K111409

510(k) SUMMARY

MAY - 3 2012

APTIMA Combo 2® Assay on the PANTHER System

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General Information

Trade Name: APTIMA Combo 2® Assay

Common or Usual Name: Ribosomal RNA (rRNA) target-amplified nucleic acid probe test for the *in vitro* diagnostic detection of *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae*

Classification Names: DNA Probe, Nucleic Acid Amplification, Chlamydia
DNA Reagents, Neisseria

APTIMA Combo 2 Assay

Device Description	DNA Probe, Nucleic Acid Amplification, Chlamydia
Medical Specialty	Microbiology
Product Code	MKZ
Device Class	1
Regulation number	866.3120

Device Description	DNA Reagents, Neisseria
Medical Specialty	Microbiology
Product Code	LSL
Device Class	2
Regulation number	866.3390

Substantially Equivalent Devices:
APTIMA Combo 2 Assay; K032194

This pre-market application is to clear the APTIMA Combo 2 Assay for use on the PANTHER System. The APTIMA Combo 2 Assay was cleared on the predicate TIGRIS System on December 24, 2003 (K032194). Clearance of this 510(k) will add the PANTHER System as an optional platform. No changes were introduced to the APTIMA Combo 2 Assay reagents.

Device Description

The APTIMA Combo 2 Assay combines the technologies of target capture, TMA, and DKA.

Specimens are collected and transferred into their respective specimen transport tubes. The transport solutions in these tubes release the rRNA targets and protect them from degradation during storage. When the APTIMA Combo 2 Assay is performed in the laboratory, the target rRNA molecules are isolated from specimens by use of capture oligomers via target capture that utilizes magnetic microparticles. The capture oligomers contain sequences complementary to specific regions of the target molecules as well as a string of deoxyadenosine residues. A separate capture oligomer is used for each target. During the hybridization step, the sequence specific regions of the capture oligomers bind to specific regions of the target molecules. The capture oligomer:target complex is then captured 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 and the supernatant is aspirated. The particles are washed to remove residual specimen matrix that may contain amplification reaction inhibitors. After the target capture steps are completed, the specimens are ready for amplification.

Target amplification assays are based on the ability of complementary oligonucleotide primers to specifically anneal and allow enzymatic amplification of the target nucleic acid strands. The APTIMA Combo 2 Assay replicates a specific region of the 23S rRNA from CT and a specific region of the 16S rRNA from GC via DNA intermediates. A unique set of primers is used for each target molecule. Detection of the rRNA amplification product sequences (amplicon) is achieved using nucleic acid hybridization. Single-stranded chemiluminescent DNA probes, which are complementary to a region of each target amplicon, are labeled with different acridinium ester molecules. The labeled DNA probes combine 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,

and are reported as Relative Light Units (RLU). In DKA, differences in the kinetic profiles of the CT and GC labeled probes allow for the differentiation of signal; kinetic profiles are derived from measurements of photon output during the detection read time. The chemiluminescent detection reaction for CT signal has very rapid kinetics and has the "flasher" kinetic type. The chemiluminescent detection reaction for GC signal is relatively slower and has the "glower" kinetic type. Assay results are determined by a cut-off based on the total RLU and the kinetic curve type.

Intended Use

The AC2 Assay intended use is stated below.

The APTIMA COMBO 2 Assay is a target amplification nucleic acid probe test that utilizes target capture for the *in vitro* qualitative detection and differentiation of ribosomal RNA (rRNA) from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC) to aid in the diagnosis of chlamydial and/or gonococcal urogenital disease using the PANTHER System as specified.

On the PANTHER System, the assay may be used to test the following specimens from symptomatic and asymptomatic individuals: clinician-collected endocervical, vaginal and male urethral swab specimens, clinician-collected gynecological specimens collected in the PreservCyt Solution, and patient-collected vaginal swab specimens[1].

[1]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.

Comparison to Predicate

A comparison of the AC2 Assay on the PANTHER System with the predicate TIGRIS System is summarized below.

Comparison to Predicate Device

Item	AC2 on TIGRIS System (Predicate Device)	AC2 on PANTHER System
Device Class	II	II
Regulation Specialty	Microbiology	Microbiology
Qualitative /Quantitative Assay	Qualitative	Qualitative
Function	Detection and differentiation of rRNA from *Chlamydia trachomatis* and *Neisseria gonorrhoeae*	Detection and differentiation of rRNA from *Chlamydia trachomatis* and *Neisseria gonorrhoeae*
Indications For Use / Intended Use	Detection and differentiation of rRNA from *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on the DTS and TIGRIS Systems.	Detection and differentiation of rRNA from *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on the PANTHER System.
Specimen Types	**Female specimens**: • Vaginal swab • Endocervical swab • ThinPrep in PreservCyt solution • Urine **Male Specimens**: • Urethral Swab • Urine	**Female specimens**: • Vaginal swab • Endocervical swab • ThinPrep in PreservCyt solution **Male Specimens**: • Urethral Swab

Item	AC2 on TIGRIS System (Predicate Device)	AC2 on PANTHER System
Specimen Transport/Storage	**Swabs:** After collection, transport and store swab in transport tube at 2-30°C and test within 60 days. If longer storage is desired, freeze at -20°C to -70°C for up to 365 days. **ThinPrep Liquid Pap in PreservCyt:** Transport and store in PreservCyt solution at 2-30°C for up to 30 days. After transfer to APTIMA specimen transfer tube, store at 15-30°C for 14 days or store at 2-8°C for 30 days. If longer storage is desired, freeze at -20°C to -70°C for up to 365 days. **Urine:** After collection, transfer urine to transport tube within 24 hours and store at 2-30°C; Must be assayed within 30 days after transfer. If held longer, freeze –at 20°C to -70°C for up to 365 days.	**Swabs:** After collection, transport and store swab in transport tube at 2-30°C and test within 60 days. If longer storage is desired, freeze at -20°C to -70°C for up to 365 days. **ThinPrep Liquid Pap in PreservCyt:** Transport and store in PreservCyt solution at 2-30°C for up to 30 days. After transfer to APTIMA specimen transfer tube, store at 15-30°C for 14 days or store at 2-8°C for 30 days. If longer storage is desired, freeze at -20°C to -70°C for up to 365 days.
Type of Assay	Nucleic Acid Amplification Test	Nucleic Acid Amplification Test
Technology*	Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA)	Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA)
Detection Format	HPA which provides relative light units (RLUs) that are assessed against an established assay cutoff	HPA which provides relative light units (RLUs) that are assessed against an established assay cutoff

*A number of Gen-Probe APTIMA assays (that are based on TC, TMA, and HPA technologies) have been cleared by FDA including: the AC2 Assay (K060652), the APTIMA CT Assay (K061413) and the APTIMA GC Assay (K061509) for use on the automated TIGRIS System and the semi-automated DTS Systems.

