*C. difficile*) in unformed (liquid or soft) stool specimens. The GenePOC™ CDiff assay kit is comprised of the disposable CDiff microfluidic cartridges (PIE), Disposable Transfer Loops (DTL), Sample Buffer Tubes (SBT), and Disposable Transfer Tools (DTT; pipette). These components are used to suspend the sample, extract, amplify, and detect *C. difficile* nucleic acid. A Process Control (PrC) is also incorporated into each PIE to verify sample processing and amplification steps. The PrC allows for the verification of potential inhibitor substances as well as microfluidic, instrument or reagent failure. The GenePOC™ CDiff assay is designed to be used on the revogene™. The revogene™ is an instrument that automates sample homogenization, sample dilution, cells lysis, DNA amplification and detection of the amplified PCR products.

Each GenePOC™ CDiff assay kit provides components for 24 tests. User intervention is required for sample preparation, transferring the stool specimen with the DTL into the SBT, using the DTT to transfer the sample into the PIE, and loading/unloading the PIE into the revogene™ carousel. Each PIE is a completely integrated closed device in which a sample is dispensed and processed through different microfluidic chambers and channels that allow for the sample processing and subsequent real-time PCR steps.

Upon completion of a run, the results are computed by the revogene™ from measured fluorescent signals and embedded calculation algorithms. The output results include positive, negative, indeterminate, and unresolved. Upon completion of a run, the user removes the used cartridges and disposes of them in normal biological waste. Results may be viewed, printed, transferred, and/or stored by the user.

H. SUBSTANTIAL EQUIVALENCE INFORMATION:

1. Predicate Device Name:
   BD MAX CDIFF ASSAY, BD MAX INSTRUMENT

2. Predicate 510(k) Number:
   K130470

3. Comparison with Predicate:

Item	GenePOC™ CDiff	BD MAX Cdiff Assay (Predicate Device)
K Number	Subject of submission	K130470
Intended Use and Indications for Use	The GenePOC CDiff assay performed on the revogene™ instrument is a qualitative in vitro diagnostic test that utilizes automated sample processing and real-time polymerase chain reaction (PCR) to detect the toxin B (*tcdB*) gene of toxigenic *Clostridium difficile* (*C. difficile*) in unformed (liquid or soft) stool specimens obtained from patients suspected of having *C. difficile* infection (CDI). The GenePOC CDiff assay is intended to aid in the diagnosis of CDI.	The BD MAX Cdiff Assay performed on the BD MAX™ System is an automated *in vitro* diagnostic test for the direct, qualitative detection of the *Clostridium difficile* toxin B gene (*tcdB*) in human liquid or soft stool specimens from patients suspected of having *C. difficile* infection (CDI). The test, performed directly on the specimen, utilizes real-time polymerase chain reaction (PCR) for the amplification of C. difficile toxin B gene DNA and fluorogenic target-specific hybridization probes for the detection of the amplified DNA. The BD MAX Cdiff Assay is intended to aid in the diagnosis of CDI.
SIMILARITIES		
Classification	Class II	Same
Product Code	OZN	Same
DNA Target	Presence of the toxin B (*tcdB*) gene	Same
Specimen type	Unformed (liquid or soft) stool	Same
Assay format	• Amplification: Real Time PCR • Detection: Fluorogenic target-specific hybridization	Same
Detection probes	TaqMan® Probe	Same
Sample preparation	Automated by revogene™	Automated by BD MAX™ system
Interpretation of test results	Automated (Diagnostic software of the revogene™)	Automated (Diagnostic software of BD MAX™ system)
Internal Process Control	To help monitor presence of potential inhibitory substances as well as any system or reagent failures	Specimen Processing Control (SPC)
DIFFERENCES		
Instrument	revogene™	BD MAX™

I. STANDARDS/GUIDANCE DOCUMENTS REFERENCED:

CLSI Guideline EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.

J. TEST PRINCIPLE:

The GenePOC revogene™ automates and integrates nucleic acid extraction and amplification, and detection of the target sequence in complex samples using real-time PCR. A liquid or soft stool specimen is collected using a standard stool collection device. Using the DTL, a disposable 5µL inoculating loop dipped into the stool specimen, stool material is transferred into SBT. After vortexing, approximately 150 µL of the inoculated sample buffer is transferred into the GenePOC microfluidic cartridge using the DTT. The loaded CDiff cartridge is placed into the revogene™ for further sample processing. No operator intervention is necessary once the clinical sample is loaded onto the revogene™.

