510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number: K081825

B. Purpose for Submission: To add the option for automated extraction of DNA from clinical specimens using the software accessory "BD ProbeTec™ *Neisseria gonorrhoeae* (GC) Q^x Amplified DNA Assay" to direct the BD Viper™ System.

C. Measurand: *Neisseria gonorrhoeae* DNA

D. Type of Test: Qualitative determination of *Neisseria gonorrhoeae* DNA using the Strand Displacement Amplification (SDA) technology

E. Applicant: BD Diagnostic System

F. Proprietary and Established Names: BD ProbeTec™ *Neisseria gonorrhoeae* (GC) Q^x Amplified DNA Assay

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LSL	Class II	21CFR 866.3390 *Neisseria* spp. direct serological test reagents	Microbiology (83)

H. Intended Use:

1.) Intended use: The BD ProbeTec GC Q^x Amplified DNA Assay, when tested with the BD Viper™ System in Extracted Mode, uses Strand Displacement Amplification technology for the direct, qualitative detection of *Neisseria gonorrhoeae* DNA in clinician-collected female endocervical and male urethral swab specimens, patient-collected vaginal swab specimens (in a clinical setting), and male and female urine specimens. The assay is indicated for use with asymptomatic and symptomatic female individuals and symptomatic male individuals to aid in the diagnosis of gonococcal urogenital disease.

2.) Indications for use: Same as intended use

3) Special conditions for use statement(s): For Prescription use only

4) Special instrument requirements: BD Viper™ System with automated nucleic acid extraction mode

I. Device Description: The **BD ProbeTec** GC Q^{x} Amplified DNA Assay is based on the simultaneous amplification and detection of target DNA using amplification primers and a fluorescently-labeled detector probe. The reagents for SDA are dried in two separate disposable microwells: the Priming Microwell contains the amplification primers, fluorescently-labeled detector probe, nucleotides and other reagents necessary for amplification, while the Amplification Microwell contains the two enzymes (a DNA polymerase and a restriction endonuclease) that are required for SDA. The **BD Viper System** pipettes a portion of the purified DNA solution from each Extraction Tube into a Priming Microwell to rehydrate the contents. After a brief incubation, the reaction mixture is transferred to a corresponding, pre-warmed Amplification Microwell which is sealed to prevent contamination and then incubated in one of the two thermally-controlled fluorescent readers. The presence or absence of *N. gonorrhoeae* DNA is determined by calculating the peak fluorescence (Maximum Relative Fluorescent Units (MaxRFU)) over the course of the amplification process and by comparing this measurement to a predetermined threshold value.

In addition to the fluorescent probe used to detect amplified *N. gonorrhoeae* target DNA, a second labeled oligonucleotide is incorporated in each reaction. The Extraction Control (EC) oligonucleotide is labeled with a different dye than that used for detection of the *N. gonorrhoeae* -specific target and is used to confirm the validity of the extraction process. The EC is dried in the Extraction Tubes and is rehydrated upon addition of the specimen and extraction reagents. At the end of the extraction process, the EC fluorescence is monitored by the **BD Viper System** and an automated algorithm is applied to both the EC and *N. gonorrhoeae* -specific signals to report results as positive, negative, or EC failure.

J. Substantial Equivalence Information:

a) Predicate device name (s):

BD ProbeTecTm ET *CT/NG* Amplified DNA Assays
Gen-Probe Aptima Combo 2 Assay

b) Predicate Numbers (s): K984631, K003395

Comparison with predicate:

Comparison of Operating and Technological Characteristics

	BD Viper System: Extracted mode of operation	BD Viper System Non-extracted mode of operation (K052481)
Thermal Module: • Priming Temperature • Priming to Amplification Transfer Temperature • Amplification Temperature	• Same as BD Viper System K052481 • 70°C • Same as BD Viper System K052481	 • 70°C • 70°C to 52.5°C • 52.5°C
Amplification Plate Sealing	• Same as BD Viper System K052481	• Automated sealing of amplification plate

Optical Module: Fluorescent readers	• Same as BD Viper System K052481 • Same as BD Viper System K052481 • Extraction control read on ROX	• Automatic amplification plate transfer into resident readers (2 readers) • Target read on FAM channel • ROX channel not used
Software Module		
Sample log-in	• Same as BD Viper System K052481 • Patient Sample Location Identification (optional)	• Bar-code or key entered accession numbers
Algorithm	• MaxRFU – Maximum (normalized) Relative Fluorescence Units	• MOTA – Method Other Than Acceleration (area under the curve)
Menu	• Same as BD Viper System K052481 • Added: CTQ, GCQ and CTQ/GCQ	• CT or CT/GC
Controls and System Checks		
Assay Controls	• Positive and negative run controls • Automated control rehydration • Extraction control • Specimen processing control procedure	• Positive and negative run controls • Manual control rehydration • Specimen processing control procedure
System Checks	• Same as BD Viper System K052481 • Extraction reagent checks • Liquid Waste reservoir check	• Consumables, Pipettor, Thermal, Optical, Fluid Volumes
Waste and Waste Disposal		
• Waste Composition • Liquid Waste Disposal Container • Liquid Waste Neutralizer	• Same as BD Viper System K052481 and liquid waste (extraction reagents) • Modified waste disposal bottle • Neutralization pouch for liquid waste	• Solid waste (pipette tips) • Waste disposal bottle resident, not used except in aborted run condition • NA

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

1. Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, May 11, 2005. http://www.fda.gov/cdrh/ode/guidance/337.pdf
2. CLSI EP5-A2 "Evaluation of Precision Performance of Quantitative Measurement Methods",
3. CLSI EP12-A "User Protocol for Evaluation of Qualitative Test Performance".

