510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number: K090971

B. Purpose for Submission: Addition of claims to the assay intended use to include asymptomatic male individuals. The BD ProbeTec™ *Neisseria gonorrhoeae* (GC) Q^{x} Amplified DNA Assay" and BD Viper™ System were previously cleared (K081825).

C. Measurand: *Neisseria gonorrhoeae* DNA

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

The BD ProbeTec GC Q^{x} Amplified DNA Assay, when tested with the BD Viper™ System in Extracted Mode, uses Strand Displacement Amplification technology (SDA) 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 and male individuals to aid in the diagnosis of gonococcal urogenital disease.

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 ProbeTec™ *Neisseria gonorrhoeae* (GC) Q^x Amplified DNA Assay

Gen-Probe Amplified *N. gonorrhoea* Assay

b) Predicate Numbers (s): K081825, K043144

Comparison with predicate:

Device Comparison: Collection Devices and Accessories

	BD ProbeTec GCQ Assay, Swab and Urine Specimens (Device)	**BD ProbeTec GCQ Assay,Swab and Urine Specimens (K081825)**	**Gen-Probe Amplified Neisseria gonorrhoeae Assay (K043144)**

Specimen Types	• Urethral swab Same as K081825 •symptomatic males included • Neat urine Same as K081825 • asymptomatic males included • UPT urine - same as K081825; symptomatic males included • Endocervical swab - Same as K081825 • Patient-collected vaginal swab (in a clinical setting) - Same as K081825 • Urethral swab	• Urethral swab symptomatic males only • Neat urine • symptomatic and symptomatic females ; symptomatic males only • UPT urine - asymptomatic and symptomatic females symptomatic males only • Endocervical swab - asymptomatic and symptomatic females • Patient-collected vaginal swab (in a clinical setting) - asymptomatic and symptomatic females	• Urethral swab symptomatic males • Neat urine • asymptomatic and symptomatic females and males • UTT urine - asymptomatic and symptomatic females and males • Endocervical swab - asymptomatic and symptomatic females • Patient-collected vaginal swab (in a clinical setting) - asymptomatic females • Clinician-collected vaginal swab (in a clinical setting) - asymptomatic and symptomatic females
Specimen Collection and Transport Accessories	• Same as K081825	• Endocervical kit • Urethral kit • Vaginal kit • UPT • Neat urine (Qx Sample Tube)	• Unisex swab kit • Vaginal swab kit • Urine collection kit

Device Comparison: Male Specimen Collection and Processing

	BD ProbeTec GCQ Assay, Swab and Urine Specimens (Device)	**BD ProbeTec GCQ Assay, Swab and Urine Specimens (K081825)**
Specimen Collection	• Same as K081825	• Urethral swab specimens are collected and placed in a BD CT/GC Qx Swab Diluent tube. • UPT urine specimens are collected and placed in a BD Qx UPT. • Neat urine specimens are collected and placed in a BD Qx Sample Tube.
Specimen Processing	• Same as K081825	• Pre-warm specimens (swabs and urines) for 15 minutes before running BD Viper System

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. Analytical performance: Same as described in K081825. No additional analytical studies were necessary to support this extended claim.

2. Comparison studies:

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

   b. *Matrix comparison:* NA

3. Clinical studies:

   a. *Clinical Sensitivity:* See under Performance Characteristics

   b. *Clinical specificity:* See under Performance Characteristics

Performance Characteristics

Clinician-collected male urethral swab specimens and male Q*x* UPT and neat urine specimens were collected from 787 symptomatic and asymptomatic male subjects attending OB/GYN, sexually transmitted disease (STD) and family planning clinics at seven geographically diverse clinical sites in North America. Thirteen 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 774 compliant male subjects.

GC Q*x* Assay Performance Compared to Patient Infected Status in asymptomatic and symptomatic male subjects (by specimen type status)

Performance Compared to Patient Infected Status								
Specimen Type	Symptomatic	N	Sensitivity	95% C.I.	Specificity	95% C.I.	PPV	NPV
MS[1]	A	508	100.0% (12/12)	(73.5% - 100.0%)	99.2% (501/505)	(98.0% - 99.8%)	75.50%	100.00%
	S	257	100.0% (100/100)	(96.4% - 100.0%)	98.7% (154/157)	(95.5% - 99.8%)	98.00%	100.00%
	Total	774	100.0% (112/112)	(96.8% - 100.0%)	99.1% (656/662)	(98.0% - 99.7%)	95.00%	100.00%
MUPT[1]	A	517	100.0% (12/12)	(73.5% - 100.0%)	99.2% (501/505)	(98.0% - 99.8%)	74.60%	100.00%
	S	257	100.0% (100/100)	(96.4% - 100.0%)	98.7% (155/157)	(95.5% - 99.8%)	98.00%	100.00%
	Total	774	100.0% (112/112)	(96.8% - 100.0%)	99.1% (656/662)	(98.0% - 99.7%)	95.00%	100.00%
MNU[1]	A	517	100.0% (12/12)	(73.5% - 100.0%)	99.2% (501/505)	(98.0% - 99.8%)	74.60%	100.00%
	S	257	100.0% (100/100)	(96.4% - 100.0%)	98.7% (155/157)	(95.5% - 99.8%)	98.00%	100.00%
	Total	774	100.0% (112/112)	(96.8% - 100.0%)	99.1% (656/662)	(98.0% - 99.7%)	95.00%	100.00%
Total		6284	99.3% (592/596)	(98.3% - 99.8%)	99.3% (5650/5688)	(99.1% - 99.5%)	93.70%	99.90%

MS: male urethral swab; MNU: male neat urine; MUPT: male UPT urine

[1] Clinical Trial enrollment for asymptomatic male subjects was extended to obtain the total number of clinical positives for this sub-population.