Each CDiff microfluidic cartridge (PIE) is a completely integrated and self-contained device. Each sample is sequentially transferred by centrifugation from one microfluidic chamber to the next and all reagents specific for the PCR reaction are incorporated and dried within the PCR wells. The stepwise process includes sample homogenization, specimen dilution and lysis of cells followed by the subsequent real-time PCR steps within 1 PCR well in the cartridge. An internal Process Control (PrC) is contained in the homogenization chamber and is therefore present in every test to verify critical steps of the analytical process (including sample homogenization, dilution, sample lysis, and nucleic acid amplification and detection) for the presence of potential inhibitory substances as well as system or reagent failures. The amplified products are detected in real time using target-specific TaqMan® chemistry-based probes. The CDiff specific designed primers and probe detect a target region of 262 base pairs (bp) of the toxin B gene (*tcdB*) of *Clostridium difficile*. The results are computed by the system from measured fluorescent signals and embedded calculation algorithms. Results may be viewed, printed, transferred, and/or stored by the user.

K. PERFORMANCE CHARACTERISTICS:

1. Analytical Performance

a. Precision/Reproducibility

For the Reproducibility and Precision study, a total of 1,022 samples (383 low positive, 384 moderate positive, and 255 negative samples) were tested with the GenePOC™ CDiff assay. Single site and multi-site precision studies were conducted to determine Between-Laboratory Reproducibility, Between-Lot Reproducibility, and Within-Laboratory Precision. A five members panel comprised of 1 negative panel member and 4 negative stool samples spiked with either a low positive (2,438 CFU/mL and 2,925 CFU/mL of SB) or a moderate positive (3,750 CFU/mL and 4,500 CFU/mL of SB) final concentration of *C. difficile* Toxinotype 0 (ATCC 43255™; ribotype 087) strain or with *C. difficile* Toxinotype IIIb (ATCC BAA-1805™; NAP1/ribotype 027) strain respectively. The negative panel member was prepared by using a pool of toxigenic *C. difficile* negative stools.

For all factors evaluated and the different panel members tested, the variation of results is consistently below 7.54% (%CV values).

Between-Laboratory Reproducibility:

The Between-Laboratory Reproducibility study was performed with one reagent lot on five days (consecutive or not) by two operators at three selected sites. Two runs were performed by each operator on each day. The overall agreement of assay results was 97.2% (95% CI = 93.6-99.1%) for Low Positive (LP) samples (both toxigenic *C. difficile* strains), 98.3% (95% CI = 95.2-99.7%) for Moderate Positive (MP) samples (both toxigenic *C. difficile* strains) and 100% (95% CI = 97.5-100%) for True Negative (TN) samples.

GenePOC™ CDiff Assay Results and Percent Agreement for Between-Laboratory Reproducibility Qualitative Analysis

Panel Type	Strain	Site 01	Site 02	Site 03	Assay Results/ Total	Agreement (%) [95% CI]
Low Positive	ATCC 43255™	27/30	28/30	30/30	85/90	94.4 [87.5%-98.2%]
	ATCC BAA-1805™	30/30	30/30	30/30	90/90	100 [96.7%-100%]
	Overall Assay Results/Total (% Agreement) [95% CI]	57/60 (95%) [86.1-99.0%]	58/60 (96.7%) [88.5-99.6]	60/60 (100%) [95.1-100]	175/180 (97.2%)	97.2 [93.6%-99.1%]
Moderate Positive	ATCC 43255™	29/30	29/30	29/30	87/90	96.7 [90.6%-99.3%]
	ATCC BAA-1805™	30/30	30/30	30/30	90/90	100 [96.7%-100%]
	Overall Assay Results/Total (% Agreement) [95% CI]	59/60 (98.3%) [91.1-100%]	59/60 (98.3%) [91.1%-100%]	59/60 (98.3%) [91.1%-100%]	177/180 (98.3%)	98.3 [95.2%-99.7%]
Negative	Overall Assay Results/Total (% Agreement) [95% CI]	40/40 (100%) [92.8-100%]	40/40 (100%) [92.8%-100%]	40/40 (100%) [92.8%-100%]	120/120 (100%)	100 [97.5%-100%]