L. Test Principle:

The BD ProbeTec GC Q^x Amplified DNA Assay is designed for use with the BD ProbeTec *Chlamydia trachomatis/Neisseria gonorrhoeae* (CT/GC) Q^x specimen

collection and transport devices, applicable reagents, the BD Viper System and BD Fox Extraction. Specimens are collected and transported in their respective transport devices which preserve the integrity of the *N. gonorrhoeae* DNA over the specified ranges of temperature and time.

Urine and swab specimens undergo a pre-warm step in the BD Viper Lysing Heater to dissolve mucus and homogenize the specimen. After cooling, the specimens are loaded onto the BD Viper System which then performs all the steps involved in extraction and amplification of target DNA, without further user intervention. The specimen is transferred to an Extraction Tube that contains ferric oxide particles in a dissolvable film and dried Extraction Control. A high pH is used to lyse the bacterial cells and liberate their DNA into solution. Acid is then added to lower the pH and induce a positive charge on the ferric oxide, which in turn binds the negatively charged DNA. The particles and bound DNA are then pulled to the sides of the Extraction Tube by magnets and the treated specimen is aspirated to waste. The particles are washed and a high pH Elution Buffer is added to recover the purified DNA. Finally, a Neutralization Buffer is used to bring the pH of the extracted solution to the optimum for amplification of the target.

The BD ProbeTec GC Q^x Amplified DNA Assay is based on the simultaneous amplification and detection of target DNA using amplification primers and a fluorescently-labeled detector probe. The reagents for SDA are dried in two separate disposable microwells: the Priming Microwell contains the amplification primers, fluorescently-labeled detector probe, nucleotides and other reagents necessary for amplification, while the Amplification Microwell contains the two enzymes (a DNA polymerase and a restriction endonuclease) that are required for SDA. The BD Viper System pipettes a portion of the purified DNA solution from each Extraction Tube into a Priming Microwell to rehydrate the contents. After a brief incubation, the reaction mixture is transferred to a corresponding, pre-warmed Amplification Microwell which is sealed to prevent contamination and then incubated in one of the two thermally-controlled fluorescent readers. The presence or absence of *N. gonorrhoeae* DNA is determined by calculating the peak fluorescence (Maximum Relative Fluorescent Units (MaxRFU)) over the course of the amplification process and by comparing this measurement to a predetermined threshold value.

In addition to the fluorescent probe used to detect amplified *N. gonorrhoeae* target DNA, a second fluorescently-labeled oligonucleotide is incorporated in each reaction. The Extraction Control (EC) oligonucleotide is labeled with a different dye than that used for detection of the N. gonorrhoeae-specific target and is used to confirm the validity of the extraction process. The EC is dried in the Extraction Tubes and is re-hydrated upon addition of the specimen and extraction reagents. At the end of the extraction process, the EC fluorescence is monitored by the BD Viper instrument and an automated algorithm is applied to both the EC and *N. gonorrhoeae*-specific signals to report specimen results as positive, negative, or EC failure.

M. Performance Characteristics (if/when applicable):
1.   <u>Analytical performance:</u>

a.   *Precision/Reproducibility:*

Reproducibility of the BD Viper System using the BD ProbeTec GC Q^x Assay was evaluated at three clinical sites on one BD Viper System per site. A panel of simulated specimens was tested that comprised CT and GC organisms seeded into swab diluent for the BD ProbeTec GC Q^x Assay. Un-inoculated swab diluent for the BD ProbeTec GC Q^x Assay was used for the GC negative samples. Nine replicates of each panel member were tested every day for five days on each BD Viper System. The data are summarized in the following table.

Summary of Reproducibility Data on the BD Viper System for the GC Q^x Assay

Specimen Type	CT EB's/ mL	GC Cells/ mL	% Correct	95% CI	MaxRFU Mean	Within Run SD	Within Run %CV	Between Runs Within Site SD	Between Runs Within Site %CV	Between Site SD	Between Site %CV
Endocervical / Urethral	0	0	99.3% (134/135)	(95.9%, 100.0%)	13.8	151.3	1096.3	0.0	0.0	0.6	4.3
	30	0	98.5% (133/135)	(94.8%, 99.8%)	28.1	220.7	785.3	0.0	0.0	33.8	120.3
	0	100	100.0% (135/135)	(97.3%, 100.0%)	1859.5	94.1	5.1	0.0	0.0	19.2	1.0
	30	250	100.0% (135/135)	(97.3%, 100.0%)	1847.3	117.6	6.4	0.0	0.0	25.9	1.4
	75	100	100.0% (135/135)	(97.3%, 100.0%)	1855.9	119.4	6.4	0.0	0.0	42.2	2.3
Urine / Vaginal	0	0	99.3% (134/135)	(95.9%, 100.0%)	15.7	162.3	1031.1	0.0	0.0	0.0	0.0
	30	0	100.0% (135/135)	(97.3%, 100.0%)	1.1	3.1	295.8	0.7	69.7	0.5	48.3
	0	100	100.0% (135/135)	(97.3%, 100.0%)	1899.0	86.1	4.5	22.8	1.2	0.0	0.0
	30	250	100.0% (135/135)	(97.3%, 100.0%)	1884.2	94.0	5.0	13.8	0.7	0.0	0.0
	75	100	100.0% (135/135)	(97.3%, 100.0%)	1867.2	87.7	4.7	0.0	0.0	19.2	1.0

A second study was conducted internally to characterize the reproducibility of test results (i.e., proportion positive or negative) at target levels below the analytical Limit of Detection (LoD) of the BD ProbeTec GC Q^x Assay. A panel of simulated specimens was tested that comprised GC and CT organisms seeded into Q^x swab diluent at two different levels each of which was below the respective analytical LoD for the organisms (1:10, 1:100). These levels were selected to fall within the dynamic range of the analytical LOD curve of the assay. Fifteen replicates of each panel member were tested every day for five days across three BD Viper Systems. The data are summarized in the table below.

