510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number: k043144

B. Purpose for Submission: New device clearance

C. Analyte: *Neisseria gonorrhoeae rRNA* (119 bp region within 16S rRNA)

D. Type of Test:
Nucleic acid (rRNA) amplification with chemiluminescent detection; the test system also incorporates an initial target capture step to separate target nucleic acid from specimen. Results are qualitative based on level of photon signals (RLU) released.

E. Applicant: Gen-Probe, Inc
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F. Proprietary and Established Names:
APTIMA Assay for Neisseria gonorrhoeae; nucleic acid (RNA) amplification for *N. gonorrhoeae*

G. Regulatory Information:

1. Regulation section: 21 CFR Part 866
.
2. Classification: II

3. Product Code: LSL, DNA reagents, Neisseria

4. Panel: 83 Microbiology

H. Intended Use:

1. Intended use(s):
The APTIMA assay for *Neisseria gonorrhoeae* is a target amplification nucleic acid probe test that utilizes target capture for the in vitro qualitative detection of ribosomal RNA from *Neisseria gonorrhoeae* (GC) to aid the diagnosis of gonococcal urogenital disease. The assay may be used to test the following specimens from symptomatic individuals: clinician-collected endocervical, vaginal and male urethral swab specimens; and female and male urine specimens. The assay may be used to test the following specimens from asymptomatic individuals: clinician-collected endocervical and vaginal swab specimens; and patient-collected vaginal swab specimens* and female and male urine specimens. *Patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated. The vaginal swab specimen collection kit is not for home use.

2. Indication(s) for use: detect gonococci in male urethral and female swab (endocervical and vaginal) and urine specimens as laboratory evidence of

gonococcal urogenital infection. It is not indicated for testing urethral swab specimens from asymptomatic males.

3. Special condition for use statement(s):

The device is for prescription use only; vaginal swab specimens are not for home use.

4. Special instrument Requirements:

Gen-Probe Leader HC+ luminometer, Gen-Probe Target Capture System (a customized workstation designed to handle TTU (ten tube unit) racks during magnetic separation and washing of the magnetic beads; this apparatus is alternately called DTS-400)

I. Device Description:

The Aptima Assay for *Neisseria gonorrhoeae* (AGC) is an in vitro diagnostic device that detects rRNA from *N. gonorrhoeae* directly in clinical specimens. The test system components are similar and in most cases the same as components used with the predicate Aptima Combo 2. Swab or urine specimens are collected and transferred into specimen transport tubes provided by the manufacturer. The transport solution contains a detergent to release the rRNA target from bacterial cells and protect it from degradation during storage. During the testing procedure, a capture oligomer isolates target rRNA (a 16S region) from the urine and swab samples by the use of a method called target capture. The capture oligomer contains a sequence complementary to a specific region of the target rRNA as well as a string of deoxyadenosine residues. The sequence specific region of the capture oligomer binds to a specific region of the target RNA. The capture oligomer:target complex is then separated out of solution by decreasing the temperature of the reaction to room temperature. This temperature reduction allows hybridization to occur between the deoxyadenosine region on the capture oligomer and the poly-deoxythymidine molecules that are covalently attached to the magnetic particles. The microparticles, including the captured target molecules bound to them, are pulled to the side of the reaction vessel using magnets allowing the supernatant to be aspirated. The particles are washed to remove residual specimen matrix that may contain amplification reaction inhibitors and other potential interferents.

During the next procedural phase, complementary oligonucleotide primers anneal with and allow enzymatic amplification of the target nucleic acid strands. The Gen-Probe TMA reaction replicates a specific region of the 16S rRNA (119 bp region) from *N. gonorrhoeae* via DNA intermediates. Detection of the rRNA amplification product sequences (amplicon) is achieved using nucleic acid hybridization. A single-stranded chemiluminescent DNA probe, which is complementary to a region of the target amplicon, is labeled with an acridinium ester molecule. The labeled DNA probe combines with amplicon to form stable RNA:DNA hybrids. The Selection Reagent differentiates hybridized from unhybridized probe, eliminating the generation of signal from unhybridized probe. During the detection step, light emitted from the labeled

RNA:DNA hybrids is measured as photon signals in a luminometer, that are reported as Relative Light Units (RLU).

The assay system includes specific reagents for the AGC assay (Amplification Reagent, Probe Reagent, Target Capture Reagent B, Probe Reconstitution Reagent, Target capture reagent, and rRNA positive and negative controls) along with component reagents used in other Aptima Assays (Enzyme Reagent, Selection Reagent, Detection reagents, etc.).

The system is performed using required equipment including pipettors, vortex mixers, water baths, Leader® HC+ Luminometer and the Target Capture System (a workstation designed to handle TTU racks during magnetic separation and washing of the magnetic beads; this setup is alternately called DTS-400). The Leader and TCS instruments/equipment are manufactured to GenProbe's specifications. Aptima Assay software installed on the Leader HC Control Unit controls sample detection, interpretation and reporting of assay results.