GCQ Assay Performance for Asymptomatic Male Subjects Compared with PIS, by Collection Site

Specimen Type	Collect Site	Prevalence %	N	Sensitivity	95% C.I.	Specificity	95% C.I.	# CT (+) and GC (+)	PPV	NPV
MS	IND	2.00%	100	100.0% (2/2)	(15.8% - 100.0%)	98.0% (96/98)	(92.8% - 99.8%)	1	50.50%	100%
	JHU	0.00%	13	NA		100.0% (13/13)	(75.3% - 100.0%)	0	NA	NA
	LSU	2.80%	218	100.0% (6/6)	(54.1% - 100.0%)	99.5% (211/212)	(97.4% - 100.0%)	4	85.20%	100%
	UAB	0.00%	18	NA		100.0% (18/18)	(81.5% - 100.0%)	0	NA	NA
	UMMC	2.50%	159	100.0% (4/4)	(39.8% - 100.0%)	99.4% (154/155)	(96.5% - 100.0%)	3	81.00%	100%
MNU	IND	2.00%	100	100.0% (2/2)	(15.8% - 100.0%)	98.0% (96/98)	(92.8% - 99.8%)	1	50.50%	100%
	JHU	0.00%	13	NA		100.0% (13/13)	(75.3% - 100.0%)	0	NA	NA

	LSU	2.80%	218	100.0% (6/6)	(54.1% - 100.0%)	99.1% (210/212)	(96.6% - 99.9%)	4	76.20%	100%
	UAB	0.00%	18	NA		100.0% (18/18)	(81.5% - 100.0%)	0	NA	NA
	UMMC	2.40%	168	100.0% (4/4)	(39.8% - 100.0%)	100.0% (164/164)	(97.8% - 100.0%)	3	100%	100%
MUPT	IND	2.00%	100	100.0% (2/2)	(15.8% - 100.0%)	99.0% (97/98)	(94.4% - 100.0%)	1	67.10%	100%
	JHU	0.00%	13	NA		100.0% (13/13)	(75.3% - 100.0%)	0	NA	NA
	LSU	2.80%	218	100.0% (6/6)	(54.1% - 100.0%)	99.1% (210/212)	(96.6% - 99.9%)	4	76.20%	100%
	UAB	0.00%	18	NA		100.0% (18/18)	(81.5% - 100.0%)	0	NA	NA
	UMMC	2.40%	168	100.0% (4/4)	(39.8% - 100.0%)	99.4% (163/164)	(96.6% - 100.0%)	3	80.40%	100%

Additional Analysis: Co-infection status

To determine the effect of CT co-infection with GC, a performance analysis was conducted to assess the GCQ assay results when compared against PIS by co-infection status. Co-infection is defined as GCQ PIS positive and CTQ PIS positive. CTQ PIS positive is defined similarly as to GCQ PIS positive (two of the three reference swabs tested positive for CT). The following table displays the co-infection status of the subjects, the number of specimens, and the calculated sensitivities and specificities for the GCQ assay.

GCQ Assay performance compared to Patient Infected Status by Co-Infection Status for Asymptomatic Males

			Performance Compared to Patient Infected Status			
Specimen Type	Co-infection	N	Sensitivity	95% C.I.	Specificity	95% C. I.
MS	N	500	100% (4/4)	(39.8% - 100.0%)	99.2% (492/496)	(97.9% - 99.8%)
	Y	8	100% (8/8)	(63.1% - 100.0%)	NA	
MNU	N	509	100% (4/4)	(39.8% - 100.0%)	99.2% (501/505)	(98.0% - 99.8%)
	Y	8	100% (8/8)	(63.1% - 100.0%)	NA	
MUPT	N	509	100% (4/4)	(39.8% - 100.0%)	99.2% (501/505)	(98.0% - 99.8%)
	Y	8	100% (8/8)	(63.1% - 100.0%)	NA	

4. Clinical cut-off**:** Clinical cut-off was validated during the swab and urine clinical trial (K081825). The cutoff was 125 MaxRFU (> 125 MaxRFU = positive; < 125 MaxRFU = negtative). The same cutoff was utilized for the clinical trial to validate the performance of the asymptomatic male specimens when tested with the GCQ assay on the BD Viper System 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 40.5% for male specimens (including both symptomatic and asymptomatic subjects).

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 99.3%, 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	99.3	74.3	100.0
5	99.3	99.3	88.2	100.0
10	99.3	99.3	94.0	99.9
20	99.3	99.3	97.3	99.8
30	99.3	99.3	98.4	99.7
40	99.3	99.3	99.0	99.5
50	99.3	99.3	99.3	99.3

N. Instrument: Same as described in K081825.

O. System Descriptions: Same as described in K081825.

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.