Characterization of System Reproducibility at Target Levels below the Analytical Limit of Detection for the GC Q^x Assay

Specimen	Dilution of Analytical LOD	% Positive	95% CI (Positive)	Max RFU Mean (Positive)	% Negative	95% CI (Negative)	Max RFU Mean (Negative)
Endocervical/Urethral	1:10	92.9 (209/225)	(88.7, 95.9)	1324.6	7.1 (16/225)	(4.1, 11.3)	41.4
Endocervical/Urethral	1:100	30.7 (69/225)	(24.7, 37.1)	835.9	69.3 (156/225)	(62.9, 75.3)	7.2
Urine/Vaginal	1:10	90.7 (204/225)	(86.1, 94.1)	1165.9	9.3 (21/225)	(5.9, 13.9)	34.2
Urine/Vaginal	1:100	22.7 (51/225)	(17.4, 28.7)	872.7	77.3 (174/225)	(71.3, 82.6)	7.8

b. *Linearity/assay reportable range*: NA

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):* The recommended Positive, Negative and Internal Control material were tested a sufficient number of times with acceptable results on all testing days.

d. *Detection limit:* Endocervical swabs and vaginal swabs were used for LoD studies because these swabs contain higher concentration of protein, mucous, and cellular debris and are considered "worst case". Urethral swabs were not tested for LoD studies.

Endocervical swabs pool - Minipool of 72 individual swab specimens in diluent showing GC negative results was divided into 6 for spiking with strain 19424 at 5 different target levels and 1 negative target level (unspiked).

Vaginal swabs pool - Minipool of 12 individual swab specimens in diluent showing GC negative results was divided into 6 for spiking with strain 19424 at 5 different target levels and 1 negative target level (unspiked).

Urine**:** Male and female urine specimens screened separately and equal volumes of negative specimens from male and female were pooled and were divided into 6 for spiking with strain 19424 at 5 different target levels and 1 negative target level (unspiked).

The Limits of Detection (LoDs) for the GC Q^x Assay with *Neisseria gonorrhoeae* strain ATCC 19424 in urine and swab specimens when extracted on the **BD Viper** System were determined to be < 50 cells per mL for neat and Q^x UPT urine and < 100 GC cells per mL for expressed vaginal and endocervical swab specimens.

The GC Q^x Assay on the **BD Viper** System in extracted mode was able to detect 17 GC strains (ATCC 19424, 27628, 27629, 27630, 27632, 27633, 27631, 21823, 51803, 23051, 31407, 31953, 35201, 31397, 31151, 43785, 51804) with ≥ 95% proportion positive at a concentration of 50 cells per mL in CT/GC Q^x Swab Diluent.

e. *Analytical specificity:*

1. Cross Reactivity: DNA from 141 organisms listed in the following table was extracted

on the BD Viper System and tested with the BD ProbeTec GC Q^x Amplified DNA Assay. All potential cross-reactive species were tested at > 1×10^8 cells/mL except where noted. Two *N. cinerea* and two *N. lactamica* strains were shown to cross-react in the GC Q^x assay.

Potential Cross-reacting Microorganisms

Acinetobacter calcoaceticus	*Enterococcus faecium*	*Peptostreptococcus asaccharolyticus*	*Neisseria elongata* subsp. *glycolytica*
Acinetobacter lwoffi	Epstein Barr Virus***	*Peptostreptococcus productus*	*Neisseria elongata* subsp. *nitroreduscens* (2)
Actinomyces israelii	*Escherichia coli*	*Plesiomonas shigelloides*	*Neisseria elongata*
Adenovirus***	*Flavobacterium meningosepticum*	*Propionibacterium acnes*	*Neisseria flava* (4)
Aeromonas hydrophilia	*Gardnerella vaginalis*	*Providencia stuartii*	*Neisseria flavescens* (4)
*Alcaligenes faecalis**	*Gemella haemolysans*	*Pseudomonas aeruginosa*	*Neisseria lactamica* (7)
*Bacillus subtilis**	*Haemophilus influenzae*	*Salmonella minnesota*	*Neisseria meningitidis* (12)
Bacteroides fragilis	Herpes Simplex Virus **	*Salmonella typhimurium*	*Neisseria mucosa* (5)
*Candida albicans**	Human papillomavirus (16 and 18)***	*Staphylococcus aureus*	*Neisseria perflava* (8)
*Candida glabrata**	*Kingella kingae*	*Staphylococcus epidermidis*	*Neisseria polysaccharea* (2)
*Candida tropicalis**	*Klebsiella pneumoniae*	*Streptococcus agalactiae*	*Neisseria sicca* (5)
Chlamydia trachomatis	*Lactobacillus acidophilus**	*Streptococcus mitis*	*Neisseria subflava* (15)
*Chlamydia pneumoniae****	*Lactobacillus brevis*	*Streptococcus mutans*	*Neisseria weaverii* (3)
*Chlamydia psittaci**	*Lactobacillus jensenii**	*Streptococcus pneumoniae**	
Citrobacter freundii	*Listeria monocytogenes*	*Streptococcus pyogenes*	
Clostridium perfringens	*Mobiluncus mulieris*	*Streptomyces griseus**	
Corynebacterium renale	*Moraxella lacunata**	*Trichomonas vaginalis**	
*Cryptococcus neoformans**	*Moraxella osloensis*	*Veillonella parvula*	
Cytomegalovirus	*Morganella*	*Vibrio*	

