K132251

510(k) SUMMARY

APTIMA Combo 2® Assay (on the PANTHER® System)

Attached is a 510(k) summary as described in 21 CFR 807.92

Sponsor Information

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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 Device:	APTIMA Combo 2® Assay (PANTHER® System); K111409 This premarket application is to clear the APTIMA Combo 2 Assay for use on the PANTHER System with the male urine specimen type.

Device Description

The APTIMA Combo 2 Assay combines the technologies of target capture, transcription-mediated amplification (TMA), and dual kinetic assay (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 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, patient-collected vaginal swab specimens,[1] and male urine 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.

Comparison to Predicate

A comparison of the APTIMA Combo 2® Assay (PANTHER® System) with the addition of the male urine specimen type to the predicate APTIMA Combo 2® Assay (PANTHER® System) (K111409) is summarized below.

Item	Predicate Device	Test Device (with Male Urine Claim)
510(k) Number	K111409	K132251
Trade Name	APTIMA Combo 2® Assay	APTIMA Combo 2® Assay
Instrument	PANTHER® System	PANTHER® System
Model Number	303094 and 302923	303094 and 302923
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*	Same
Indications For Use / 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,	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,

Item	Predicate Device	Test Device (with Male Urine Claim)
Indications For Use / Intended Use (Continued)	clinician-collected gynecological specimens collected in the PreservCyt Solution, 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.	clinician-collected gynecological specimens collected in the PreservCyt Solution, patient-collected vaginal swab specimens[1], **and male urine 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.
Specimen Types	**Female specimens**: • Vaginal swab • Endocervical swab • ThinPrep in PreservCyt solution **Male Specimens**: • Urethral Swab	**Female specimens**: • Vaginal swab • Endocervical swab • ThinPrep in PreservCyt solution **Male Specimens**: • Urethral Swab • **Urine**
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.	**Swabs:** Same
	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.	**ThinPrep Liquid Pap in PreservCyt**: Same

Item	Predicate Device	Test Device (with Male Urine Claim)
Specimen Transport/Storage (Continued)		**Urine:** After collection, transport the processed urine specimens in the APTIMA urine specimen transport tube at 2°C to 30°C and store at 2°C to 30°C until tested. Processed urine specimens should be assayed with the APTIMA Combo 2 Assay within 30 days of collection. If longer storage is needed, freeze at -20°C to -70°C for up to 12 months after collection.
Type of Assay	Nucleic Acid Amplification Test	Same
Technology*	Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA)	Same
Detection Format	HPA which provides relative light units (RLUs) that are assessed against an established assay cutoff	Same

*A number of Gen-Probe APTIMA assays (that are based on TC, TMA, and HPA technologies) have been cleared by FDA including: the APTIMA Combo 2 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 analytical studies were conducted to support clearance of the male urine claim for the APTIMA Combo 2 Assay on the PANTHER System.

Analytical Sensitivity Study

Chlamydia trachomatis analytical sensitivity (limit of detection) was determined by testing 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, 5.0 IFU/mL urine). However, dilutions of less than 1 IFU/assay tested positive in the APTIMA Combo 2 Assay for the following 12 CT serovars: D, E, F, G, H, I, J, K, L1, L2, L2a and L3 (≥95% positivity was observed in samples containing CT concentrations of 1.89 IFU/mL).

Neisseria gonorrhoeae analytical sensitivity (limit of detection) was determined by testing dilutions of GC organisms in 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, 250 cells/mL urine). However, dilutions of less than 50 cell/assay tested positive in the APTIMA Combo 2 Assay for 30 different strains of GC (≥95% positivity was observed in samples containing GC concentrations of 0.36 CFU/mL).

Carryover Studies for the Panther System

Two studies were conducted to evaluate carryover on the PANTHER System. In the first study, carryover was assessed in multiple runs on three PANTHER Systems with 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 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. Five runs were performed on each of three PANTHER Systems. Carryover was calculated from a total of 2938 valid negative results. The overall carryover rate from this study was 0% with a 95% confidence interval of 0–0.1%.