J. Substantial Equivalence Information:

Predicate device name(s): Gen-Probe™ Aptima Combo 2 Assay (*Chlamydia trachomatis* and *Neisseria Gonorrhoeae*)

1. Predicate K number(s): k003395

2. Comparison with predicate:

Similarities		
Item	Device	Predicate
Target Nucleic acid	16S RNA	16S RNA
Target Capture	Capture oligomer has same GC binding region	
Positive Control	*APTIMA Positive Control, GC/Negative Control, CT* : 250 fg/400 μL *N. gonorrhoeae* rRNA and nonspecific nucleic acid, calf thymus DNA.	
Negative Control	*APTIMA Positive Control-CT/Negative Control-GC,* 5 fg/400 μL *C. trachomatis* rRNA and nonspecific nucleic acid, calf thymus DNA	
Amplification	Enzymes: reverse transcriptase and T7 RNA Polymerase	
Other Reagents	Enzyme , Enzyme Reconstitution, Selection, Wash, Oil Deactivation Fluid Buffer, Auto Detect	

Similarities		
Item	Device	Predicate
Collection & Transport Materials	APTIMA Assay Unisex Swab Specimen Collection Kit for Endocervical and Male Urethral Swab Specimens; APTIMA Assay Urine Specimen Collection Kit for Male and Female Urine Specimens; or APTIMA Vaginal Swab Specimen Collection Kit	
Instrumentation	LEADER HC+ Luminometer and Target Capture System	
Other Equipment	Vortexers, water baths, Pipettors, Reconstitution collars and sealing cards	

Differences		
Item	Device	Predicate
Primer	27-base DNA oligonucleotide	28 base oligonucleotide
Promotor Primer	64-nucleotide DNA polymer	53 nucleotide polymer
Helper Probes	36- and 40-nucleotide	Single 39-nucleotide
Detection probe	20-nucleotide DNA	24-nucleotide
Amplification Reagent	Amplification Reagent, GC	Combo 2 Amplification Reagent
Amplicon	119 nucleotide RNA strand	109 nucleotide RNA strand
Detection Method	Single Kinetic	Dual Kinetic
Probe Label	N-methyl acridinium ester	N-methyl 2'-methyl acridinium ester
Amplification Reconstitution Solution and Probe Reagent	GC	Combo 2
Detection kinetics	Single algorithm	Dual algorithm
Software	APTIMA Assay Software with APTIMA Assay Protocol Disk	APTIMA Assay Software with APTIMA Combo 2 Protocol Disk

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

L. Test Principle:

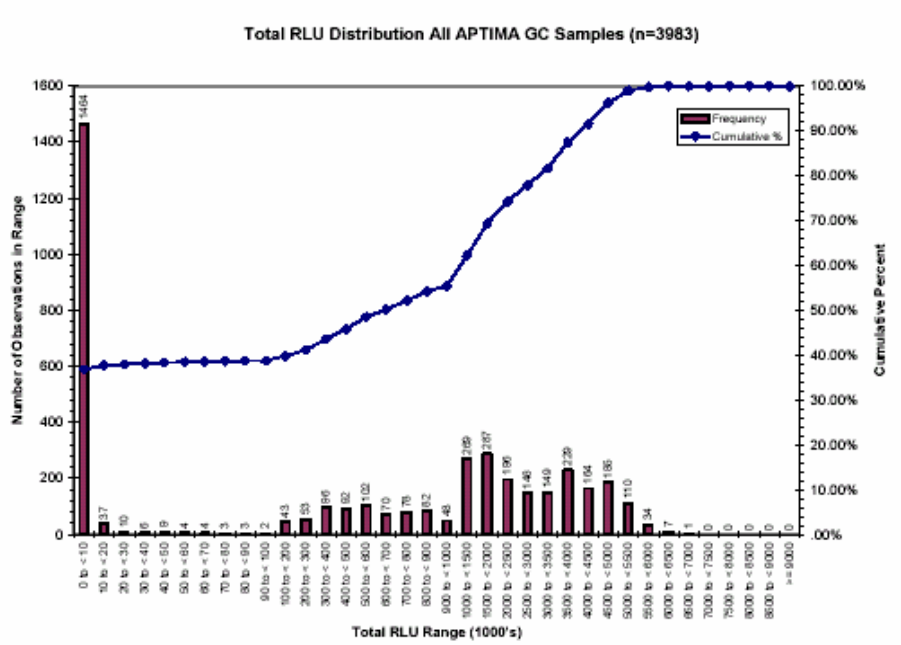
The APTIMA GC Assay combines nucleic acid (rRNA) amplification (Transcription-Mediated Amplification or TMA) with chemiluminescent detection (Hybridization Protection Assay or HPA). The test system also incorporates an initial target capture step to separate target nucleic acid from specimen.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision: Several concentrations of GC rRNA were tested repeatedly under varied conditions. This testing was done at 2 external laboratories and at the manufacturer's facility. Reproducibility for samples with organism in matrix was not assessed. The labeling includes a warning that reproducibility when testing swab and urine specimens containing target organism has not been determined.

b. Linearity/assay reportable range: RLU output values range from 0 to 12 million RLU. With analytical samples tested, highest RLU values were ~7 million. The luminometer counts the number of photons each 20 msec time interval over a 2 sec total read time, resulting in a kinetic profile of the chemiluminescent reaction. The light



output in each interval is reported as relative light units (RLU), which is directly proportional to the number of photons counted.