**	*morganii*	*parahaemolyticus*
Edwardsiella tarda	*Mycobacterium gordonae*	*Yersinia enterocolitica*
Enterobacter cloacae	*Mycobacterium smegmatis*	*Branhamella catarrhalis* (5)
Enterococcus faecalis	*Peptostreptococcus anaerobius*	*Neisseria cinerea* (2)

(n) number of strains tested in the BD ProbeTec GC Q^x Assay

* Tested at $> 1x10^7$ cells or EB/mL; **Tested at $> 1x10^6$ cells or viral particles per mL; ***Tested at $> 1x10^6$ genomic equivalents per mL;**** tested at $> 1x10^5$ TCID$_{50}$/mL

2. Interference: The performance of the BD ProbeTec GC Q^x Assay on the BD Viper System in extracted mode was evaluated in the presence of potential interfering substances which may be encountered in swab and/or urine specimens. Potential interfering substances were spiked into UPT urine and vaginal swab specimen matrices in both the presence and the absence of GC organisms (150 GC cells/mL in urine matrix and 300 GC cells/mL in swab matrix). Results are summarized in the following table.

GC Q^x Interfering Substances

Interpretation	Swab	Urine
No Interference Observed	Blood ($\leq$ 60%) Seminal Fluid Mucus Over The Counter vaginal products and contraceptives Hemorrhoidal cream Prescription vaginal treatments Leukocytes ($1x10^6$ cells/mL) $1x10^6$ EB/mL Chlamydia trachomatis	Blood ($\leq$1%) Seminal fluid Mucus Antibiotics Analgesics Over The Counter deodorant sprays and powders Hormones Leukocytes Albumin <1 mg/mL Glucose Acidic urine (pH 4.0) Alkaline urine (pH 9.0) Bilirubin $1x10^6$ EB/mL Chlamydia trachomatis Organisms associated with Urinary Tract Infections
May cause extraction control (EC) failures	Blood (> 60%)	Not applicable

f.   Assay cut-off: NA

g. Cross Contamination and Carryover

An internal study was conducted to evaluate the risk of producing a false positive result in either the same run on the BD Viper System in extracted mode (within run cross-contamination) or in a subsequent run (between run carryover). Testing was conducted using negative and positive samples on three BD Viper Systems. Negative samples consisted of CT/GC Q^x Swab Diluent. Positive samples consisted of a representative analyte (10^5 CT EB/mL) spiked into CT/GC Q^x Swab Diluent. The overall rate of cross-contamination (i.e., with alternating columns of positive and negative samples and a prevalence of 50%) was 0.41% (9/2208). The overall rate of carryover contamination (i.e., carryover between successive runs when the prevalence was 50% in the previous run) was 0.36% (8/2208). Cross-contamination and carryover rates across the three BD Viper Systems are summarized in the table.

Cross Contamination and Carryover Contamination

Assay Dispense Mode Selected	BD Viper System	Cross-Contamination			Carryover Contamination		
		n	Positive Results	Percent Positive	n	Positive Results	Percent Positive
Dual Assay	1	736	5	0.68	736	1	0.14
	2	736	0	0.00	736	3	0.41
	3	736	4	0.54	736	4	0.54
	Overall	2208	9	0.41	2208	8	0.36
Single Assay	1	190	0	0.00	186	0	0.00
	2	188	1	0.53	186	1	0.54
	3	188	0	0.00	186	0	0.00
	Overall	566	1	0.18	568	1	0.18

2. Comparison studies:

   a. *Method comparison with predicate method:* See below under Performance Characteristics

   b. *Matrix comparison:* NA

3. Clinical studies:

   a. *Clinical Sensitivity:* NA

   b. *Clinical specificity:* NA

Performance Characteristics

Clinician-collected endocervical and male urethral swab specimens, patient-collected vaginal swab specimens (in a clinical setting), and male and female Q^x UPT and neat

urine specimens were collected from 1059 female subjects and 479 male subjects attending OB/GYN, sexually transmitted disease (STD) and family planning clinics at seven geographically diverse clinical sites in North America. Subjects were classified as symptomatic if they reported symptoms such as dysuria, urethral discharge, coital pain/difficulty/bleeding, testicular or scrotum pain/swelling, abnormal vaginal discharge, or pelvic/uterine/adnexal pain. Subjects were classified as asymptomatic if they did not report symptoms. Sixty five female subjects and 7 male subjects were excluded from the data analysis due to age requirement violations, antibiotic treatment in the last 21 days, opting to withdraw from the study after initially consenting, failure to obtain paired swab and urine specimens, urine quantity less than 20 mL, or transport and storage errors related to specimen collection. Therefore, the final data analysis included 994 compliant female subjects and 472 compliant male subjects.

Five specimens were collected from each of the 994 eligible female subjects. A urine specimen was collected and split into Q^x UPT, neat urine and the two reference urine specimen collection devices followed by a vaginal swab specimen and three randomized endocervical swab specimens. Up to four specimens were collected from each of the 472 eligible male subjects. Up to three randomized urethral swab specimens were collected followed by a urine specimen that was split into Q^x UPT, neat urine and the two reference urine specimen collection devices. BD ProbeTec GC Q^x assay results were generated from the Q^x UPT and neat urine specimens, the vaginal swab specimen, one endocervical swab specimen and one male urethral swab specimen. The remaining two endocervical swab specimens, up to two male urethral swab specimens, and the two reference urine specimens for each male and female subject were tested using two reference methods: the BD ProbeTec ET GC/AC assay and another commercially available NAAT (Nucleic Acid Amplification Test). Specimen testing was conducted either at the site of collection or at a designated BD Viper testing site.