The second carryover study was conducted on one PANTHER System with high titer GC positive samples (GC rRNA spiked into STM at the equivalent of 2.5×10^5 CFU/mL) alternately processed with negative samples in a checkerboard format. Five checkerboard runs were performed. The overall carryover rate from this study was 0.74% (1/135 negative samples).

Freeze-Thaw Study

Gen-Probe conducted an in-house analytical study that compared the APTIMA Combo 2 Assay (PANTHER System) performance of fresh (non-frozen) versus frozen urines. These data support the use of prospectively-collected frozen specimens to establish the male urine specimen performance claims. Performance of sixty individual urine specimens was assessed after exposure to fresh (non-frozen) and frozen storage conditions.

There were no significant differences in sensitivity and specificity between fresh and frozen samples (upper and lower bound of the 95% CI for the difference in sensitivity and specificity was <10%).

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, is shown in **Tables 1** and **2** for two multi-center clinical studies by clinical site and overall.

Table 1: Clinical Study 1. Prevalence of CT and GC Infections as Determined by the APTIMA Combo 2 Assay in Male Urethral Swab, Vaginal Swab, PreservCyt Solution Liquid Pap, and Endocervical Swab Samples by Clinical Site.

	Prevalence % (# positive/# tested with valid results)											
	MS			CVS/PVS			PCyt			FS		
Site	CT+/GC-	CT-/GC+	CT+/GC+	CT+/GC-	CT-/GC+	CT+/GC+	CT+/GC-	CT-/GC+	CT+/GC+	CT+/GC-	CT-/GC+	CT+/GC+
1	0 (-)	0 (-)	0 (-)	9.9 (21/212)	3.3 (7/212)	3.8 (8/212)	8.9 (20/225)	2.7 (6/225)	3.1 (7/225)	10.4 (20/193)	3.1 (6/193)	3.6 (7/193)
2	13.9 (28/202)	5.9 (12/202)	3.0 (6/202)	8.3 (19/230)	3.9 (9/230)	1.3 (3/230)	8.8 (21/239)	4.6 (11/239)	0.8 (2/239)	8.2 (19/231)	4.8 (11/231)	0.9 (2/231)
3	1.3 (1/76)	1.3 (1/76)	0.0 (0/76)	2.7 (6/222)	0.5 (1/222)	0.0 (0/222)	3.1 (7/226)	0.4 (1/226)	0.0 (0/226)	2.7 (6/223)	0.4 (1/223)	0.0 (0/223)
4	24.4 (33/135)	1.5 (2/135)	4.4 (6/135)	11.7 (40/342)	1.5 (5/342)	1.2 (4/342)	10.2 (35/342)	1.5 (5/342)	0.9 (3/342)	11.3 (38/337)	1.8 (6/337)	0.9 (3/337)
5	0 (-)	0 (-)	0 (-)	4.5 (1/22)	0.0 (0/22)	0.0 (0/22)	4.8 (1/21)	0.0 (0/21)	0.0 (0/21)	4.3 (1/23)	0.0 (0/23)	0.0 (0/23)
6	21.5 (28/130)	5.4 (7/130)	0.8 (1/130)	11.9 (13/109)	3.7 (4/109)	0.9 (1/109)	8.7 (10/115)	1.7 (2/115)	0.9 (1/115)	8.8 (10/114)	1.8 (2/114)	0.9 (1/114)
7	16.7 (1/6)	0.0 (0/6)	0.0 (0/6)	3.2 (5/157)	2.5 (4/157)	0.6 (1/157)	2.5 (4/161)	2.5 (4/161)	0.6 (1/161)	2.6 (4/152)	2.6 (4/152)	0.7 (1/152)
All	16.6 (91/549)	4.0 (22/549)	2.4 (13/549)	8.1 (105/1294)	2.3 (30/1294)	1.3 (17/1294)	7.4 (98/1329)	2.2 (29/1329)	1.1 (14/1329)	7.7 (98/1273)	2.4 (30/1273)	1.1 (14/1273)

CVS = clinician-collected vaginal swab, FS = female endocervical swab, MS = male urethral swab, PCyt = PreservCyt Solution liquid Pap, PVS = patient-collected vaginal swab.