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

The positive control is rRNA prepared from a broth growth of *Neisseria gonorrhoeae*, ATCC #19424 Type Strain, and purified by sucrose gradient and chloroform-ethanol

extraction. The positive control and a 1:5 dilution were used to assess assay parameters. Testing done for critical parameters in the capture, amplification, and detection stages of the AGC are shown below.

a. Capture Stage Parameters

Step		Condition	50 fg GC		250 fg GC	
			Avg RLU	Result, % Pos	Avg RLU	Result, % Pos
Temp	A-T Binding	7 °C	3,055,000	100%	4,680,000	100%
		RT	3,392,000	100%	4,808,000	100%
		42 °C	4,988,000	100%	4,646,000	100%
	Target Capture	50 °C	2,021,000	100%	3,688,000	100%
		55 °C	3,281,000	100%	4,359,000	100%
		62 °C	3,128,000	100%	4,568,000	100%
		95 °C	1,029,000	100%	2,964,000	100%
Time	A-T Binding	0 min	4,124,000	100%	4,872,000	100%
		15 min	4,199,000	100%	4,641,000	100%
		30 min	4,008,000	100%	5,256,000	100%
		60 min	3,698,000	100%	5,098,000	100%
	Magnetic Separation	1 min	3,514,000	100%	5,403,000	100%
		5 min	3,631,000	100%	5,246,000	100%
		9 min	3,178,000	100%	5,180,000	100%
	Target Capture	0 min	78,000	20%	475,000	100%
		15 min	2,636,000	100%	4,789,000	100%
		30 min	3,976,000	100%	4,898,000	100%
		60 min	3,899,000	100%	4,771,000	100%
Volume	Control	200 µl	2,146,000	100%	4,341,000	100%
		300 µl	3,448,000	100%	5,178,000	100%
		400 µl	4,238,000	100%	5,456,000	100%
		600 µl	4,763,000	100%	5,607,000	100%
		800 µl	5,057,000	100%	5,706,000	100%
	TCR	0 µl	2,770,000	80%	376,000	40%
		50 µl	5,033,000	100%	6,079,000	100%
		100 µl	4,238,000	100%	5,456,000	100%
		150 µl	2,906,000	100%	4,394,000	100%
		200 µl	1,886,000	100%	3,657,000	100%
	Wash Solution	0 ml	2,828,000	100%	3,511,000	80%
		0.5 ml	3,208,000	100%	4,844,000	100%
		1 ml	3,338,000	100%	5,054,000	100%
		2 ml	2,736,000	100%	4,634,000	100%

b. Amplification stage parameters

Step		Condition	50 fg GC		250 fg GC	
			Avg RLU	Result, % Pos	Avg RLU	Result, % Pos
Temp	Amplification	37°C	3,064,000	100%	4,954,000	100%
		42°C	3,857,000	100%	5,298,000	100%
		44°C	230,000	100%	339,000	100%
	Primer Binding	RT	1,370,000	100%	3,462,000	100%
		62 °C	3,933,000	100%	5,413,000	100%
		75 °C	4,216,000	100%	5,386,000	100%
		95 °C	3,397,000	100%	5,332,000	100%
Time	Amplification	30 min	1,977,000	100%	3,929,000	100%
		60 min	2,822,000	100%	4,339,000	100%
		90 min	3,010,000	100%	4,561,000	100%
	Pre-Enzyme Incubation	0 min	2,872,000	100%	4,609,000	100%
		5 min	2,579,000	100%	4,450,000	100%
		15 min	2,452,000	100%	4,790,000	100%
	Primer Binding	0 min	746,000	100%	2,422,000	100%
		10 min	3,204,000	100%	4,793,000	100%
		30 min	3,177,000	100%	4,773,000	100%
Volume	Amplification Reagent	25 µl	2,965,000	100%	4,761,000	100%
		75 µl	3,764,000	100%	5,412,000	100%
		100 µl	4,298,000	100%	5,182,000	100%
		125 µl	3,839,000	100%	5,078,000	100%
	Enzyme Reagent	10 µl	2,018,000	100%	4,484,000	100%
		15 µl	3,478,000	100%	4,931,000	100%
		25 µl	4,238,000	100%	5,456,000	100%
		35 µl	4,221,000	100%	5,424,000	100%
		40 µl	3,990,000	100%	5,490,000	100%
	Oil Reagent	0 µl	4,099,000	100%	5,306,000	100%
		200 µl	3,947,000	100%	5,707,000	100%
		400 µl	3,853,000	100%	5,061,000	100%

c. Detection stage parameters.

Step		Condition	50 fg GC		250 fg GC	
			Avg RLU	Result, % Pos	Avg RLU	Result, % Pos
Temp	Hybridization & Selection	60 °C	4,160,000	100%	5,273,000	100%
		61 °C	4,738,000	100%	5,930,000	100%
		62 °C	4,015,000	100%	5,514,000	100%
		63 °C	4,039,000	100%	5,354,000	100%
		64 °C	2,937,000	100%	4,262,000	100%
	Pre-Selection Incubation	7 °C	3,783,000	100%	5,218,000	100%
		RT	3,854,000	100%	4,992,000	100%
		42 °C	3,794,000	100%	4,961,000	100%
	Pre-Detection Incubation	7 °C	3,472,000	100%	5,122,000	100%
		RT	3,854,000	100%	4,992,000	100%
		60 °C	2,292,000	100%	3,398,000	100%
Time	Hybridization	5 min	2,165,000	100%	4,540,000	100%
		20 min	2,481,000	100%	4,522,000	100%
		30 min	2,788,000	100%	4,638,000	100%
	Pre-Selection Incubation	0 min	2,709,000	100%	3,720,000	100%
		5 min	2,889,000	100%	4,617,000	100%
		15 min	2,792,000	100%	4,702,000	100%
	Pre-Detection Incubation	8 min	3,462,000	100%	5,259,000	100%
		15 min	3,395,000	100%	5,186,000	100%
		19 min	3,110,000	100%	4,935,000	100%
	Selection	5 min	3,841,000	100%	6,390,000	100%
		7 min	3,484,000	100%	5,879,000	100%
		8 min	3,941,000	100%	5,981,000	100%
		10 min	4,284,000	100%	5,283,000	100%
		15 min	2,653,000	100%	4,343,000	100%
Volume	Probe Reagent	50 µl	2,579,000	100%	2,991,000	100%
		100 µl	3,947,000	100%	5,707,000	100%
		150 µl	4,966,000	100%	7,031,000	100%
		200 µl	5,973,000	100%	8,481,000	100%
	Selection Reagent	100 µl	4,283,000	100%	5,616,000	100%
		200 µl	4,167,000	100%	5,585,000	100%
		250 µl	3,947,000	100%	5,707,000	100%
		300 µl	4,239,000	100%	5,527,000	100%
		500 µl	3,858,000	100%	5,306,000	100%