All performance calculations were based on the total number of BD ProbeTec GC Q^x assays results for endocervical, vaginal and male urethral swab specimens, and male and female Q^x UPT and neat urine specimens compared to a patient infected status (PIS) algorithm for each gender. In the algorithm, the designation of a subject as being infected with GC or not was based on endocervical swab and urine specimen results from the commercially available BD ProbeTec ET GC/AC assay and the other commercially available NAAT. Subjects were considered infected with GC if two of the four endocervical swab and urine specimens (or two of the three or four urethral swab and urine specimens) tested positive in the BD ProbeTec ET GC/AC assay and the other reference NAAT (one specimen testing positive in each NAAT). Subjects were considered non-infected if less than two reference NAAT results were positive. A total of 5387 BD ProbeTec GC Q^x assay results was used to calculate sensitivity and specificity. Sensitivity and specificity by specimen type and symptomatic status are presented in the table below.

Performance of the assay with endocervical swabs, patient collected vaginal swabs specimens (in a clinical setting), female UPT and neat urine was assessed in the clinical study. Separate performance was calculated for specimens collected from pregnant females. Sensitivity compared to patient infected status for FS, FV, FNU, and FUPT was 100% (3/3). In each case, specificity was 100% (24/24) for FS, FV, FNU, and FUPT separately.

GC Q^x Assay Performance Compared to Patient Infected Status (by specimen type and symptomatic status)

Specimen Type	Symptomatic	N	Sensitivity	95% C.I.	Specificity	95% C.I.	PPV%	NPV%	Error Initial/Final
FS	N	450	96.3% (26/27)	(81.0% - 99.9%)	99.5% (421/423)	(98.3% - 99.9%)	92.9	99.8	3/0
	Y	542	100.0% (38/38)	(90.7% - 100.0%)	99.8% (503/504)	(98.9% - 100.0%)	97.4	100.0	2/2
	Total	992	98.5% (64/65)	(91.7% - 100.0%)	99.7% (924/927)	(99.1% - 99.9%)	95.5	99.9	5/2
FV	N	449	100.0% (27/27)	(87.2% - 100.0%)	98.6% (416/422)	(96.9% - 99.5%)	81.8	100.0	0/0
	Y	544	100.0% (38/38)	(90.7% - 100.0%)	99.6% (504/506)	(98.6% - 100.0%)	95.0	100.0	0/0
	Total	993	100.0% (65/65)	(94.5% - 100.0%)	99.1% (920/928)	(98.3% - 99.6%)	89.0	100.0	0/0
FN	N	450	96.3% (26/27)	(81.0% - 99.9%)	99.3% (420/423)	(97.9% - 99.9%)	89.7	99.8	0/0
	Y	543	97.4% (37/38)	(86.2% - 99.9%)	99.6% (503/505)	(98.6% - 100.0%)	94.9	99.8	0/0
	Total	993	96.9% (63/65)	(89.3% - 99.6%)	99.5% (923/928)	(98.7% - 99.8%)	92.6	99.8	0/0
FUPT	N	450	100.0% (27/27)	(87.2% - 100.0%)	99.5% (421/423)	(98.3% - 99.9%)	93.1	100.0	0/0
	Y	543	97.4% (37/38)	(86.2% - 99.9%)	99.8% (504/505)	(98.9% - 100.0%)	97.4	99.8	0/0
	Total	993	98.5% (64/65)	(91.7% - 100.0%)	99.7% (925/928)	(99.1% - 99.9%)	95.5	99.9	0/0
MS	N	215	100.0% (7/7)	(59.0% - 100.0%)	100.0% (208/208)	(98.2% - 100.0%)	100.0	100.0	0/0
	Y	257	100.0% (100/100)	(96.4% - 100.0%)	98.7% (155/157)	(95.5% - 99.8%)	98.0	100.0	1/0
	Total	472	100.0% (107/107)	(96.6% - 100.0%)	99.5% (363/365)	(98.0% - 99.9%)	98.2	100.0	1/0
MN	N	215	100.0% (7/7)	(59.0% - 100.0%)	100.0% (208/208)	(98.2% - 100.0%)	100.0	100.0	0/0
	Y	257	100.0% (100/100)	(96.4% - 100.0%)	98.1% (154/157)	(94.5% - 99.6%)	97.1	100.0	0/0
	Total	472	100.0% (107/107)	(96.6% - 100.0%)	99.2% (362/365)	(97.6% - 99.8%)	97.3	100.0	0/0
MUPT	N	215	100.0% (7/7)	(59.0% - 100.0%)	99.5% (207/208)	(97.4% - 100.0%)	87.5	100.0	0/0
	Y	257	100.0% (100/100)	(96.4% - 100.0%)	98.7% (155/157)	(95.5% - 99.8%)	98.0	100.0	0/0
	Total	472	100.0% (107/107)	(96.6% - 100.0%)	99.2% (362/365)	(97.6% - 99.8%)	97.3	100.0	0/0
Total		5387	99.3% (577/581)	(98.2% - 99.8%)	99.4% (4779/4806)	(99.2% - 99.6%)	95.5	99.9	6/2

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GC Q^x Assay Performance Compared to Patient Infected Status (by clinical site)