Performance Data

Brief Description of Non-Clinical Data

The following studies were conducted to support analytical performance of the PANTHER System.

Analytical Sensitivity Study

Chlamydia trachomatis analytical sensitivity (limits of detection) was determined by directly comparing dilutions of CT organisms in the APTIMA COMBO 2 assay. The analytical sensitivity claim for the assay is 1 IFU/assay (7.25 IFU/swab, 9.75 IFU/mL, PreservCyt Solution liquid Pap). However, dilutions of less than 1 IFU/assay tested positive in the APTIMA COMBO 2 Assay (for this study, 100% positivity was observed in samples containing CT concentrations of 0.03 IFU/mL).

Neisseria gonorrhoeae analytical sensitivity (limits of detection) was determined by directly comparing dilutions of GC organismsin the APTIMA COMBO 2 Assay. The analytical sensitivity claim for the assay is 50 cells/assay (362 cells/swab, 488 cells/mL PreservCyt Solution liquid Pap). However, dilutions of less than 50 cells/assay tested positive in the APTIMA COMBO 2 Assay (for this study, 100% positivity was observed in samples containing GC concentrations of 0.04 CFU/mL).

Within Laboratory Precision Study

APTIMA COMBO 2 Assay precision was evaluated at Gen-Probe using the PANTHER System. Testing was performed using three PANTHER Systems and three lots of assay reagents. Testing was performed over 24 days.

Reproducibility panel members were created using negative PreservCyt Solution liquid Pap specimens and STM. The positive panel members were created by spiking CT and/or GC organisms to the targeted concentrations shown in **Table 1**.

For each panel member, **Table 1** presents mean RLU, between-instrument, between-lot, between-run, within-run, and overall variation as SD and percent CV. Percent agreement with expected results is also shown.

Table 1. PANTHER System Within Laboratory Precision Data

Matrix	Target Concentration		Agreed/ N	Agrmt (%)	Mean RLU (x1000)	Between Instruments		Between Lots		Between Runs		Within Runs		Total	
	CT (IFU/mL)	GC (CFU/mL)				SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)
STM	0	0	96/96	100	6	0.1	1.0	0.9	13.5	0.0	0.0	1.0	15.7	1.3	20.1
	0.25	0	95/95	100	1226	70.0	5.7	20.0	1.6	8.4	0.7	47.1	3.8	87.1	7.1
	2.5	0	96/96	100	1249	78.0	6.2	6.1	0.5	0.0	0.0	32.9	2.6	84.8	6.8
	25	0	95/95	100	1268	72.9	5.7	15.3	1.2	0.0	0.0	39.6	3.1	84.3	6.6
	0	12.5	96/96	100	1081	18.4	1.7	28.6	2.6	0.0	0.0	26.7	2.5	43.2	4.0
	0	125	96/96	100	1266	29.8	2.4	0.0	0.0	8.9	0.7	27.6	2.2	41.6	3.3
	0	1250	96/96	100	1309	29.4	2.2	0.0	0.0	9.8	0.8	31.8	2.4	44.4	3.4
	2.5	125	96/96	100	2456	86.6	3.5	0.0	0.0	0.0	0.0	53.0	2.2	101.5	4.1
	2.5	2500	96/96	100	2509	73.1	2.9	0.0	0.0	19.8	0.8	46.8	1.9	89.0	3.5
	1000	2500	96/96	100	2496	31.7	1.3	6.1	0.2	0.0	0.0	193.7	7.8	196.3	7.9
	1000	125	96/96	100	2471	83.6	3.4	9.4	0.4	0.0	0.0	52.4	2.1	99.1	4.0
PCyt	0	0	96/96	100	7	0.0	0.0	0.8	11.7	0.0	0.0	1.5	22.4	1.7	24.7
	0.25	0	96/96	100	1113	92.3	8.3	30.1	2.7	0.0	0.0	63.6	5.7	116.0	10.4
	2.5	0	96/96	100	1194	62.5	5.2	24.8	2.1	0.0	0.0	47.0	3.9	82.1	6.9
	25	0	95/95	100	1222	65.1	5.3	26.4	2.2	14.7	1.2	35.0	2.9	79.8	6.5
	0	12.5	93/93	100	994	33.3	3.3	36.9	3.7	16.0	1.6	26.2	2.6	58.4	5.9
	0	125	95/95	100	1189	40.1	3.4	4.5	0.4	10.9	0.9	21.4	1.8	47.0	4.0
	0	1250	95/95	100	1239	37.7	3.0	7.5	0.6	13.6	1.1	18.0	1.5	44.6	3.6
	2.5	125	95/95	100	2333	99.7	4.3	35.3	1.5	12.6	0.5	48.9	2.1	117.2	5.0

Agrmt = agreement, CV = coefficient of variation, N = number of samples, PCyt = PreservCyt Solution liquid Pap, RLU = relative light unit, SD = standard deviation, STM = swab transport medium.

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with standard deviation and %CV is set to 0.

Carryover Studies for the PANTHER System

A multi-run analytical study was conducted using spiked panels on three PANTHER Systems. Carryover was assessed using approximately 20% high titer GC samples dispersed between negative samples. The runs included clusters of high positive samples with clusters of negative samples as well as single high positives dispersed in a specific pattern within the run. High titer samples were made using GC rRNA spiked into STM to give a final concentration equivalent to 2.5×10^5 CFU/mL. Testing was carried out using 5 runs on each of three PANTHER Systems. Carryover was calculated from a total of 2938 valid negative results. The overall carryover rate was 0% with a 95% confidence interval of 0–0.1%.