Results for the Ct Values Analysis of Between-Laboratory Reproducibility Study

C. difficile													
Panel Type	**Strain**	**Mean Ct (CDiff)**	**N**	**Between-Laboratory**		**Between-Operators**		**Between-Days**		**Residual Error**		**Overall**	
				SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Low Positive	ATCC 43255™	38.48	85	0.23	0.61	0.00	0.00	0.00	0.00	1.54	4.00	1.56	4.05
	ATCC BAA-1805™	36.37	90	1.12	3.07	0.00	0.00	0.00	0.00	2.50	6.89	2.74	7.54
Moderate Positive	ATCC 43255™	37.68	87	0.46	1.23	0.00	0.00	0.00	0.00	1.56	4.14	1.63	4.32
	ATCC BAA-1805™	36.57	90	0.54	1.48	0.19	0.52	0.16	0.43	1.54	4.21	1.65	4.52
PrC													
Panel Type	**Strain**	**Mean Ct (PrC)**	**N**	**Between-Laboratory**		**Between-Operators**		**Between-Days**		**Residual Error**		**Overall**	
				SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Negative	N/A	33.09	120	0.45	1.36	0.19	0.58	0.07	0.20	0.89	2.70	1.02	3.09

Between-Lot Reproducibility:

The Between-Lot Reproducibility study was performed at one site with three lots for a total of 15 days of testing (5 days per reagent lot) and two runs performed by each operator on each day. The overall agreement of assay results was 95.0% (95% CI = 90.7- 97.7%) for Low Positive (LP) samples (both toxigenic *C. difficile* strains), 98.3% (95% CI = 95.2-99.7%) for Moderate Positive (MP) samples (both toxigenic *C. difficile* strains) and 100% (95% CI = 97.5-100%) for True Negative (TN) samples.

GenePOC™ CDiff Assay Results and Percent Agreement for Between-Lot Reproducibility Qualitative Analysis

Panel Type	Strain	Kit lot #1 (L1906151)	Kit lot #2 (L1906091)	Kit lot #3 (L1906141)	Assay Results/ Total	Agreement (%) [95% CI]
Low Positive	ATCC 43255™	27/30	27/30	28/30	82/90	91.1 [83.2%-96.1%]
	ATCC BAA-1805™	30/30	29/30	30/30	89/90	98.9 [94.0%-100%]
	Overall Assay Results/Total (% Agreement) [95% CI]	57/60 (95%) [86.1-99.0%]	56/60 (93.3%) [83.8-98.2%]	58/60 (96.7%) [88.5-99.6%]	171/180 (95%)	95.0 [90.7%-97.7%]
Moderate Positive	ATCC 43255™	29/30	30/30	28/30	87/90	96.7 [90.6%-99.3%]
	ATCC BAA-1805™	30/30	30/30	30/30	90/90	100 [96.7%-100%]
	Overall Assay Results/Total (% Agreement) [95% CI]	59/60 (98.3%) [91.1-100%]	60/60 (100%) [95.1-100%]	58/60 (96.7%) [88.5-99.6%]	177/180 (98.3%)	98.3 [95.2%-99.7%]
Negative	Overall Assay Results/Total (% Agreement) [95% CI]	40/40 (100%) [92.8-100%]	40/40 (100%) [92.8-100%]	40/40 (100%) [92.8-100%]	120/120 (100%)	100 [97.5%-100%]

Results for the Ct Values Analysis of Between-Lot Reproducibility Study

C. difficile													
Panel Type	Strain	Mean Ct (CDiff)	N	Between-Lot		Between-Operators		Between-Days		Residual Error		Overall	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low Positive	ATCC 43255™	38.57	82	0.08	0.20	0.10	0.26	0.15	0.40	1.71	4.43	1.72	4.46
	ATCC BAA-1805™	37.02	89	0.59	1.60	0.46	1.24	0.00	0.00	1.83	4.96	1.98	5.35
Moderate Positive	ATCC 43255™	37.55	87	0.70	1.86	1.02	2.71	0.00	0.00	1.77	4.72	2.16	5.75
	ATCC BAA-1805™	36.86	90	0.16	0.42	0.72	1.96	0.18	0.48	1.07	2.90	1.31	3.56
PrC													
Panel Type	Strain	Mean Ct (PrC)	N	Between-Lot		Between-Operators		Between-Days		Residual Error		Overall	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Negative	N/A	33.21	120	0.34	1.02	0.23	0.68	0.18	0.55	0.78	2.35	0.90	2.71