d. Detection limit: The kit positive control contains 250 fg *N. gonorrhoeae* rRNA. This control was diluted serially10-fold. Results are shown below. At a 100-fold dilution, all RLU values are in the low positive region.

fg GC rRNA	Replicate 1		Replicate 2		Replicate 3		Replicate 4		Replicate 5	
	RLU	Result	RLU	Result	RLU	Result	RLU	Result	RLU	Result
250	5,696,000	GC+	5,804,000	GC+	6,040,000	GC+	5,979,000	GC+	6,202,000	GC+
25	86,000	GCeq	2,684,000	GC+	2,829,000	GC+	2,830,000	GC+	1,245,000	GC+
2.5	392,000	GC+	483,000	GC+	322,000	GC+	483,000	GC+	6,000	GC-
0.25	8,000	GC-	17,000	GC-	69,000	GCeq	50,000	GCeq	23,000	GC-
0.025	7,000	GC-	2,000	GC-	26,000	GC-	3,000	GC-	2,000	GC-
0.0025	3,000	GC-	3,000	GC-	2,000	GC-	2,000	GC-	2,000	GC-

Serial dilutions of 51 N. gonorrhoeae clinical isolates were prepared from McFarland preparations. Five dilutions were quantified by plate counts and microscopically with a

hemocytometer. One hundred microliters (100 µL) of the stock McFarland suspension was added to 3.9 mL of Swab Transport Media. After quantitation of the McFarland suspensions, the appropriate amounts of the Swab Transport Media stock that would result in 0.5, 5, and 50 cells per assay were added to KOVA-Trol/Urine Transport Media and Swab Transport Media. These dilutions were tested by APTIMA GC in triplicate. The source and characterization of these strains was not indicated. Most of the strains tested were detected with high RLU levels (>2,000,000) at each of the three levels (50, 5, and 0.5 cells per assay). The labeling claims detection of 50 cells per assay (calculated to be equivalent to 362 CFU/swab or 250 CFU/mL urine). Based on these data, most strains would be detected at lower levels (5 or 0.5 cells/assay). Some strains (for example, #337) yield lower RLU values at all levels. Results for dilutions in swab transport media are shown below:

Swab Transport Media

Isolate	GC Cells	Replicate 1		Replicate 2		Replicate 3	
#	Per Assay	RLU	Result	RLU	Result	RLU	Result
337	50	393,000	GC (+)	497,000	GC (+)	440,000	GC (+)
	5	69,000	GC (e)	51,000	GC (e)	40,000	GC (-)
	0.5	16,000	GC (-)	10,000	GC (-)	15,000	GC (-)
343	50	687,000	GC (+)	930,000	GC (+)	1,084,000	GC (+)
	5	85,000	GC (e)	83,000	GC (e)	118,000	GC (+)
	0.5	9,000	GC (-)	7,000	GC (-)	19,000	GC (-)
322	50	5,907,000	GC (+)	6,124,000	GC (+)	6,075,000	GC (+)
	5	5,758,000	GC (+)	5,748,000	GC (+)	5,726,000	GC (+)
	0.5	3,898,000	GC (+)	3,726,000	GC (+)	3,591,000	GC (+)
323	50	3,720,000	GC (+)	3,459,000	GC (+)	4,287,000	GC (+)
	5	1,228,000	GC (+)	1,439,000	GC (+)	1,036,000	GC (+)
	0.5	116,000	GC (+)	103,000	GC (+)	106,000	GC (+)
324	50	1,060,000	GC (+)	339,000	GC (+)	1,108,000	GC (+)
	5	83,000	GC (e)	150,000	GC (+)	156,000	GC (+)
	0.5	21,000	GC (-)	14,000	GC (-)	4,000	GC (-)
329	50	5,277,000	GC (+)	5,304,000	GC (+)	5,538,000	GC (+)
	5	3,629,000	GC (+)	3,544,000	GC (+)	3,490,000	GC (+)
	0.5	423,000	GC (+)	481,000	GC (+)	775,000	GC (+)
332	50	5,355,000	GC (+)	5,274,000	GC (+)	5,335,000	GC (+)
	5	4,829,000	GC (+)	4,785,000	GC (+)	4,798,000	GC (+)