Brief Description of Clinical Data

Prevalence

The prevalence of CT and GC in patient populations depends on risk factors such as age, gender, the presence or absence of symptoms, the type of clinic, and the sensitivity of the test used to detect infections. A summary of the prevalence of three CT and GC disease outcomes, as determined by the APTIMA COMBO 2 Assay on the PANTHER System in the clinical trial, is shown in **Tables 2, 3, and 4** by specimen type and clinical site.

Table 2. Prevalence of CT+/GC- Infections as Determined by the APTIMA COMBO 2 Assay by Specimen Type and Clinical Site

Site	CT+/GC- Prevalence % (# positive/# tested with valid results)			
	Male Urethral Swab	Clinician-Collected/Patient-collected Vaginal Swab	PreservCyt	Endocervical Swab
1	0 (-)	9.9 (21/212)	8.9 (20/225)	10.4 (20/193)
2	13.9 (28/202)	8.3 (19/230)	8.8 (21/239)	8.2 (19/231)
3	1.3 (1/76)	2.7 (6/222)	3.1 (7/226)	2.7 (6/223)
4	24.4 (33/135)	11.7 (40/342)	10.2 (35/342)	11.3 (38/337)
5	0 (-)	4.5 (1/22)	4.8 (1/21)	4.3 (1/23)
6	21.5 (28/130)	11.9 (13/109)	8.7 (10/115)	8.8 (10/114)
7	16.7 (1/6)	3.2 (5/157)	2.5 (4/161)	2.6 (4/152)
All	16.6 (91/549)	8.1 (105/1294)	7.4 (98/1329)	7.7 (98/1273)

PreservCyt = PreservCyt Solution Liquid Pap

Table 3. Prevalence of CT-/GC+ Infections as Determined by the APTIMA COMBO 2 Assay by Specimen Type and Clinical Site

Site	CT-/GC+ Prevalence % (# positive/# tested with valid results)			
	Male Urethral Swab	Clinician-Collected/Patient-collected Vaginal Swab	PreservCyt	Endocervical Swab
1	0 (-)	3.3 (7/212)	2.7 (6/225)	3.1 (6/193)
2	5.9 (12/202)	3.9 (9/230)	4.6 (11/239)	4.8 (11/231)
3	1.3 (1/76)	0.5 (1/222)	0.4 (1/226)	0.4 (1/223)
4	1.5 (2/135)	1.5 (5/342)	1.5 (5/342)	1.8 (6/337)
5	0 (-)	0.0 (0/22)	0.0 (0/21)	0.0 (0/23)
6	5.4 (7/130)	3.7 (4/109)	1.7 (2/115)	1.8 (2/114)
7	0.0 (0/6)	2.5 (4/157)	2.5 (4/161)	2.6 (4/152)
All	4.0 (22/549)	2.3 (30/1294)	2.2 (29/1329)	2.4 (30/1273)

PreservCyt = PreservCyt Solution Liquid Pap

Table 4. Prevalence of CT+/GC+ Infections as Determined by the APTIMA COMBO 2 Assay by Specimen Type and Clinical Site

Site	CT+/GC+ Prevalence % (# positive/# tested with valid results)			
	Male Urethral Swab	Clinician-Collected/Patient-collected Vaginal Swab	PreservCyt	Endocervical Swab
1	0 (-)	3.8 (8/212)	3.1 (7/225)	3.6 (7/193)
2	3.0 (6/202)	1.3 (3/230)	0.8 (2/239)	0.9 (2/231)
3	0.0 (0/76)	0.0 (0/222)	0.0 (0/226)	0.0 (0/223)
4	4.4 (6/135)	1.2 (4/342)	0.9 (3/342)	0.9 (3/337)
5	0 (-)	0.0 (0/22)	0.0 (0/21)	0.0 (0/23)
6	0.8 (1/130)	0.9 (1/109)	0.9 (1/115)	0.9 (1/114)
7	0.0 (0/6)	0.6 (1/157)	0.6 (1/161)	0.7 (1/152)
All	2.4 (13/549)	1.3 (17/1294)	1.1 (14/1329)	1.1 (14/1273)

PreservCyt = PreservCyt Solution Liquid Pap

Positive and Negative Predictive Values for Hypothetical Prevalence Rates

The estimated positive and negative predictive values (PPV and NPV) of the APTIMA COMBO 2 Assay for different hypothetical prevalence rates are shown for each specimen type in **Table 5**. The PPV and NPV are derived for different hypothetical prevalence rates using the sensitivity and specificity estimates for each specimen type from the clinical performance study (see **Table 6** and **Table 9**).

Table 5. Positive and Negative Predictive Values for Hypothetical Prevalence Rates by Specimen Type

Specimen Type	Hypothetical Prevalence (%)	CT Detection		GC Detection	
		PPV (%)	NPV (%)	PPV (%)	NPV (%)
Male Urethral Swab	1	53.1	100	100	100
	2	69.6	100	100	100
	5	85.5	100	100	100
	10	92.6	100	100	100
	15	95.2	100	100	100
	20	96.6	100	100	100
	25	97.4	100	100	100
Clinician-Collected Vaginal Swab/ Patient-Collected Vaginal Swab	1	38.9	100	70.6	100
	2	56.3	99.9	82.9	100
	5	76.8	99.9	92.6	99.9
	10	87.5	99.7	96.3	99.7
	15	91.7	99.5	97.7	99.6
	20	94.0	99.3	98.3	99.4
	25	95.5	99.1	98.8	99.2
PreservCyt Solution Liquid Pap	1	100	100	100	100
	2	100	100	100	100
	5	100	99.9	100	100
	10	100	99.8	100	100
	15	100	99.7	100	100
	20	100	99.6	100	100
	25	100	99.4	100	100
Endocervical Swab	1	58.5	100	85.8	100
	2	74.0	99.9	92.4	100
	5	88.0	99.9	96.9	100
	10	93.9	99.7	98.5	100
	15	96.1	99.5	99.1	100
	20	97.2	99.3	99.3	100
	25	97.9	99.1	99.5	100

Clinical Study Results

A prospective, multicenter clinical study was conducted to establish the performance characteristics of the APTIMA COMBO 2 Assay on the PANTHER System. Specimens were collected from symptomatic and asymptomatic men (n=580) and women (n=1332) enrolled from 7 geographically and ethnically diverse US clinical sites, including obstetrics and gynecology, family planning, public health, and STD clinics. Subjects were classified as symptomatic if symptoms were reported by the subject. Subjects were classified as asymptomatic if the subject did not report symptoms. Of the 580 male subjects, none were <18 years of age, 72 were 18 to 20 years of age, 201 were 21 to 25 years of age, and 307 were >25 years of age. Of the 1332 female subjects, 11 were 14 to 15 years of age, 59 were 16 to 17 years of age, 319 were 18 to 20 years of age, 401 were 21 to 25 years of age, and 542 were >25 years of age.