Within-Laboratory Precision:

The Within-Laboratory Precision of the assay was performed at one site and tested specimens with one reagent lot for a total of 12 days of testing with two runs performed by each operator on each day. The overall agreement of assay results was 94.4% (95% CI = 89.3-97.6%) for Low Positive (LP) samples (both toxigenic *C. difficile* strains), 96.5% (95% CI = 92.1-98.9%) for Moderate Positive (MP) samples (both toxigenic *C. difficile* strains) and 100% (95% CI = 96.9-100%) for True Negative

(TN) samples.

GenePOC™ CDiff Assay Results and Percent Agreement for Within-Laboratory Precision Qualitative Analysis

Panel Type	Strain	Assay Results/ Total	Agreement (%) [95% CI]
Low Positive	ATCC 43255™	64/72	88.9 [79.3%-95.1%]
	ATCC BAA-1805™	71/71	100 [95.9%-100%]
	Overall Assay Results/Total (% Agreement) [95% CI]	135/143 (94.4%)	94.4 [89.3%-97.6%]
Moderate Positive	ATCC 43255™	69/72	95.8 [88.3%-99.1%]
	ATCC BAA-1805™	70/72	97.2 [90.3%-99.7%]
	Overall Assay Results/Total (% Agreement) [95% CI]	139/144 (96.5%)	96.5 [92.1%-98.9%]
Negative	Overall Assay Results/Total (% Agreement) [95% CI]	95/95 (100%)	100 [96.9%-100%]

b. Linearity/Assay Reportable Range

Not applicable.

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

There are three types of controls for the GenePOC™ CDiff assay including an internal process control (PrC), positive external control (PEC) and negative external control (NEC). The PrC is provided in each GenePOC™ CDiff assay. The PrC is extracted, amplified, and detected along with each specimen tested and verifies the efficacy of the dilution, cell lysis, PCR amplification, and detection processes. For the PEC and NEC, GenePOC recommends using commercially available control materials (e.g., ATCC 43255™, a *C. diffic*ile strain bearing the *tcdB* gene for PEC, and ATCC 43593, a non-toxigenic *C. difficile* strain for NEC). It is recommended that the positive bacterial strain be freshly prepared in saline to a turbidity of 0.5 McFarland from isolated colonies and subsequently diluted ½ in saline before its addition into the SBT with the DTL. The negative strain could be prepared the same way while added directly to the SBT without the dilution step.

d. Detection Limit

The LoD was established and confirmed in two separate studies. The confirmation of the LoD included three GenePOC™ CDiff reagent lots, six revogene™ instruments, and two operators. There were 4 runs per instrument per day, and the study was conducted over four days. Strain *C. difficile* ATCC 43255™ and strain *C. difficile* ATCC BAA-1805™ were used in the study. The LoD was defined as the lowest concentration at which 95% or greater of all replicates tested positive. The LoD of the GenePOC™ CDiff assay was 1,500 CFU/mL of SB for each strain.

e. Analytical Inclusivity

The analytical reactivity (inclusivity) of the GenePOC™ CDiff assay was evaluated by testing 20 strains of toxigenic *C. difficile* from various geographic origins representing eight different toxinotypes. Three lots of GenePOC™ CDiff assay kits were used for sample testing and n=1 sample/strain/reagent lot. All toxigenic *C. difficile* strains tested were detected at 3,750 CFU/mL SB (2 - 3xLOD).