Specimen Type	Site	Prevalence	n	Sensitivity	95% C.I.	Specificity	95% C.I.	# CT (+) and GC (+)	PPV%	NPV%
FS[1]	1	8.4%	155	100.0% (13/13)	(75.3% - 100.0%)	99.3% (141/142)	(96.1% - 100.0%)	5	92.9%	100.0%
	2	10.4%	154	93.8% (15/16)	(69.8% - 99.8%)	99.3% (137/138)	(96.0% - 100.0%)	6	93.7%	99.3%
	3	6.8%	73	100.0% (5/5)	(47.8% - 100.0%)	98.5% (67/68)	(92.1% - 100.0%)	2	83.3%	100.0%
	4	19.0%	105	100.0% (20/20)	(83.2% - 100.0%)	100.0% (85/85)	(95.8% - 100.0%)	6	100.0%	100.0%
	5	1.4%	70	100.0% (1/1)	(2.5% - 100.0%)	100.0% (69/69)	(94.8% - 100.0%)	0	100.0%	100.0%
	6	2.2%	365	100.0% (8/8)	(63.1% - 100.0%)	100.0% (357/357)	(99.0% - 100.0%)	3	100.0%	100.0%
	7	2.9%	70	100.0% (2/2)	(15.8% - 100.0%)	100.0% (68/68)	(94.7% - 100.0%)	0	100.0%	100.0%
FV[2]	1	8.4%	155	100.0% (13/13)	(75.3% - 100.0%)	99.3% (141/142)	(96.1% - 100.0%)	5	92.9%	100.0%
	2	10.3%	155	100.0% (16/16)	(79.4% - 100.0%)	97.1% (135/139)	(92.8% - 99.2%)	6	80.0%	100.0%
	3	6.8%	73	100.0% (5/5)	(47.8% - 100.0%)	100.0% (68/68)	(94.7% - 100.0%)	2	100.0%	100.0%
	4	19.0%	105	100.0% (20/20)	(83.2% - 100.0%)	97.6% (83/85)	(91.8% - 99.7%)	6	90.9%	100.0%
	5	1.4%	70	100.0% (1/1)	(2.5% - 100.0%)	100.0% (69/69)	(94.8% - 100.0%)	0	100.0%	100.0%
	6	2.2%	365	100.0% (8/8)	(63.1% - 100.0%)	99.7% (356/357)	(98.4% - 100.0%)	3	88.9%	100.0%
	7	2.9%	70	100.0% (2/2)	(15.8% - 100.0%)	100.0% (68/68)	(94.7% - 100.0%)	0	100.0%	100.0%
FNU[3]	1	8.4%	155	100.0% (13/13)	(75.3% - 100.0%)	98.6% (140/142)	(95.0% - 99.8%)	5	86.7%	100.0%
	2	10.3%	155	93.8% (15/16)	(69.8% - 99.8%)	97.8% (136/139)	(93.8% - 99.6%)	6	83.3%	99.3%
	3	6.8%	73	100.0% (5/5)	(47.8% - 100.0%)	100.0% (68/68)	(94.7% - 100.0%)	2	100.0%	100.0%
	4	19.2%	104	100.0% (20/20)	(83.2% - 100.0%)	100.0% (84/84)	(95.7% - 100.0%)	6	100.0%	100.0%
	5	1.4%	70	100.0% (1/1)	(2.5% - 100.0%)	100.0% (69/69)	(94.8% - 100.0%)	0	100.0%	100.0%

[1] 22 of the 65 FS PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (22/22).

[2] 22 of the 65 FV PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (22/22).

[3] 22 of the 65 FNU PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 95.5% (21/22).

Specimen Type	Site	Prevalence	n	Sensitivity	95% C.I.	Specificity	95% C.I.	# CT (+) and GC (+)	PPV%	NPV%
FUPT[4]	6	2.2%	366	100.0% (8/8)	(63.1% - 100.0%)	100.0% (358/358)	(99.0% - 100.0%)	3	100.0%	100.0%
	7	2.9%	70	50.0% (1/2)	(1.3% - 98.7%)	100.0% (68/68)	(94.7% - 100.0%)	0	100.0%	98.6%
	1	8.4%	155	100.0% (13/13)	(75.3% - 100.0%)	99.3% (141/142)	(96.1% - 100.0%)	5	92.9%	100.0%
	2	10.3%	155	93.8% (15/16)	(69.8% - 99.8%)	99.3% (138/139)	(96.1% - 100.0%)	6	93.8%	99.3%
	3	6.8%	73	100.0% (5/5)	(47.8% - 100.0%)	100.0% (68/68)	(94.7% - 100.0%)	2	100.0%	100.0%
	4	19.2%	104	100.0% (20/20)	(83.2% - 100.0%)	98.8% (83/84)	(93.5% - 100.0%)	6	95.2%	100.0%
	5	1.4%	70	100.0% (1/1)	(2.5% - 100.0%)	100.0% (69/69)	(94.8% - 100.0%)	0	100.0%	100.0%
MS[5]	6	2.2%	366	100.0% (8/8)	(63.1% - 100.0%)	100.0% (358/358)	(99.0% - 100.0%)	3	100.0%	100.0%
	7	2.9%	70	100.0% (2/2)	(15.8% - 100.0%)	100.0% (68/68)	(94.7% - 100.0%)	0	100.0%	100.0%
	1	15.3%	203	100.0% (31/31)	(88.8% - 100.0%)	100.0% (172/172)	(97.9% - 100.0%)	9	100.0%	100.0%
	2	42.1%	76	100.0% (32/32)	(89.1% - 100.0%)	95.5% (42/44)	(84.5% - 99.4%)	10	94.1%	100.0%
	4	33.7%	101	100.0% (34/34)	(89.7% - 100.0%)	100.0% (67/67)	(94.6% - 100.0%)	11	100.0%	100.0%
	5	12.7%	71	100.0% (9/9)	(66.4% - 100.0%)	100.0% (62/62)	(94.2% - 100.0%)	3	100.0%	100.0%
	7	4.8%	21	100.0% (1/1)	(2.5% - 100.0%)	100.0% (20/20)	(83.2% - 100.0%)	0	100.0%	100.0%
MNU[6]	1	15.3%	203	100.0% (31/31)	(88.8% - 100.0%)	100.0% (172/172)	(97.9% - 100.0%)	9	100.0%	100.0%
	2	42.1%	76	100.0% (32/32)	(89.1% - 100.0%)	95.5% (42/44)	(84.5% - 99.4%)	10	94.1%	100.0%
	4	33.7%	101	100.0% (34/34)	(89.7% - 100.0%)	98.5% (66/67)	(92.0% - 100.0%)	11	97.1%	100.0%
	5	12.7%	71	100.0% (9/9)	(66.4% - 100.0%)	100.0% (62/62)	(94.2% - 100.0%)	3	100.0%	100.0%
	7	4.8%	21	100.0% (1/1)	(2.5% - 100.0%)	100.0% (20/20)	(83.2% - 100.0%)	0	100.0%	100.0%