Up to 2 specimens were collected from each male subject (1 urethral swab and 1 first-catch urine, in that order) and up to 4 specimens were collected from each female subject (1 first-catch urine, 1 vaginal swab, 1 PreservCyt Solution liquid Pap specimen, and 1 endocervical swab, in that order). All specimens were clinician-collected except urine specimens and approximately half of the vaginal swab specimens, which were collected by the subject at the clinic. Approximately half of the PreservCyt Solution liquid Pap specimens were collected with a broom-type device and half were collected with a spatula and cytobrush. Samples were prepared for APTIMA testing in accordance with the appropriate APTIMA specimen collection kit package insert instructions.

All evaluable samples (567 male urethral swab, 1319 vaginal swab, 1330 PreservCyt, and 1310 endocervical swab samples) were tested with the APTIMA COMBO 2 Assay on the PANTHER System in accordance with package insert instructions. The samples were split amongst three laboratories (two external laboratories and GEN-PROBE). Samples with initial invalid, equivocal, or error results were retested. Eighteen (18) male urethral swab, 25 vaginal swab, 1 PreservCyt, and 37 endocervical swab specimens had final invalid results and were excluded from the analyses. Most of the invalid results were due to insufficient sample volume. One vaginal swab and 1 endocervical swab had final CT equivocal results and 1 PreservCyt and 1 endocervical swab had final GC equivocal results and were excluded from the analyses.

Male urethral swab, male and female urine, and PreservCyt samples were tested with cleared nucleic acid amplification tests (NAATs) to establish the infected status. The infected status algorithm used results from two specimen types and two reference NAATs. Subjects were categorized as infected if a positive result occurred in each of the 2 reference NAATs. For female subjects, if the positive NAAT results occurred only in the urine specimens and not in the PreservCyt specimens, the subject was categorized as infected; however, for the evaluation of the non-urine specimen types, the specimens were considered non-infected. Subjects that could not be categorized as infected or not infected were excluded from the performance analyses.

Chlamydia trachomatis Performance Results

Performance characteristics of the APTIMA COMBO 2 Assay were estimated by comparing PANTHER System results to the infected status algorithm. **Table 6** shows the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the APTIMA COMBO 2 Assay for CT detection and the prevalence of CT (based on the infected status) in each specimen type.

Table 6. Performance Characteristics of the APTIMA COMBO 2 Assay for CT Detection

Spec Type	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
MS	549	100	4	445	0	18.2	100 (96.3-100)	99.1 (97.7-99.7)	96.2 (90.8-98.9)	100 (99.2- 100)
CVS/ PVS	1274	104	18	1149	3	8.4	97.2 (92.1-99.0)	98.5 (97.6-99.0)	85.2 (78.8-90.5)	99.7 (99.3-99.9)
PCyt	1311	112	0	1197	2	8.7	98.2 (93.8-99.5)	100 (99.7-100)	100 (96.9- 100)	99.8 (99.4- 100)
FS	1254	104	8	1139	3	8.5	97.2 (92.1-99.0)	99.3 (98.6-99.6)	92.9 (87.1-96.7)	99.7 (99.3-99.9)

CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

Table 7 shows the sensitivity, specificity, PPV, and NPV of the APTIMA COMBO 2 Assay for CT detection and the prevalence of CT (based on the infected status) in each specimen type by symptom status. CT prevalence was higher in symptomatic men and women.

Table 7. Performance Characteristics of the APTIMA COMBO 2 Assay for CT Detection by Symptom Status

Spec Type	Sx Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
MS	Sym	238	59	1	178	0	24.8	100 (93.9-100)	99.4 (96.9-99.9)	98.3 (91.5- 100)	100 (98.0- 100)
	Asym	311	41	3	267	0	13.2	100 (91.4-100)	98.9 (96.8-99.6)	93.2 (82.5-98.5)	100 (98.7- 100)
CVS/ PVS	Sym	810	73	8	729	0	9.0	100 (95.0-100)	98.9 (97.9-99.4)	90.1 (82.3-95.5)	100 (99.5- 100)
	Asym	464	31	10	420	3	7.3	91.2 (77.0-97.0)	97.7 (95.8-98.7)	75.6 (63.1-86.2)	99.3 (98.1-99.8)
PCyt	Sym	838	76	0	762	0	9.1	100 (95.2-100)	100 (99.5-100)	100 (95.4- 100)	100 (99.5- 100)
	Asym	473	36	0	435	2	8.0	94.7 (82.7-98.5)	100 (99.1-100)	100 (91.1- 100)	99.5 (98.5-99.9)
FS	Sym	794	71	5	718	0	8.9	100 (94.9-100)	99.3 (98.4-99.7)	93.4 (85.9-97.8)	100 (99.5- 100)
	Asym	460	33	3	421	3	7.8	91.7 (78.2-97.1)	99.3 (97.9-99.8)	91.7 (79.9-98.0)	99.3 (98.1-99.8)

Asym = asymptomatic, CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, Sx = symptom, Sym = symptomatic, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

Table 8 shows the sensitivity, specificity, PPV, and NPV of the APTIMA COMBO 2 Assay for CT detection and the prevalence of CT (based on the infected status) in each specimen type by clinical site. CT prevalence varied across clinical sites, as expected.