***C. difficile* Strain**	**Toxinotype, Toxin**
ATCC 9689	Toxinotype 0, A+, B+
ATCC 700792	Toxinotype 0, A+, B+
ATCC 17858	Toxinotype 0, A+, B+
ATCC BAA-1382	Toxinotype 0, A+, B+
ATCC 51695	Toxinotype 0, A+, B+
ATCC 43600	Toxinotype 0, A+, B+
ATCC 43599	Toxinotype 0, A+, B+
ATCC 43596	Toxinotype 0, A+, B+
ATCC 43594	Toxinotype 0, A+, B+
ATCC 17857	Toxinotype 0, A+, B+
ATCC 43598	Toxinotype VIII, A-, B+
CCUG 8864	Toxinotype X, A-, B+
ATCC BAA-1870	Toxinotype IIIb, NAP1, A+, B+
ATCC BAA-1812	Toxinotype XII, A+, B+
ATCC BAA-1803	Toxinotype IIIc, NAP1, A+, B+
ATCC BAA-1814	Toxinotype XXII, A+, B+
ATCC BAA-1804	Toxinotype 0, A+, B+
ATCC BAA-1875	Toxinotype V, A+, B+
ATCC BAA-2155	Toxinotype XXII, A+, B+
ATCC BAA-1873	Toxinotype 0, A+, B+

f. Analytical Specificity

A total of 58 various analytes (1 yeast, 6 viruses, 50 bacteria, and human DNA) found in clinical unformed stool specimens (different from toxigenic *C. difficile*) were selected. These included:

- Commensal and pathogenic microorganisms (bacteria, yeasts and viruses) from the intestinal tract;
- Species phylogenetically related to *C. difficile*;
- *C. difficile* non-pathogenic strains; and
- Human DNA.

Under the condition of the study, *Clostridium sordellii* was detected by the CDiff assay at approximately 10^6 CFU/mL of SB for one replicate out of 3, but was found non-reactive at a load of 10^5 CFU/mL of SB. *Clostridium novyi* and *Clostridium scindens* produced false positive reactions in 1 replicate out of 6 tested at approximately 10^6 CFU/mL of SB. No reactivity was observed for three replicates tested at 10^5 CFU/mL of SB. *Enterococcus faecalis* produced false positive reaction in one replicate out of three tested at approximately 10^7 CFU/mL of SB. No reactivity was observed for three replicates tested at 10^6 CFU/mL of SB.

Name	Identification	Name	Identification
Bacteria (non-toxigenic *C. difficile* and other *Clostridium* species)			
Clostridium difficile (non-toxigenic)	ATCC 43593	*Clostridium perfringens*	ATCC 13124
Clostridium difficile (non-toxigenic)	ATCC 43601	*Clostridium scindens*	ATCC 35704
Clostridium bifermentans	ATCC 638	*Clostridium septicum*	ATCC 12464
Clostridium butyricum	ATCC 860	*Clostridium sordellii*	ATCC 9714
Clostridium haemolyticum	ATCC 9650	*Clostridium sporogenes*	ATCC 15579
Clostridium novyi	ATCC 19402	*Flavonifractor plautii (anc. design. Clostridium orbiscindens)*	ATCC 49531
Bacteria (potentially present in gastrointestinal tract)			
Abiotrophia defectiva	ATCC 49176	*Peptostreptococcus anaerobius*	ATCC 27337
Acinetobacter baumannii	ATCC 19606	*Plesiomonas shigelloides*	ATCC 14029
Aeromonas hydrophila	ATCC 7966	*Porphyromonas asaccharolytica*	ATCC 25260
Alcaligenes faecalis subsp. faecalis	ATCC 15554	*Prevotella melaninogenica*	ATCC 25845
Bacillus cereus	ATCC 14579	*Proteus mirabilis*	ATCC 33583
Bacteroides fragilis	ATCC 25285	*Providencia alcalifaciens*	ATCC 9886
Campylobacter jejuni sub sp. jejuni	ATCC 33560	*Pseudomonas aeruginosa*	ATCC 35554
Campylobacter jejuni (anc. design. Campylobacter coli)	ATCC 43479	*Salmonella enterica* subsp. *arizonae*	ATCC 13314
Citrobacter freundii	ATCC 8090	*Salmonella enterica* subsp. *enterica serovar Choleraesuis*	ATCC 7001
Edwardsiella tarda	ATCC 15947	*Salmonella enterica* subsp. *enterica serovar Typhimurium*	ATCC 14028
Enterobacter aerogenes	ATCC 13048	*Serratia liquefaciens*	ATCC 27592
Enterobacter cloacae subsp. *cloacae*	ATCC 13047	*Serratia marcescens* subsp. *marcescens*	ATCC 13880
Enterococcus faecalis	ATCC 19433	*Shigella boydii*	ATCC 9207
Escherichia coli	ATCC 11775	*Shigella dysenteriae*	CCRI-7792
Escherichia coli O157:H7	CCRI-22391	*Shigella sonnei*	ATCC 29930