[4] 22 of the 65 FUPT PIS positive subjects were co-infected with CT. BD ProbeTec GC Qˣ Amplified DNA Assay sensitivity was 95.5% (21/22).

[5] 33 of the 107 MS PIS positive subjects were co-infected with CT. BD ProbeTec GC Qˣ Amplified DNA Assay sensitivity was 100% (33/33).

[6] 33 of the 107 MNU PIS positive subjects were co-infected with CT. BD ProbeTec GC Qˣ Amplified DNA Assay sensitivity was 100% (33/33).

Specimen Type	Site	Prevalence	n	Sensitivity	95% C.I.	Specificity	95% C.I.	# CT (+) and GC (+)	PPV%	NPV%
MUPT[7]	1	15.3%	203	100.0% (31/31)	(88.8% - 100.0%)	99.4% (171/172)	(96.8% - 100.0%)	9	96.9%	100.0%
	2	42.1%	76	100.0% (32/32)	(89.1% - 100.0%)	97.7% (43/44)	(88.0% - 99.9%)	10	97.0%	100.0%
	4	33.7%	101	100.0% (34/34)	(89.7% - 100.0%)	100.0% (67/67)	(94.6% - 100.0%)	11	100.0%	100.0%
	5	12.7%	71	100.0% (9/9)	(66.4% - 100.0%)	98.4% (61/62)	(91.3% - 100.0%)	3	90.0%	100.0%
	7	4.8%	21	100.0% (1/1)	(2.5% - 100.0%)	100.0% (20/20)	(83.2% - 100.0%)	0	100.0%	100.0%

[1] 22 of the 65 FS PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (22/22).

[2] 22 of the 65 FV PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (22/22).

[3] 22 of the 65 FNU PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 95.5% (21/22).

[4] 22 of the 65 FUPT PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 95.5% (21/22).

[5] 33 of the 107 MS PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (33/33).

[6] 33 of the 107 MNU PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (33/33).

[7] 33 of the 107 MUPT PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (33/33).

[7] 33 of the 107 MUPT PIS positive subjects were co-infected with CT. BD ProbeTec GC Q^x Amplified DNA Assay sensitivity was 100% (33/33).

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Analysis of GC Positive/Negative Specimens from Female Subjects Based on Patient Infected
Status

PIS GC	NAAT 1		NAAT 2		BD ProbeTec GC Q^x Amplified DNA Assay				Symptomatic Status		
	Endocervical Swab	Urine	Endocervical Swab	Urine	Q^x Endocervical Swab	Q^x Vaginal Swab	Neat Urine	Q^x UPT Urine	A	S	Total
+	-	+	+	+	-	+	+	+	1	0	1
	+	-	+	-	+	+	-	-	0	1	1
	+	-	+	-	+	+	+	+	3	0	3
	+	-	+	+	+	+	+	+	1	1	2
	+	+	+	-	+	+	+	+	2	1	3
	+	+	+	+	+	+	-	+	1	0	1
	+	+	+	+	+	+	+	+	19	35	54
Total PIS Positive									27	38	65
-	NA	-	-	-	-	-	-	-	12	2	14
	-	NA	E	-	-	-	NA	NA	0	1	1
	-	NA	-	-	-	-	-	-	1	1	2
	-	I	-	-	-	-	-	-	5	1	6
	-	-	NA	-	-	-	-	-	1	2	3
	-	-	E	-	-	-	-	-	1	0	1
	-	-	-	-	ET	-	-	-	0	1	1
	-	-	-	-	LE	-	-	-	0	1	1
	-	-	-	-	-	NA	-	-	1	0	1
	-	-	-	-	-	-	-	-	390	484	874
	-	-	-	-	-	-	-	+	0	1	1
	-	-	-	-	-	-	+	-	1	1	2
	-	-	-	-	-	+	-	-	4	1	5
	-	-	-	-	-	+	+	-	0	1	1
	-	-	-	-	-	+	+	+	1	0	1
	-	-	-	-	+	-	-	-	0	1	1
	-	-	+	-	-	-	-	-	1	3	4
	-	-	+	-	+	-	-	-	1	0	1
	-	+	-	-	-	-	-	-	1	2	3
	+	-	-	-	-	-	-	-	2	3	5
	+	+	-	-	+	+	+	+	1	0	1
Total PIS Negative									423	506	929