Table 8. Performance Characteristics of the APTIMA COMBO 2 Assay for CT Detection by Clinical Site

Spec Type	Site	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
MS	1	0	0	0	0	0	NC	NC	NC	NC	NC
	2	202	34	0	168	0	16.8	100 (89.8-100)	100 (97.8-100)	100 (90.3- 100)	100 (98.0- 100)
	3	76	0	1	75	0	0.0	NC	98.7 (92.9-99.8)	0.0 (NC)	100 (NC)
	4	135	36	3	96	0	26.7	100 (90.4-100)	97.0 (91.5-99.0)	92.3 (80.9-98.3)	100 (96.6- 100)
	5	0	0	0	0	0	NC	NC	NC	NC	NC
	6	130	29	0	101	0	22.3	100 (88.3-100)	100 (96.3-100)	100 (88.9- 100)	100 (96.7- 100)
	7	6	1	0	5	0	16.7	100 (20.7-100)	100 (56.6-100)	100 (6.9- 100)	100 (80.4- 100)
CVS/ PVS	1	211	23	6	182	0	10.9	100 (85.7-100)	96.8 (93.2-98.5)	79.3 (64.2-91.2)	100 (98.2- 100)
	2	230	18	4	206	2	8.7	90.0 (69.9-97.2)	98.1 (95.2-99.3)	81.8 (64.7-93.9)	99.0 (97.1-99.9)
	3	213	6	0	206	1	3.3	85.7 (48.7-97.4)	100 (98.2-100)	100 (64.1- 100)	99.5 (98.1- 100)
	4	335	40	4	291	0	11.9	100 (91.2-100)	98.6 (96.6-99.5)	90.9 (79.8-97.3)	100 (98.8- 100)
	5	21	1	0	20	0	4.8	100 (20.7-100)	100 (83.9-100)	100 (6.5- 100)	100 (95.3- 100)
	6	107	11	3	93	0	10.3	100 (74.1-100)	96.9 (91.2-98.9)	78.6 (56.4-94.6)	100 (96.8- 100)
	7	157	5	1	151	0	3.2	100 (56.6-100)	99.3 (96.4-99.9)	83.3 (47.4-99.5)	100 (98.3- 100)
PCyt	1	225	27	0	198	0	12.0	100 (87.5-100)	100 (98.1-100)	100 (88.1- 100)	100 (98.3- 100)
	2	239	23	0	216	0	9.6	100 (85.7-100)	100 (98.3-100)	100 (86.3- 100)	100 (98.4- 100)
	3	217	7	0	210	0	3.2	100 (64.6-100)	100 (98.2-100)	100 (65.7- 100)	100 (98.7- 100)
	4	335	38	0	295	2	11.9	95.0 (83.5-98.6)	100 (98.7-100)	100 (91.5- 100)	99.3 (97.8-99.9)
	5	21	1	0	20	0	4.8	100 (20.7-100)	100 (83.9-100)	100 (6.5- 100)	100 (95.3- 100)
	6	113	11	0	102	0	9.7	100 (74.1-100)	100 (96.4-100)	100 (75.2- 100)	100 (97.0- 100)
	7	161	5	0	156	0	3.1	100 (56.6-100)	100 (97.6-100)	100 (57.8- 100)	100 (98.4- 100)

CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

Table 8. Performance Characteristics of the APTIMA COMBO 2 Assay for CT Detection by Clinical Site (continued)

Spec Type	Site	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
FS	1	193	24	3	166	0	12.4	100 (86.2-100)	98.2 (94.9-99.4)	88.9 (73.6-97.5)	100 (98.0- 100)
	2	231	19	2	209	1	8.7	95.0 (76.4-99.1)	99.1 (96.6-99.7)	90.5 (73.4-98.6)	99.5 (97.7- 100)
	3	214	6	0	207	1	3.3	85.7 (48.7-97.4)	100 (98.2-100)	100 (64.1- 100)	99.5 (98.1- 100)
	4	330	39	2	288	1	12.1	97.5 (87.1-99.6)	99.3 (97.5-99.8)	95.1 (84.8-99.3)	99.7 (98.2- 100)
	5	22	1	0	21	0	4.5	100 (20.7-100)	100 (84.5-100)	100 (6.5- 100)	100 (95.5- 100)
	6	112	11	0	101	0	9.8	100 (74.1-100)	100 (96.3-100)	100 (75.2- 100)	100 (97.0- 100)
	7	152	4	1	147	0	2.6	100 (51.0-100)	99.3 (96.3-99.9)	80.0 (40.0-99.4)	100 (98.4- 100)

CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

Table 9 shows the sensitivity, specificity, PPV, and NPV of the APTIMA COMBO 2 Assay for GC detection and the prevalence of GC (based on the infected status) in each specimen type.

Table 9. Performance Characteristics of the APTIMA COMBO 2 Assay for GC Detection

Spec Type	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
MS	546	34	0	512	0	6.2	100 (89.8-100)	100 (99.3-100)	100 (90.2- 100)	100 (99.3- 100)
VS	1258	42	5	1210	1	3.4	97.7 (87.9-99.6)	99.6 (99.0-99.8)	89.4 (78.6-96.1)	99.9 (99.6- 100)
PCyt	1293	43	0	1250	0	3.3	100 (91.8-100)	100 (99.7-100)	100 (92.1- 100)	100 (99.7- 100)
FS	1238	42	2	1194	0	3.4	100 (91.6-100)	99.8 (99.4- 100)	95.5 (85.4-99.4)	100 (99.7- 100)

CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

Table 10 shows the sensitivity, specificity, PPV, and NPV of the APTIMA COMBO 2 Assay for GC detection and the prevalence of GC (based on the infected status) in each specimen type by symptom status. GC prevalence was higher in symptomatic men but similar in symptomatic and asymptomatic women.