Swab Transport Media							
Isolate #	GC Cells Per Assay	Replicate 1		Replicate 2		Replicate 3	
		RLU	Result	RLU	Result	RLU	Result
799	50	5,835,000	GC (+)	5,748,000	GC (+)	5,890,000	GC (+)
	5	5,919,000	GC (+)	6,118,000	GC (+)	5,808,000	GC (+)
	0.5	5,605,000	GC (+)	5,538,000	GC (+)	5,627,000	GC (+)
806	50	5,709,000	GC (+)	5,699,000	GC (+)	5,576,000	GC (+)
	5	5,934,000	GC (+)	5,821,000	GC (+)	5,989,000	GC (+)
	0.5	5,256,000	GC (+)	5,079,000	GC (+)	5,190,000	GC (+)
827	50	6,057,000	GC (+)	6,096,000	GC (+)	6,064,000	GC (+)
	5	5,863,000	GC (+)	5,930,000	GC (+)	5,825,000	GC (+)
	0.5	5,109,000	GC(+)	4,997,000	GC (+)	4,987,000	GC (+)
800	50	5,681,000	GC (+)	5,779,000	GC (+)	5,811,000	GC (+)
	5	5,845,000	GC (+)	5,918,000	GC (+)	5,943,000	GC (+)
	0.5	4,558,000	GC (+)	5,799,000	GC (+)	5,803,000	GC (+)
793	50	6,011,000	GC (+)	5,897,000	GC (+)	5,806,000	GC (+)
	5	5,331,000	GC (+)	5,579,000	GC (+)	5,757,000	GC (+)
	0.5	4,961,000	GC (+)	4,403,000	GC (+)	4,852,000	GC (+)
787	50	5,964,000	GC (+)	6,128,000	GC (+)	6,029,000	GC (+)
	5	5,804,000	GC (+)	5,720,000	GC (+)	5,730,000	GC (+)
	0.5	5,015,000	GC (+)	1,000	GC (-)	4,756,000	GC (+)
795	50	5,838,000	GC (+)	6,154,000	GC (+)	6,071,000	GC (+)
	5	5,641,000	GC (+)	5,722,000	GC (+)	5,886,000	GC (+)
	0.5	4,981,000	GC (+)	2,552,000	GC (+)	5,063,000	GC (+)
790	50	5,944,000	GC (+)	5,890,000	GC (+)	5,787,000	GC (+)
	5	3,857,000	GC (+)	5,795,000	GC (+)	5,657,000	GC (+)
	0.5	5,085,000	GC (+)	4,892,000	GC (+)	4,696,000	GC (+)
802	50	5,933,000	GC (+)	6,049,000	GC (+)	5,885,000	GC (+)
	5	5,361,000	GC (+)	5,408,000	GC (+)	5,488,000	GC (+)
	0.5	122,000	GC (+)	4,632,000	GC (+)	5,293,000	GC (+)
334	50	6,113,000	GC (+)	5,979,000	GC (+)	6,036,000	GC (+)
	5	5,375,000	GC (+)	5,252,000	GC (+)	5,294,000	GC (+)
	0.5	2,140,000	GC (+)	1,935,000	GC (+)	1,992,000	GC (+)
335	50	5,705,000	GC (+)	5,799,000	GC (+)	5,732,000	GC (+)
	5	3,986,000	GC (+)	3,781,000	GC (+)	3,344,000	GC (+)
	0.5	645,000	GC (+)	673,000	GC (+)	548,000	GC (+)
336	50	5,690,000	GC (+)	5,612,000	GC (+)	5,661,000	GC (+)
	5	3,327,000	GC (+)	3,074,000	GC (+)	3,900,000	GC (+)
	0.5	541,000	GC (+)	553,000	GC (+)	533,000	GC (+)
750	50	6,002,000	GC (+)	5,965,000	GC (+)	5,826,000	GC (+)
	5	4,995,000	GC (+)	4,859,000	GC (+)	4,639,000	GC (+)
	0.5	1,292,000	GC (+)	1,078,000	GC (+)	1,029,000	GC (+)
327	50	5,899,000	GC (+)	5,792,000	GC (+)	5,717,000	GC (+)
	5	5,993,000	GC (+)	5,934,000	GC (+)	5,808,000	GC (+)
	0.5	5,570,000	GC (+)	5,316,000	GC (+)	5,317,000	GC (+)
339	50	5,764,000	GC (+)	5,684,000	GC (+)	5,694,000	GC (+)
	5	5,573,000	GC (+)	4,556,000	GC (+)	5,517,000	GC (+)
	0.5	5,279,000	GC (+)	5,474,000	GC (+)	5,404,000	GC (+)
758	50	5,913,000	GC (+)	5,714,000	GC (+)	5,776,000	GC (+)
	5	5,727,000	GC (+)	5,856,000	GC (+)	5,802,000	GC (+)
	0.5	5,489,000	GC (+)	5,238,000	GC (+)	5,246,000	GC (+)
774	50	5,650,000	GC (+)	5,632,000	GC (+)	5,646,000	GC (+)
	5	5,689,000	GC (+)	5,575,000	GC (+)	5,609,000	GC (+)