Table 2: Clinical Study 1 and Clinical Study 2. Prevalence of CT and GC Infections as Determined by the APTIMA Combo 2 Assay in Male Urine Samples by Clinical Site

Site	Prevalence % (# positive/# tested with valid results)		
	CT+/GC-	CT-/GC+	CT+/GC+
1	6.0 (6/100)	0.0 (0/100)	0.0 (0/100)
2	3.0 (2/67)	3.0 (2/67)	0.0 (0/67)
3	0.0 (0/109)	0.9 (1/109)	0.0 (0/109)
4	13.0 (13/100)	3.0 (3/100)	1.0 (1/100)
5	13.6 (17/125)	5.6 (7/125)	0.0 (0/125)
6	15.1 (43/284)	7.0 (20/284)	2.1 (6/284)
7	1.4 (3/212)	0.9 (2/212)	0.0 (0/212)
8	1.3 (1/75)	0.0 (0/75)	0.0 (0/75)
9	16.7 (42/251)	5.2 (13/251)	3.2 (8/251)
10	20.5 (17/83)	1.2 (1/83)	0.0 (0/83)
11	4.1 (6/146)	0.7 (1/146)	0.7 (1/146)
12	14.3 (16/112)	4.5 (5/112)	2.7 (3/112)
13	8.9 (10/112)	2.7 (3/112)	2.7 (3/112)
14	7.7 (2/26)	0.0 (0/26)	0.0 (0/26)
All	9.9 (178/1802)	3.2 (58/1802)	1.2 (22/1802)

Note: CT and GC prevalence was estimated using symptomatic male urine samples from Clinical Study 2 and asymptomatic male urine samples from both studies.

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 3**. For each specimen type, the PPV and NPV are derived for different hypothetical prevalence rates using the sensitivity and specificity estimates from the two multi-center clinical studies (see **Table 4 and Table 7**).

Table 3: Positive and Negative Predictive Values for Hypothetical Prevalence Rates by Specimen Type

Specimen Type	Hypothetical Prevalence (%)	CT Detection		GC Detection	
		PPV (%)	NPV (%)	PPV (%)	NPV (%)
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
Female 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
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
Male Urine	1	83.6	100	77.4	100
	2	91.2	99.9	87.4	100
	5	96.4	99.7	94.7	99.9
	10	98.2	99.5	97.4	99.9
	15	98.9	99.2	98.4	99.8
	20	99.2	98.8	98.8	99.7
	25	99.4	98.4	99.1	99.6

Note: APTIMA Combo 2 Assay performance was estimated using vaginal swab, PreservCyt Solution Liquid Pap, female endocervical swab, and male urethral swab sample results from Clinical Study 1, symptomatic male urine samples from Clinical Study 2, and asymptomatic male urine samples from both studies.

Clinical Study Results

Two clinical studies were performed. APTIMA Combo 2 Assay clinical performance was estimated with male urethral swab, vaginal swab, PreservCyt Solution liquid Pap, and endocervical swab specimens in Clinical Study 1, and with male urine specimens in Clinical Study 2.

Clinical Study 1: Vaginal Swab, PreservCyt Solution Liquid Pap, Female Endocervical Swab, and Male Urethral Swab Specimen Clinical Study[1]

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, 580 male urine, 1319 vaginal swab, 1330 PreservCyt Solution liquid Pap, and 1310 endocervical swab samples) were tested with the APTIMA Combo 2 Assay on the PANTHER System in accordance with package insert

[1] This study included testing of male urine samples with the APTIMA Combo 2 Assay on the PANTHER System that were not included in the original performance results due to the low prevalence of GC in the study population.

instructions. The samples were split amongst three laboratories (two external laboratories and in-house). Samples with initial invalid, equivocal, or error results were retested. Eighteen (18) male urethral swab, 25 vaginal swab, 1 PreservCyt Solution liquid Pap, and 37 endocervical swab samples 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 Solution liquid Pap sample and 1 endocervical swab had final GC equivocal results and were excluded from the analyses.