Table 10. Performance Characteristics of the APTIMA COMBO 2 Assay for GC Detection by Symptom Status

Spec Type	Sx Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
MS	Sym	236	31	0	205	0	13.1	100 (89.0-100)	100 (98.2-100)	100 (89.5- 100)	100 (98.3- 100)
	Asym	310	3	0	307	0	1.0	100 (43.9-100)	100 (98.8-100)	100 (44.4- 100)	100 (99.3- 100)
CVS/ PVS	Sym	802	27	4	771	0	3.4	100 (87.5-100)	99.5 (98.7- 99.8)	87.1 (72.6-96.1)	100 (99.6- 100)
	Asym	456	15	1	439	1	3.5	93.8 (71.7-98.9)	99.8 (98.7- 100)	93.8 (74.0-99.8)	99.8 (98.9- 100)
PCyt	Sym	829	27	0	802	0	3.3	100 (87.5-100)	100 (99.5-100)	100 (88.0- 100)	100 (99.6- 100)
	Asym	464	16	0	448	0	3.4	100 (80.6-100)	100 (99.1-100)	100 (81.3- 100)	100 (99.3- 100)
FS	Sym	785	26	1	758	0	3.3	100 (87.1-100)	99.9 (99.3- 100)	96.3 (82.4-99.9)	100 (99.5- 100)
	Asym	453	16	1	436	0	3.5	100 (80.6-100)	99.8 (98.7- 100)	94.1 (74.3-99.8)	100 (99.3- 100)

Asym = asymptomatic, CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, Sx = symptom, Sym = symptomatic, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

Table 11 shows the sensitivity, specificity, PPV, and NPV of the APTIMA COMBO 2 Assay for GC detection and the prevalence of GC (based on the infected status) in each specimen type by clinical site for the clinical performance study. GC prevalence varied across clinical sites, as expected.

Table 11. Performance Characteristics of the APTIMA COMBO 2 Assay for GC Detection by Clinical Site

Spec Type	Site	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
MS	1	0	0	0	0	0	NC	NC	NC	NC	NC
	2	201	18	0	183	0	9.0	100 (82.4-100)	100 (97.9-100)	100 (83.1- 100)	100 (98.2- 100)
	3	76	1	0	75	0	1.3	100 (20.7-100)	100 (95.1-100)	100 (6.4- 100)	100 (98.7- 100)
	4	135	8	0	127	0	5.9	100 (67.6-100)	100 (97.1-100)	100 (68.8- 100)	100 (97.7- 100)
	5	0	0	0	0	0	NC	NC	NC	NC	NC
	6	128	7	0	121	0	5.5	100 (64.6-100)	100 (96.9-100)	100 (65.8- 100)	100 (97.7- 100)
	7	6	0	0	6	0	0.0	NC	100 (61.0-100)	NC	100 (NC)
CVS/ PVS	1	207	13	2	192	0	6.3	100 (77.2-100)	99.0 (96.3-99.7)	86.7 (64.6-98.3)	100 (98.4- 100)
	2	230	12	0	217	1	5.7	92.3 (66.7-98.6)	100 (98.3-100)	100 (77.8- 100)	99.5 (97.9- 100)
	3	206	1	0	205	0	0.5	100 (20.7-100)	100 (98.2-100)	100 (6.4- 100)	100 (99.5- 100)
	4	331	8	1	322	0	2.4	100 (67.6-100)	99.7 (98.3-99.9)	88.9 (59.1-99.7)	100 (99.1- 100)
	5	21	0	0	21	0	0.0	NC	100 (84.5-100)	NC	100 (NC)
	6	106	3	2	101	0	2.8	100 (43.9-100)	98.1 (93.2-99.5)	60.0 (24.6-92.8)	100 (98.0- 100)
	7	157	5	0	152	0	3.2	100 (56.6-100)	100 (97.5-100)	100 (57.8- 100)	100 (98.3- 100)
PCyt	1	220	13	0	207	0	5.9	100 (77.2-100)	100 (98.2-100)	100 (78.0- 100)	100 (98.5- 100)
	2	239	13	0	226	0	5.4	100 (77.2-100)	100 (98.3-100)	100 (78.0- 100)	100 (98.6- 100)
	3	210	1	0	209	0	0.5	100 (20.7-100)	100 (98.2-100)	100 (6.4- 100)	100 (99.5- 100)
	4	331	8	0	323	0	2.4	100 (67.6-100)	100 (98.8-100)	100 (68.6- 100)	100 (99.1- 100)
	5	21	0	0	21	0	0.0	NC	100 (84.5-100)	NC	100 (NC)
	6	111	3	0	108	0	2.7	100 (43.9-100)	100 (96.6-100)	100 (44.6- 100)	100 (98.1- 100)
	7	161	5	0	156	0	3.1	100 (56.6-100)	100 (97.6-100)	100 (57.8- 100)	100 (98.4- 100)

CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

Table 11. Performance Characteristics of the APTIMA COMBO 2 Assay for GC Detection by Clinical Site (continued)

Spec Type	Site	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV% (95% CI)[2]
FS	1	189	12	1	176	0	6.3	100 (75.8-100)	99.4 (96.9-99.9)	92.3 (68.6-99.8)	100 (98.2- 100)
	2	231	13	0	218	0	5.6	100 (77.2-100)	100 (98.3-100)	100 (78.0- 100)	100 (98.5- 100)
	3	207	1	0	206	0	0.5	100 (20.7-100)	100 (98.2-100)	100 (6.4- 100)	100 (99.5- 100)
	4	327	8	1	318	0	2.4	100 (67.6-100)	99.7 (98.2-99.9)	88.9 (59.1-99.7)	100 (99.1- 100)
	5	22	0	0	22	0	0.0	NC	100 (85.1-100)	NC	100 (NC)
	6	110	3	0	107	0	2.7	100 (43.9-100)	100 (96.5-100)	100 (44.6- 100)	100 (98.1- 100)
	7	152	5	0	147	0	3.3	100 (56.6-100)	100 (97.5-100)	100 (57.9- 100)	100 (98.3- 100)

CI = confidence interval, CVS = clinician-collected vaginal swab, FN = false negative, FP = false positive, FS = female endocervical swab, MS = male urethral swab, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, Spec = specimen, TN = true negative, TP = true positive.

[1] Score CI

[2] PPV 95% CI computed from the exact 95% CI for the positive likelihood ratio, NPV 95% CI computed from the exact 95% CI from the negative likelihood ratio.

The frequency of test outcomes from reference NAAT and investigational PANTHER System testing is summarized in **Table 12** and **Table 13** for CT and in **Tables 16** and **Table 15** for GC.