Name	Identification	Name	Identification
Helicobacter pylori	ATCC 43504	*Staphylococcus aureus subsp. aureus*	ATCC 33592
Klebsiella oxytoca	ATCC 8724	*Staphylococcus epidermidis*	ATCC 14990
Lactobacillus acidophilus	ATCC 4356	*Streptococcus sp.(S.agalactiae)*	ATCC 12973
Listeria monocytogenes	ATCC 7644	*Vibrio parahaemolyticus*	ATCC 17802
Viruses			
Human Adenovirus 1 (DNA)	ATCC VR-1D	Enterovirus (RNA)	ATCC VR-1823D
Rotavirus (RNA)	ATCC VR-2018DQ	Echovirus (RNA)	ATCC VR-1734D
Norovirus (RNA)	ATCC VR-3235SD (GII)	Human Herpesvirus 5 (Cytomegalovirus) (DNA)	ATCC VR-538D
Yeast			
Candida albicans	ATCC 10231		
Other Organisms			
Human DNA	Kit, TQMN control genomic DNA		

g. Interference with Non-Target Organisms

The potentially inhibitory effect of 30 organisms, that may be present in the normal intestinal flora and which are not targeted by the test, was assessed using organisms selected from the cross-reactivity study. Each organism category (i.e., 27 bacteria, 1 yeast, 2 viruses) was represented with a special attention to include the most frequent causative agents of intestinal tract infections. Groups of 2 to 6 organisms were prepared in toxigenic *C. difficile*-negative liquid stool matrix, and tested in duplicate in presence of either 3,750 CFU/mL of SB of the toxigenic *C. difficile* ATCC® 43255™ strain or 4,500 CFU/mL of SB of the toxigenic *C. difficile* ATCC® BAA-1805™ strain, to assess their potential interference on detection of toxigenic *C. difficile* or PrC. Each organism within group was diluted to reach a load of $\geq 10^6$ CFU/mL of SB for bacterium and yeast, and $\geq 10^5$ copies/mL of SB for viruses.

None of the 30 organisms present at $\geq 10^6$ CFU/mL of SB for bacteria and yeast and $\geq 10^5$ copies/mL of SB for viruses interfered with detection of PrC and with the toxigenic *C. difficile* ATCC® BAA-1805™ strain. Two groups showed a potentially inhibitory effect on detection of the toxigenic *C. difficile* strain ATCC® 43255™. Nevertheless, when each bacterium from these groups was tested individually at a load of $\geq 10^6$ CFU/ mL of SB in presence of *C. difficile* strain ATCC® 43255™, none interfered.

h. Interference with Exogenous and Endogenous Substances

Interference on the GenePOC™ CDiff assay was evaluated with 21 potentially interfering exogenous and endogenous substances in absence and in presence of 2 *C. difficile* strains ATCC® 43255™ and ATCC® BAA- 1805™ tested at 2-3xLoD (3,750 CFU/mL of SB or 4,500 CFU/mL of SB respectively) across 3 reagent lots.

N=16 exogenous substances occasionally used or found in the intestinal tract were tested including: Nystatin, Personnelle Hydrocortisone cream, Preparation H®, Tums®,

Stomaax®, Life BRAND™ Heavy Mineral Oil USP, Mesalazine, Trojan® with spermicidal Lubricant Condoms, Pepto Bismol ™, Imodium®, Senokot®, Vancomycin, Metronidazole, Aleve®, Equate™ Flushable Moist Wipes, and Wet Ones®. Interference was observed with Tums and Stomaax® at concentrations of > 0.5 mg/mL of SB and > 0.5 µL/mL of SB respectively.