Swab Transport Media							
Isolate #	GC Cells Per Assay	Replicate 1		Replicate 2		Replicate 3	
		RLU	Result	RLU	Result	RLU	Result
	0.5	3,158,000	GC (+)	3,023,000	GC (+)	2,981,000	GC (+)
344	50	4,874,000	GC (+)	4,947,000	GC (+)	4,958,000	GC (+)
	5	2,985,000	GC (+)	2,905,000	GC (+)	2,888,000	GC (+)
	0.5	568,000	GC (+)	566,000	GC (+)	504,000	GC (+)
345	50	1,689,000	GC (+)	1,778,000	GC (+)	1,769,000	GC (+)
	5	371,000	GC (+)	478,000	GC (+)	414,000	GC (+)
	0.5	23,000	GC (-)	15,000	GC (-)	34,000	GC (-)
347	50	4,810,000	GC (+)	4,871,000	GC (+)	4,820,000	GC (+)
	5	2,855,000	GC (+)	3,220,000	GC (+)	3,073,000	GC (+)
	0.5	542,000	GC (+)	615,000	GC (+)	583,000	GC (+)
3063	50	1,747,000	GC (+)	5,852,000	GC (+)	5,788,000	GC (+)
	5	4,747,000	GC (+)	4,984,000	GC (+)	4,916,000	GC (+)
	0.5	696,000	GC (+)	1,274,000	GC (+)	960,000	GC (+)
3064	50	5,831,000	GC (+)	5,809,000	GC (+)	5,671,000	GC (+)
	5	5,195,000	GC (+)	5,204,000	GC (+)	5,331,000	GC (+)
	0.5	1,960,000	GC (+)	2,020,000	GC (+)	2,024,000	GC (+)
3091	50	5,981,000	GC (+)	5,863,000	GC (+)	5,887,000	GC (+)
	5	5,438,000	GC (+)	5,356,000	GC (+)	5,380,000	GC (+)
	0.5	2,323,000	GC (+)	2,350,000	GC (+)	2,325,000	GC (+)
3092	50	5,654,000	GC (+)	5,433,000	GC (+)	5,679,000	GC (+)
	5	2,849,000	GC (+)	1,859,000	GC (+)	3,773,000	GC (+)
	0.5	648,000	GC (+)	609,000	GC (+)	1,000	GC (-)
3100	50	5,900,000	GC (+)	5,912,000	GC (+)	5,936,000	GC (+)
	5	4,845,000	GC (+)	5,168,000	GC (+)	4,790,000	GC (+)
	0.5	2,297,000	GC (+)	2,211,000	GC (+)	2,285,000	GC (+)
3101	50	5,271,000	GC (+)	5,303,000	GC (+)	5,436,000	GC (+)
	5	4,345,000	GC (+)	4,241,000	GC (+)	4,415,000	GC (+)
	0.5	1,532,000	GC (+)	1,576,000	GC (+)	1,491,000	GC (+)
3103	50	5,979,000	GC (+)	5,852,000	GC (+)	5,702,000	GC (+)
	5	5,224,000	GC (+)	4,926,000	GC (+)	5,169,000	GC (+)
	0.5	29,000	GC (-)	2,053,000	GC (+)	1,953,000	GC (+)
3047	50	6,020,000	GC (+)	6,171,000	GC (+)	6,009,000	GC (+)
	5	5,550,000	GC (+)	701,000	GC (+)	5,747,000	GC (+)
	0.5	5,078,000	GC (+)	5,662,000	GC (+)	5,352,000	GC (+)
3024	50	5,634,000	GC (+)	5,743,000	GC (+)	5,826,000	GC (+)
	5	5,442,000	GC (+)	5,520,000	GC (+)	5,581,000	GC (+)
	0.5	5,628,000	GC (+)	5,468,000	GC (+)	5,574,000	GC (+)
3045	50	635,000	GC (+)	5,899,000	GC (+)	6,001,000	GC (+)
	5	5,892,000	GC (+)	5,566,000	GC (+)	205,000	GC (+)
	0.5	5,510,000	GC (+)	5,693,000	GC (+)	5,601,000	GC (+)
3043	50	5,826,000	GC (+)	5,745,000	GC (+)	6,011,000	GC (+)
	5	6,031,000	GC (+)	4,175,000	GC (+)	5,868,000	GC (+)
	0.5	3,102,000	GC (+)	5,353,000	GC (+)	5,307,000	GC (+)
813	50	5,777,000	GC (+)	5,928,000	GC (+)	7,856,000	GC (+)
	5	5,812,000	GC (+)	6,031,000	GC (+)	5,839,000	GC (+)
	0.5	5,128,000	GC (+)	5,090,000	GC (+)	4,519,000	GC (+)
801	50	5,846,000	GC (+)	5,697,000	GC (+)	5,834,000	GC (+)
	5	5,609,000	GC (+)	5,741,000	GC (+)	5,751,000	GC (+)
	0.5	5,284,000	GC (+)	5,157,000	GC (+)	5,158,000	GC (+)

2. Comparison studies: NA

3. Clinical studies:

The data in support of this submission is from a prospective, single-arm, multi-center clinical study to determine the performance characteristics and precision of the Aptima GC (AGC) Assay for the detection of *Neisseria gonorrhoeae* GC in female endocervical swab, patient-collected vaginal swab (PVS), clinician-collected vaginal swab (CVS), and first catch urine (FCU) specimens and in male urethral swab and first catch urine specimens.
The first study enrolled 2,851 symptomatic and asymptomatic, male and female subjects from Ob-Gyn clinic settings and STD, teen and family planning clinics from eight geographically diverse, and high and low prevalence sites; a ninth site performed specimen testing using the BD Assay, and a tenth site, GenProbe, performed specimen testing using the AC2 Assay as well as the alternate TMA amplification assay for GC. Five specimens were collected from each female subject enrolled in the study: two endocervical swabs, one FCU specimen, one PVS, and one CVS. Three different specimens were collected from each male subject enrolled in the study: two urethral swabs and one patient-collected FCU specimen. The clinical study evaluated the performance characteristics of the AGC Assay in terms of sensitivity, specificity and predictive values. Four specimen results were used to determine each male or female subject's GC infected status. An "infected status +" is any one assay positive with a positive by a 2nd assay with a different target and a different format (regardless of specimen).