Male urethral swab, male and female urine, and PreservCyt Solution liquid Pap 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 two reference NAATs (see **Tables 10, 11, 13,** and **14** for the infected status algorithms). For female subjects, if the positive NAAT results occurred only in the urine specimens and not in the PreservCyt Solution liquid Pap 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.

In addition, male urine samples tested with the APTIMA Combo 2 Assay on the PANTHER System were excluded from the performance analyses due to the low prevalence of GC in the study population, particularly in the asymptomatic subjects.

Clinical Study 2: Male Urine Specimen Clinical Study

A prospective, multicenter clinical study was conducted to establish the performance characteristics of the APTIMA Combo 2 Assay on the PANTHER System in male urine specimens. Specimens were collected from symptomatic and asymptomatic men (n=1492) enrolled from 13 geographically and ethnically diverse US clinical research sites, and family planning, public health, men's 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 1492 subjects enrolled, 14 were withdrawn.

Two specimens were collected from each subject (1 urethral swab and 1 first-catch urine, in that order). The urethral swab specimens were clinician-collected, and urine specimens were collected by the subject at the clinic. Urine specimens from each subject were processed into

multiple samples for CT/GC testing with different NAATs in accordance with the instructions in the appropriate specimen collection kit package insert. The male urine samples for APTIMA Combo 2 Assay testing on the PANTHER System were split among three external laboratories. All 1478 male urine samples from non-withdrawn subjects were tested with the APTIMA Combo 2 Assay on the PANTHER System in accordance with the APTIMA Combo 2 Assay package insert instructions. Samples with initial invalid, equivocal, or error results were retested. One male urine sample had a final invalid result and was excluded from the analyses. The invalid result was due to insufficient sample volume. Of the remaining 1477 evaluable male subjects, 46 were 16 to 17 years of age, 155 were 18 to 20 years of age, 524 were 21 to 30 years of age, 279 were 31 to 40 years of age, and 473 were >40 years of age.

Male urethral swab and urine samples were tested with cleared NAATs to establish the infected status (see **Tables 13** and **15** for the infected status algorithms). The infected status algorithm used urethral swab and urine sample results from one reference CT and GC NAAT and urine sample results from two additional reference CT and GC NAATs to generate four reference results for each analyte. Subjects were categorized as infected if a positive result occurred in at least two of the reference NAATs. Subjects that could not be categorized as infected or not infected were excluded from the performance analyses; 1 subject had an indeterminate CT infected status and was excluded from the performance analyses for detection of CT.

Chlamydia trachomatis Performance Results

Performance characteristics of the APTIMA Combo 2 Assay for CT detection were estimated for each specimen type and are displayed in **Tables 4** and **5** combining data from the two clinical studies. **Table 6** displays the clinical performance results by individual study. Performance was calculated by comparing PANTHER System results to an infected status algorithm, which differed between the two clinical studies (see **Tables 10** through **12** for the CT infected status algorithms). **Table 4** 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 4: Performance Characteristics of the APTIMA Combo 2 Assay for CT Detection

Specimen Type[1]	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[2]	Specificity % (95% CI)[2]	PPV % (95% CI)[3]	NPV% (95% CI)[3]
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)
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)
MU	1799	197	3	1589	10	11.5	95.2 (91.3-97.4)	99.8 (99.4-99.9)	98.5 (95.8- 99.7)	99.4 (98.9-99.7)

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

[1] Male urethral swab, vaginal swab, PreservCyt liquid Pap, and endocervical swab sample results are from Clinical Study 1, symptomatic male urine sample results are from Clinical Study 2, and asymptomatic male urine sample results are from both studies.