N=5 endogenous agents were tested including: Triglyceride Mix (C2-C10), Palmitic acid, Stearic acid, Whole blood, and Mucus. No interference was observed.

i. Carry-Over and Cross Contamination Studies

The within-run and between-run carry-over and cross- contamination were assessed using positive samples prepared in a toxigenic C. difficile-negative liquid stool matrix to reach a final concentration of $>10^7$ CFU/mL of SB of the toxigenic *C. difficile* ATCC® 43255™ strain. True negative samples, prepared with the toxigenic *C. difficile*-negative liquid stool matrix only, were also tested.

For the within-run study, a total of 10 runs were performed by two operators with the CDiff assay on one revogene. Four (4) high positive samples and 4 negative samples were tested by alternating positive and negative samples in each run. For the between-run study, a run of 8 replicates of high positive samples followed by a run of 8 replicates of negative samples were performed by two operators, for a total of 10 runs on one revogene.

Absence of carry-over and cross-contamination was demonstrated.

j. Sample Storage

Collected specimens should be stored between 2˚C and 25˚C during transport.

Stool specimens can be stored at 25°C for up to 2 days, or at 2-8°C for up to 4 days. Inoculated SBT can be stored at 25°C for up to 2 days, or at 2-8°C for up to 3 days.

Store the CDiff kit at 2-25°C. The expiration date is indicated on the box kit's label.

Do not open a pouch until ready to perform testing. Use the PIE within 1 hour after opening the pouch.

2. Comparison Studies

a. Method Comparison with predicate device

Not applicable

b. Matrix Comparison

Not applicable.

3. Clinical Studies

GenePOC conducted a prospective multicenter trial at 7 geographically diverse clinical trial sites (US and Canada). Unformed (liquid or soft) stool specimens were collected from patients suspected of having *C. difficile* infection (CDI). Samples were tested with both the reference method (Combined Direct and Enriched Culture) and the GenePOC™ CDiff assay. The direct culture method consisted in the transfer of a swab of the stool specimen from Anaerobic Transport Medium to pre-reduced selective anaerobic media, a standard cycloserine cefoxitin and fructose agar plate (CCFA), followed by cytotoxicity testing on characterized *C. difficile* colonies isolated from stool. For the enriched culture method, the same swab that was utilized to inoculate the CCFA plate was used to inoculate a cycloserine cefoxitin mannitol broth with taurocholate and lysozyme (CCMB-TAL) tube. The enrichment broth was sub-cultured on another CCFA plate and followed the same procedure used for the direct method. A specimen was considered positive for toxigenic *C. difficile* if *C. difficile* was recovered from stool either by direct or enriched culture and if bacterial isolates tested positive by CCNA. If *C. difficile* was isolated from the direct culture and the isolate tested positive by cytotoxicity testing, the enrichment culture was not further analyzed. Specimens were classified as negative for toxigenic *C. difficile* only if they tested negative by both direct, and combined culture i.e. direct and enriched culture.

The study design consisted of testing fresh samples and prospectively testing retrospectively collected samples that were stored frozen.

The study population demographics are presented below.

Subjects	All Subjects	Fresh	Frozen
	N=2461	N=797	N=1664
Source of specimens			
In-patient	1804 (73,3%)	617 (77,4%)	1187 (71,3%)
Out-patient	420 (17,1%)	123 (15,4%)	297 (17,8%)
Emergency	234 (9,5%)	57 (7,2%)	177 (10,6%)
Missing	3 (0,1%)	0 (0,0%)	3 (0,2%)
Age Class			
< 2	9 (0,4%)	4 (0,5%)	5 (0,3%)
3-18	105 (4,3%)	30 (3,8%)	75 (4,5%)
19-60	1199 (48,7%)	399 (50,1%)	800 (48,1%)
> 60	1148 (46,6%)	364 (45,7%)	784 (47,1%)

Two thousand four hundred and sixty-three (2,463) specimens were used to establish the performance of the GenePOC CDiff test by comparison with Combined Direct and Enriched Culture method. All 2,463 freshly collected specimens were tested in culture, 798 were tested with GenePOC™ CDiff assay as fresh specimens and a subset of 1,665 specimens were frozen before testing with the GenePOC™ CDiff assay.