Summary of Performance of the Aptima GC Assay:

Specimen type	Symptoms	N	Sensitivity (CI)	Specificity(CI)	Prevalence	PPV	NPV
Male urethral swab	Symptomatic	575	99.4 (96.8-100)	97.5 (95.5-98.8)	29. 7%	94%	99.70%
	Asymptomatic	742	100 (69.2-100)	97.0 (95.5-98.1)	1.30%	31%	100%
Male urine	Symptomatic	576	99.4 (96.8-100)	99.0 (97.5-99.7)	29.70%	97.70%	99.70%
	Asymptomatic	745	90.0 (55.5-99.7)	99.3 (98.4-99.8)	1.30%	64%	99.90%
Female endocervical swab	Symptomatic	805	98.1 (89.9-100)	98.9 (97.9-99.5)	6.40%	86.70%	99.90%
	Asymptomatic	635	95.2 (76.2-99.9)	99.2 (98.1-99.7)	3.10%	80%	99.80%
Female urine	Symptomatic	810	90.6 (79.3-96.9)	99.7 (99.0-100)	5.90%	96%	96.80%
	Asymptomatic	639	95.5 (77.2-99.9)	99.8 (99.1-100)	3.20%	95%	99.80%
Patient-collected Vag Swab	Asymptomatic	629	100 (83.9-100)	99.3 (98.3-99.8)	3.30%	84%	100%
	All	1422	97.3 (90.6-99.7)	99.2 (98.5-99.6)	5.20%	86.70%	99. 9%
Clinician-collected Vag Swab	Symptomatic	809	98.1 (89.9-100)	99.1 (98.1-99.6)	6.40%	88%	99.90%
	Asymptomatic	637	95.5 (77.2-99.9)	99.3 (98.3-99.8)	3.30%	84%	99.80%

The clinical evaluation with testing swabs from asymptomatic males raised concerns about false positivity. Out of 746 asymptomatic male patients who had urethral swab specimens tested by AGC, there were 10 infected individuals defined by the reference assays and an additional 22 patients that had positive AGC results; the consequent positive predictive value is 31% for AGC testing of urethral swabs from asymptomatic males. The use of swab specimens for asymptomatic males was not indicated in the final labeling.

a. Clinical cut-off: During the clinical evaluation, a 100,000 RLU cutoff used to separate positive AGC results from equivocal results. The majority of infected patients in all groups had AGC RLU results >2,000,000. Overall there was a preponderance of presumed false positives with RLU levels between 100,000 and 2,000,000 (See below). The labeling advises that AGC tests with RLU results in that range are more likely to be falsely positive. The numbers of presumed false positives in different measurement ranges was broken out as follows:

Breakout by specimen type – distribution of FP&TP across "positive" range

neg=1220 (3FN)	100k-1,000k	1-2 M	2-3 M	3 -4 M	4-5 M	5-6 M	>6M
Endocx swab							
Total n	12	1	1	7	1	15	47
# FP	11	1	0	0	0	0	0
#TP	1	0	1	7	1	15	47
Proportion TP	8.3%			100	100	100	100

neg=1446 (2 FN)	100k-1,000k	1-2 M	2-3 M	3 -4 M	4-5 M	5-6 M	>6M
Vag Swab(CC)							
Total n	6	3	1	6	1	19	48
# FP	5	3	0	1	0	2	0
#TP	1	0	1	5	1	17	48
Proportion TP	16.7%	0		83.3%		89.5%	100%

neg=1422 (3 FN)	100k-1,000k	1-2 M	2-3 M	3 -4 M	4-5 M	5-6 M	>6M
Vag Swab(PC)							
Total n	9	0	2	9	1	20	42
# FP	7	0	1	2	0	1	1
#TP	2	0	1	7	1	19	41
Proportion TP	22.2%		50%	77.8%		95%	97.6%

neg=1057 (5FN)	100k-1,000k	1-2 M	2-3 M	3 -4 M	4-5 M	5-6 M	>6M
Urethral swab							
Total n	28	3	3	5	4	31	139
# FP	25	1	2	2	0	0	0
#TP	3	2	1	3	4	31	139
Proportion TP	10.7%	66.7%	33.3%	60.0%	100%	100%	100%