Table 12. CT Infected Status for Performance Evaluation in Male Urethral Swab Specimens

	Assay Results						
	AC2 DTS		ACT TIGRIS		AC2 PANTHER	Symptom Status	
CT Infected Status	MS	MU	MS	MU	MS	Sym	Asym
Infected	+	+	+	+	+	50	37
Infected	+	+	+	+	NA	4	1
Infected	+	+	+	-	+	2	0
Infected	+	-	+	+	+	4	2
Infected	+	-	+	-	+	3	2
Not Infected	+	+	-	-	-	0	1
Not Infected	+	-	-	-	+	0	1
Not Infected	+	-	-	-	-	1	1
Not Infected	-	-	+	-	-	3	2
Not Infected	-	-	-	+	-	1	1
Not Infected	-	-	-	-	+	1	2
Not Infected	-	-	-	-	-	173	262
Not Infected	-	-	-	-	NA	10	9
Not Infected	NA	-	-	-	NA	1	2

AC2 = APTIMA COMBO 2, ACT = APTIMA CT Assay, Asym = asymptomatic, DTS = DTS Systems, MS = male urethral swab, MU = male urine, NA = result not available, PANTHER = PANTHER System, Sym = symptomatic, TIGRIS = TIGRIS DTS System

Table 13. CT Infected Status for Performance Evaluation in Female Vaginal Swab, PreservCyt Solution Liquid Pap, and Endocervical Swab Specimens

CT Infected Status	Assay Results							Symptom Status	
	AC2 TIGRIS		ACT TIGRIS		AC2 PANTHER				
	PCyt	FU	PCyt	FU	CVS/PVS	PCyt	FS	Sym	Asym
Infected	+	+	+	+	+	+	+	62	26
Infected	+	+	+	+	+	+	-	0	1
Infected	+	+	+	+	+	+	NA	3	0
Infected	+	+	+	+	+	-	+	0	2
Infected	+	+	+	+	-	+	+	0	1
Infected	+	+	+	+	NA	+	+	1	1
Infected	+	+	+	+	NA	+	NA	2	1
Infected	+	-	+	+	+	+	+	4	1
Infected	+	-	+	+	NA	+	NA	0	1
Infected	+	-	+	-	+	+	+	4	0
Infected	+	-	+	-	-	+	-	0	1
Infected	+	-	+	-	NA	+	+	0	1
Infected	+	NA	+	NA	+	+	+	0	1
Infected	+	NA	+	NA	-	+	-	0	1
Infected[1]	-	+	-	+	+	-	+	1	0
Infected[1]	-	+	-	+	+	-	-	2	0
Infected[1]	-	+	-	+	-	-	-	1	1
Not Infected	+	-	-	-	-	-	-	0	2
Not Infected	-	+	-	-	-	-	-	1	0
Not Infected	-	-	+	-	+	-	+	0	1
Not Infected	-	-	+	-	-	-	-	5	0
Not Infected	-	-	-	+	+	-	-	0	1
Not Infected	-	-	-	+	+	-	NA	0	1
Not Infected	-	-	-	+	-	-	-	1	3
Not Infected	-	-	-	-	+	-	+	1	0
Not Infected	-	-	-	-	+	-	-	2	7
Not Infected	-	-	-	-	+	-	NA	2	0
Not Infected	-	-	-	-	-	-	+	2	2
Not Infected	-	-	-	-	-	-	-	680	396
Not Infected	-	-	-	-	-	-	NA	29	8
Not Infected	-	-	-	-	-	NA	-	1	0
Not Infected	-	-	-	-	NA	-	-	17	4
Not Infected	-	-	-	-	NA	-	NA	8	1
Not Infected	-	NA	-	-	-	-	-	8	6
Not Infected	-	NA	-	-	-	-	NA	0	1
Not Infected	NA	-	-	-	-	-	-	0	1
Not Infected	NA	-	-	-	-	-	NA	1	0
Not Infected	NA	-	-	-	NA	-	+	1	0

AC2 = APTIMA COMBO 2, ACT = APTIMA CT Assay, Asym = asymptomatic, CVS = clinician-collected vaginal swab, FS = female endocervical swab, FU = female urine, NA = result not available, PANTHER = PANTHER System, PCyt = PreservCyt Solution liquid Pap, PVS = patient-collected vaginal swab, Sym = symptomatic, TIGRIS = TIGRIS DTS System

[1] For the evaluation of the non-urine specimen types, the specimens were considered non-infected.

Table 14. GC Infected Status for Performance Evaluation in Male Urethral Swab Specimens

	Assay Results						
	AC2 DTS		AGC DTS		AC2 PANTHER	Symptom Status	
GC Infected Status	MS	MU	MS	MU	MS	Sym	Asym
Infected	+	+	+	+	+	30	2
Infected	+	+	+	+	NA	0	1
Infected	+	-	+	-	+	1	1
Infected	NA	+	NA	+	NA	1	0
Not Infected	-	-	NA	NA	-	205	307
Not Infected	-	-	NA	NA	NA	14	9

AC2 = APTIMA COMBO 2, AGC = APTIMA GC Assay, Asym = asymptomatic, DTS = DTS Systems, MS = male urethral swab, MU = male urine, NA = result not available, PANTHER = PANTHER System, Sym = symptomatic, TIGRIS = TIGRIS DTS System

Table 15. GC Infected Status for Performance Evaluation in Female Vaginal Swab, PreservCyt Solution Liquid Pap, and Endocervical Swab Specimens

	Assay Results								
	AC2 TIGRIS		AGC TIGRIS		AC2 PANTHER			Symptom Status	
GC Infected Status	PCyt	FU	PCyt	FU	CVS/ PVS	PCyt	FS	Sym	Asym
Infected	+	+	+	+	+	+	+	22	10
Infected	+	+	+	+	+	+	NA	1	0
Infected	+	+	+	-	+	+	+	1	0
Infected	+	+	+	=	+	+	+	0	1
Infected	+	-	+	-	+	+	+	3	3
Infected	+	-	+	-	-	+	+	0	1
Infected	+	NA	+	NA	+	+	+	0	1
Not Infected	+	NA	-	-	-	=	-	0	1
Not Infected	-	-	NA	NA	+	-	+	0	1
Not Infected	-	-	NA	NA	+	-	-	3	0
Not Infected	-	-	NA	NA	+	-	NA	1	0
Not Infected	-	-	NA	NA	-	-	+	1	0
Not Infected	-	-	NA	NA	-	-	-	736	429
Not Infected	-	-	NA	NA	-	-	=	1	0
Not Infected	-	-	NA	NA	-	-	NA	32	9
Not Infected	-	-	NA	NA	-	NA	-	1	0
Not Infected	-	-	NA	NA	NA	-	-	18	6
Not Infected	-	-	NA	NA	NA	-	NA	10	3

AC2 = APTIMA COMBO 2, ACT = APTIMA CT Assay, Asym = asymptomatic, CVS = clinician-collected vaginal swab, FS = female endocervical swab, FU = female urine, NA = result not available, PANTHER = PANTHER System, PCyt = PreservCyt Solution liquid Pap, PVS = patient-collected vaginal swab, Sym = symptomatic, TIGRIS = TIGRIS DTS System.