Of the 798 fresh and 1,665 frozen eligible specimens that were compliant at the specimen and PCR level, 9 and 13 were respectively reported unresolved at initial testing (1,1% for the fresh specimens and 0,8% for the frozen specimens) and only one fresh specimen remained unresolved following repeat testing. The unresolved rate after repeat testing was 0,1% (1/798) for the fresh specimens and 0,0% (0/1665) for the frozen specimens.

Of the 798 fresh and 1,665 frozen eligible specimens that were compliant at the specimen and PCR level, 12 and 28 were respectively reported indeterminate at initial testing (1,5% for the fresh specimens and 1,7% for the frozen specimens) and only one frozen specimen remained indeterminate following repeat testing. The indeterminate rate after repeat testing was 0,0% (0/798) for the fresh specimen and 0,1% (1/1665) for the frozen specimens.
A total of 2,461 fully compliant fresh (n=797) and frozen (n=1,664) samples were tested with both the reference method (Combined Direct and Enriched Culture) and the GenePOC™ CDiff assay. The GenePOC™ CDiff assay sensitivity and specificity obtained with the fresh stool specimens were 80.5% (91/113) and 97.1% (664/684), respectively. The GenePOC™ CDiff assay sensitivity and specificity obtained with the frozen stool specimens were 87.3% (192/220) and 97.3% (1,405/1,444) respectively. In addition, the GenePOC™ CDiff assay agreement with the Direct Culture method was 95.5% (63/66) for the PPA and 93.4% (683/731) for the NPA for the fresh stool specimens, whereas for the frozen stool specimens, 95.2% (160/168) for the PPA and 95.3% (1,425/1,496) for the NPA were obtained

Overall performance (all sites combined) with the GenePOC™ CDiff assay in comparison with the Direct Culture and Reference Method (Combined Direct and Enriched Culture) obtained with fresh specimens

Overall performance		Direct Culture		Total	Reference Method		Total
		Positive	Negative		Positive	Negative	
GenePOC™ CDiff test	Positive	63	48	111	91	20[B]	111
	Negative	3	683	686	22[C]	664	686
	Total	66	731	797	113	684	797
PPA[A]		95.5% [87.3 - 99.1%]			n/a		
NPA		93.4% [91.4 - 95.1%]			n/a		
Sensitivity		n/a			80.5% [72.0 - 87.4%]		
Specificity		n/a			97.1% [95.5 - 98.2%]		

[A] Numbers between parentheses indicate exact binomial 95% CI.
[B] Of the 20 specimens with false-positive GenePOC CDiff test results relative to the combined direct and enrichment culture 8 were positive and 4 were negative by a second NAAT method (Sites' Routine PCR Assay).
[C] Of the 22 specimens with false-negative GenePOC CDiff test results relative to the combined direct and enrichment culture 13 were negative and 4 were positive by a second NAAT method (Sites' Routine PCR Assay).

Overall performance (all sites combined) with the GenePOC™ CDiff assay in comparison with the Direct Culture and Reference Method (combined Direct and Enriched Culture) obtained with frozen specimens

Overall performance		Direct Culture		Total	Reference Method		Total
		Positive	Negative		Positive	Negative	
GenePOC™ CDiff test	Positive	160	71	231	192	39[B]	231
	Negative	8	1,425	1,433	28[C]	1,405	1,433
	Total	168	1,496	1,664	220	1,444	1,664
PPA[A]		95.2% [90.8 - 97.9%]			n/a		
NPA		95.3% [94.1 - 96.3%]			n/a		
Sensitivity		n/a			87.3% [82.1 - 91.4%]		
Specificity		n/a			97.3% [96.3 - 98.1%]		

[A] Numbers between parentheses indicate exact binomial 95% CI.
[B] Of the 39 specimens with false-positive GenePOC CDiff test results relative to the combined direct and enrichment culture 17 were positive and 15 were negative by a second NAAT method (Sites' Routine PCR Assay).
[C] Of the 28 specimens with false-negative GenePOC CDiff test results relative to the combined direct and enrichment culture 14 were negative and 12 were positive by a second NAAT method (Sites' Routine PCR Assay).

4. Clinical Cut-off
   Not applicable.

L. CONCLUSION:

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