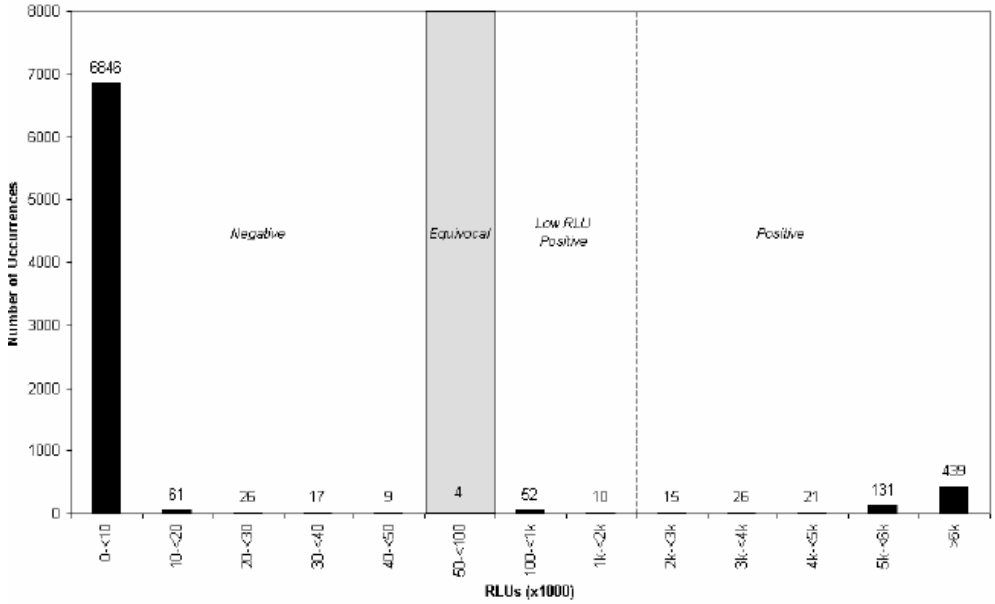
neg=1074 (9FN)	100k-1,000k	1-2 M	2-3 M	3 -4 M	4-5 M	5-6 M	>6M
Male Urine							
Total n	5	4	2	1	8	36	133
# FP	5	2	1	1	0	0	0
#TP	0	2	1	0	8	36	133
Proportion TP	0%	50%	50%		100%	100%	100%

neg=1257 (10FN)	100k-1,000k	1-2 M	2-3 M	3 -4 M	4-5 M	5-6 M	>6M
Female Urine							
Total n	9	0	7	3	6	13	34
# FP	2	0	0	1	0	0	0
#TP	7	0	7	2	6	13	34
Proportion TP	77.8%	0	100%	66.7%	100%	100%	100%

Note: calculations not done when fewer than 2 results in any one region. Gray areas are where numbers although mostly small suggest an equivocal region.

b. Expected values/Reference range: As discussed above, an RLU region immediately above the designated equivocal region, was determined to be a low measurement region in which results were more likely falsely positive. The distribution of RLU responses from all specimen types tested in the clinical study are shown below:

Figure 2 Frequency of RLU Distribution for the APTIMA GC Assay



d. **Instrument Name:** Leader HC Luminometer and Target Capture System (specifications shown below)

Component	Specifications
Main Workstation	5 in. high x 19 in. wide x 19 in. deep (approximately 35.5 cm high x 48.25 cm wide x 48.25 cm deep). Requires approximately 12 in. (30 cm) of space above the unit to maneuver the Aspiration Manifold dispense handles.
Dispense Manifold and Station	4 in. high x 9 in. wide x 10 in. deep (approximately 9 cm high x 22.75 cm wide x 25.5 cm deep).
Vacuum Trap	18 in. high x 15 in. wide x 7 in. deep (approximately 45.75 cm high x 38 cm wide x 17.75 cm deep).
Vacuum Pump Requirement	Absolute vacuum and open-flow rate specifications are dependent upon altitude. Contact Technical Service for the appropriate specifications.
Weight	Workstation & Aspiration Manifold: 23.6 lbs. (10.7 kg) Dispense Station & Manifold: 4.8 lbs. (2.2 kg) Vacuum Trap: 16.4 lbs. (7.5 kg) Vacuum Pump: 30 lbs. (13.6 kg) Total weight: 74. 8 lbs. (34 kg)
Voltage	115V 60 Hz
Injector Volumes	Provides delivery of 1.0 ml +/- 10% volume of fluid from the Wash Reagent Bottle via an operator-activated Dispense Manifold, without splash-back.
Operating Environment	Operates in a controlled environment of 15° C to 30° C and 20% to 90% relative humidity, non-condensing.

7.1 LEADER HC+ Luminometer Specifications

Component	Specifications
Dimensions	19.1 cm H x 45.7 cm W x 67.3 cm D (7.5 in. H x 18.0 in. W x 26.5 in. D)
Weight	23 kg (50 lb)
Power Requirements	100-140VAC 50-60 Hz, OR 200-250VAC 50-60 Hz Main supply fluctuation not to exceed ±10% of nominal voltage. Transient over-voltages according to installation Categories I, II, and III. For main supply, the minimum and normal category is II.
Operating Environment	Indoor use; maximum relative humidity of 10 to 90%; temperature range 15°C to 30°C unless specified otherwise in assay package inserts; altitude up to 2000m
Injector Volumes	200 µL, Accuracy ±10%, Coefficient of Variation ≤2% CV
Instrument Precision Capability	Photon (see glossary) counting < 2% CV at 1000 RLU or greater
Serial Output	RS-232, 9600 baud; 8 data bits; odd parity; 1 stop bit
Test Tubes	Due to the special requirements of luminescence measurements, not every type or brand of reaction tube can be used (see the assay package insert). Use individual polypropylene or polystyrene 12 x 75mm tubes for pump volume verification.
Cassettes	Processes up to 25 Cassettes per run, each capable of holding ten (10), 12 x 75 mm tubes, or one TTU.

Note: Specifications are subject to change without notice.

O. System Descriptions:

1. Modes of Operation:

   The Aptima software is resident in an internal hard drive and performs an array of functions including: hardware control, measurement, patient sample identification, systems parameters, communication, self-diagnosis and maintenance.

2. Software:

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

   Yes ____x____ or No _____

3. Specimen Identification: no comments

4. Specimen Sampling and Handling: no comments

5. Calibration: no comments

6. Quality Control: no comments

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

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.