The equal symbol (=) represents an equivocal result on repeat testing.

RLU Distribution of APTIMA COMBO 2 Controls

The distribution of the RLU values for the APTIMA COMBO 2 controls is presented in **Table 16** from all valid PANTHER System runs performed during the clinical performance study.

Table 16. RLU Distribution of APTIMA COMBO 2 Controls

Control	Statistic	Total RLU (×1000)
Positive Control, CT/ Negative Control, GC	N	66
	Maximum	1335
	Median	1081.5
	Minimum	624
	CV%	11.2
Positive Control, GC/ Negative Control, CT	N	66
	Maximum	1241
	Median	1172.0
	Minimum	1063
	CV%	3.2

Reproducibility Study

APTIMA Combo 2 Assay reproducibility was evaluated at two external US laboratories and at Gen-Probe using the PANTHER System. Testing was performed using one lot of assay reagents and a total of six operators (two at each site). At each site, testing was performed over at least 10 days.

Reproducibility panel members were created using negative specimens processed with the APTIMA Specimen Collection Kit. The positive panel members were created by spiking with CT and/or GC organisms to result in panel members with expected targeted concentrations.

Table 17 shows the CT and GC concentrations for each panel member. **Table 17** presents, for each panel member, RLU data in terms of mean, standard deviation (SD), and coefficient of variation (CV) between sites, between operators, between days, between runs, within runs, and overall. Percent agreement with expected results is also shown. Samples with valid results were included in the analyses.

Table 17. Reproducibility Data

Target Concentration					Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
CT (IFU/mL)	GC (CFU/mL)	Agreed/N	Agrmt (%)	Mean RLU (x1000)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)
0	0	178/180	98.9	6.2	1.2	19.0	0.0	0.0	0.0	0.0	0.0	0.0	8.2	131.7	8.3	133.0
0.25	0	180/180	100	1202.1	92.4	7.7	0.0	0.0	0.0	0.0	62.9	5.2	50.3	4.2	122.6	10.2
2.5	0	178/178	100	1184.5	90.9	7.7	0.0	0.0	0.0	0.0	53.8	4.5	34.6	2.9	111.1	9.4
25	0	180/180	100	1265.4	97.4	7.7	18.9	1.5	0.0	0.0	62.4	4.9	35.1	2.8	122.4	9.7
1000	0	180/180	100	1278.5	101.9	8.0	15.7	1.2	20.6	1.6	61.4	4.8	31.8	2.5	125.9	9.8
0	0.25	177/179	98.9	421.9	40.3	9.5	21.9	5.2	27.6	6.5	35.3	8.4	72.7	17.2	96.9	23.0
0	12.5	179/180	99.4	1141.8	11.9	1.0	0.0	0.0	44.4	3.9	37.3	3.3	75.8	6.6	96.2	8.4
0	125	180/180	100	1223.7	31.4	2.6	13.0	1.1	11.1	0.9	19.8	1.6	34.3	2.8	53.4	4.4
0	1250	180/180	100	1262.9	16.7	1.3	9.4	0.7	21.0	1.7	14.0	1.1	30.6	2.4	44.1	3.5
0	2500	180/180	100	1308.7	20.7	1.6	13.4	1.0	0.0	0.0	21.7	1.7	25.3	1.9	41.4	3.2
2.5	125	180/180	100	2467.6	71.9	2.9	31.5	1.3	21.7	0.9	64.8	2.6	44.4	1.8	113.1	4.6
2.5	2500	180/180	100	2453.3	76.2	3.1	30.9	1.3	0.0	0.0	62.5	2.5	51.6	2.1	115.4	4.7
1000	125	179/179	100	2503.8	74.0	3.0	38.5	1.5	0.0	0.0	59.1	2.4	39.1	1.6	109.4	4.4
1000	2500	180/180	100	2357.1	79.1	3.4	0.0	0.0	0.0	0.0	74.2	3.1	55.2	2.3	121.7	5.2

Agrmt = agreement, CV = coefficient of variation, N = number of samples, RLU = relative light unit, SD = standard deviation.

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with standard deviation and %CV is set to 0.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Gen-Probe, Inc.
Jody Fleming
Regulatory Affairs Specialist
10210 Genetic Center Drive
San Diego, CA 92121

MAY - 3 2012

Re: k111409

Trade/Device Name: APTIMA COMBO 2® Assay on the (PANTHER® System)
Regulation Number: 21 CFR 866.3120
Regulation Name: DNA Reagents, Neisseria
Regulatory Class: II
Product Code: LSL, MKZ, NSU
Dated: April 20, 2012
Received: April 23, 2012

Dear Ms. Fleming:

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

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

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

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

Sincerely yours,

Sally A. Hojvat, Ph.D.
Director,
Division of Microbiology Devices
Office of In Vitro Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use Form

510(k) Number (if known): K111409

Device Name: APTIMA COMBO 2® Assay

Indications For Use:

The PANTHER System is intended to fully automate amplified nucleic acid test (NAT) diagnostic assays currently developed by Gen-Probe Incorporated (San Diego, CA).

Intended Use -- APTIMA COMBO 2 Assay

Intended Use

The APTIMA COMBO 2 Assay is a target amplification nucleic acid probe test that utilizes target capture for the *in vitro* qualitative detection and differentiation of ribosomal RNA (rRNA) from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC) to aid in the diagnosis of chlamydial and/or gonococcal urogenital disease using the PANTHER System as specified.

On the PANTHER System, the assay may be used to test the following specimens from symptomatic and asymptomatic individuals: clinician-collected endocervical, vaginal and male urethral swab specimens, clinician-collected gynecological specimens collected in the PreservCyt Solution, and patient-collected vaginal swab specimens.

[1]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.

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

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

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

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K 111409