I Indeterminate
E Error
LE Liquid Level Error
ET Extraction Transfer Error

Analysis of GC Positive/Negative Specimens from Male Subjects Based on Patient Infected Status

PIS GC	NAAT 1		NAAT 2		BD ProbeTec GC Q^x Amplified DNA Assay			Symptomatic Status		
	Urethral Swab	Urine	Urethral Swab	Urine	Q^x Urethral Swab	Neat Urine	Q^x UPT Urine	A	S	Total
+	NA	+	+	+	+	+	+	0	6	6
	+	+	NA	+	+	+	+	0	13	13
	+	+	+	+	+	+	+	7	81	88
Total PIS Positive								7	100	107
-	NA	-	-	-	-	-	-	3	11	14
	NA	-	+	-	-	-	-	1	0	1
	NA	-	+	+	+	+	+	0	1	1
	NA	+	-	-	-	-	-	0	1	1
	-	I	NA	-	-	-	-	1	0	1
	-	I	-	-	-	-	-	4	1	5
	-	-	NA	-	-	-	-	13	11	24
	-	-	E	-	-	-	-	2	0	2
	-	-	-	E	-	-	-	0	1	1
	-	-	-	-	-	-	-	180	124	304
	-	-	-	-	-	-	+	1	1	2
	-	-	-	-	-	+	-	0	1	1
	-	-	-	+	-	-	-	2	1	3
	-	-	+	-	-	-	-	1	1	2
	-	-	+	+	+	+	-	0	1	1
	+	-	-	-	-	-	-	0	1	1
	+	+	NA	-	-	-	-	0	1	1
Total PIS Negative								208	157	365

4. Clinical cut-off: Clinical cut-off was estimated by evaluating GCQ assay results obtained from a total of 696 unique subjects for a total of 4878 assay results. This dataset included both the initial and repeat assay results: specimens were tested and then retested, and both results were included in the analysis in order to generate a larger data pool for use in training the algorithm. The optimal cutoff for the GCQ Assay was located between 50 and 250 MaxRFU based on the analysis of this dataset. When evaluating assay sensitivity and specificity over this range of values across all specimen types, the assay sensitivity and specificity were relatively constant at approximately 92 and 99%, respectively. In order to guard against false positive results (protect specificity), the preliminary cutoff was set at 125 MaxRFU. These preliminary cutoff values were incorporated into the version of algorithm software that was utilized in the Cutoff Trial by the BD Viper System operating in extracted mode.

5. Expected values/Reference range:

A. Prevalence: The prevalence of positive *N. gonorrhoeae* specimens in patient

populations depends upon: clinic type, age, risk factors, gender, and test method. The prevalence observed with the GC Q^x Amplified DNA Assay during a multi-center clinical trial ranged from 1.4% to 19.1% for female specimens and 4.8% to 42.1% for male specimens.

B. Positive and Negative Predictive Value: Hypothetical positive and negative predictive values (PPV & NPV) for the GC Q^x Assay are shown in the following table. These calculations are based on hypothetical prevalence and overall sensitivity and specificity (compared to the patient infected status) of 99.3% and 99.4%, respectively. In addition, PPV and NPV based on actual prevalence, sensitivity and specificity are shown in the tables under performance characteristics section (See "GC Q^x Assay Performance Compared to Patient Infected Status (by specimen type and symptomatic status)" and "GC Q^x Assay Performance Compared to Patient Infected Status (by clinical site)." PPV was calculated using: (Sensitivity * Prevalence) / (Sensitivity*Prevalence + (1 - Specificity) * (1 - Prevalence)). NPV was calculated using: (Specificity * (1 - Prevalence)/ (1-Sensitivity) * Prevalence + Specificity * (1-Prevalence)).

GC Hypothetical Positive and Negative Predictive Values Compared to Patient Infected Status

Prevalence (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
2	99.3	99.4	78.3	100.0
5	99.3	99.4	90.3	100.0
10	99.3	99.4	95.2	99.9
20	99.3	99.4	97.8	99.8
30	99.3	99.4	98.7	99.7
40	99.3	99.4	99.2	99.5
50	99.3	99.4	99.4	99.3

N. Instrument:

BD Viper™ System in extracted mode with the addition of the CTQ and GCQ Assays: The BD Viper System with the capability of automated nucleic acid extraction is the third generation of the BD Viper robotic platform for amplified DNA analysis. The system builds upon its predecessors, the BD Viper Instrument (K023955) and the BD Viper System (K052481).

O. System Descriptions:

Viewing the BD Viper System from the perspective of assay workflow, the level of automation added to enable automated nucleic acid extraction on the existing BD Viper System includes the following:
(1) chemical lysis of organisms in clinical specimens,
(2) chemical extraction and purification of DNA using paramagnetic particles facilitated by employment of an extractor block containing a movable magnet assembly;

(3) elution of extracted DNA into SDA-compatible buffer; and
(4) transfer of the eluate from the extraction tube to the assay priming microwells.

Beyond these additions to the existing BD Viper System's workflow, the following processing functions are common to both systems (extracted and non-extracted):
(5) priming microwell heat spike;
(6) transfer of sample from priming microwells to prewarmed amplification microwells located directly on the reader stage/heater;
(7) amplification microwell plate sealing and movement of the sealed amplification microwells into the fluorescent reader;
(8) amplification temperature control and fluorescent photodetection; and
(9) calculation and result interpretation.

2. Software: The FDA has reviewed applicant's Hazard Analysis and Software development processes for the device

 P. Other Supportive Device and Instrument Information: NA

 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.