[2] Score CI

[3] 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 5 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 5: Performance Characteristics of the APTIMA Combo 2 Assay for CT Detection by Symptom Status

Specimen Type[1]	Symptom Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[2]	Specificity % (95% CI)[2]	PPV % (95% CI)[3]	NPV% (95% CI)[3]
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)
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)
MU	Sym	497	85	1	406	5	18.1	94.4 (87.6-97.6)	99.8 (98.6-100)	98.8 (94.1-100)	98.8 (97.3-99.6)
	Asym	1302	112	2	1183	5	9.0	95.7 (90.4-98.2)	99.8 (99.4-100)	98.2 (94.1-99.8)	99.6 (99.1-99.9)

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

[1]Male urethral swab, vaginal swab, PreservCyt liquid Pap, and endocervical swab sample results are from Clinical Study 1, symptomatic male urine sample results are from Clinical Study 2, and asymptomatic male urine sample results are from both studies.

[2] Score CI

[3] 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 6: Clinical Performance of the AC2 Assay on PANTHER for Detection of *Chlamydia Trachomatis* in Male Urine, by Study and Symptom Status

Study	Symptom Status	n	TP	FP	TN	FN	Prev (%)	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV % (95% CI)[2]
Study 1	Asymp	323	40	1	280	2	13.0	95.2 (84.2 to 98.7)	99.6 (98.0 to 99.9)	97.6 (88.3 to 99.9)	99.3 (97.6 to 99.9)
Study 2	Asymp	979	72	1	903	3	7.7	96.0 (88.9 to 98.6)	99.9 (99.4 to 100.0)	98.6 (93.0 to 100.0)	99.7 (99.1 to 99.9)
	Sympt	497	85	1	406	5	18.1	94.4 (87.6 to 97.6)	99.8 (98.6 to 100.0)	98.8 (94.1 to 100.0)	98.8 (97.3 to 99.6)
	Total	1476	157	2	1309	8	11.2	95.2 (90.7 to 97.5)	99.8 (99.4 to 100.0)	98.7 (95.7 to 99.8)	99.4 (98.8 to 99.7)

Asympt = asymptomatic, Prev = prevalence, Sympt = symptomatic

[1]Score CI.

[2]PPV 95% CI computed from the exact 95% CI for Positive Likelihood Ratio, NPV 95% CI computed from the exact 95% CI for Negative Likelihood Ratio.

Neisseria gonorrhoeae Performance Results

Performance characteristics of the APTIMA Combo 2 Assay for GC detection were estimated for each specimen type and are displayed in **Tables 7** and **8** combining data from the two clinical studies. **Table 9** displays the clinical performance results by individual study. The infected status algorithm differed between the two clinical studies (see **Tables 13** through **15** for the GC infected status algorithms). **Table 7** 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 7: Performance Characteristics of the APTIMA Combo 2 Assay for GC Detection

Specimen Type[1]	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[2]	Specificity % (95% CI)[2]	PPV % (95% CI)[3]	NPV% (95% CI)[3]
CVS/ PVS	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)
MS	546	34	0	512	0	6.2	100 (89.8-100)	100 (99.3-100)	100 (90.2-100)	100 (99.3-100)
MU	1797	75	5	1716	1	4.2	98.7 (92.9-99.8)	99.7 (99.3-99.9)	93.8 (86.7-97.8)	99.9 (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, MU = male urine, NPV = negative predictive value, PCyt = PreservCyt Solution liquid Pap, PPV = positive predictive value, Prev = prevalence, PVS = patient-collected vaginal swab, TN = true negative, TP = true positive.

[1] Vaginal swab, PreservCyt liquid Pap, endocervical swab, and male urethral swab sample results are from Clinical Study 1, symptomatic male urine sample results are from Clinical Study 2, and asymptomatic male urine sample results are from both studies..

[2] Score CI

[3] 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 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 8: Performance Characteristics of the APTIMA Combo 2 Assay for GC Detection by Symptom Status

Specimen Type[1]	Symptom Status	n	TP	FP	TN	FN	Prev %	Sensitivity % (95% CI)[2]	Specificity % (95% CI)[2]	PPV % (95% CI)[3]	NPV% (95% CI)[3]
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)
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)
MU	Sym	497	66	1	430	0	13.3	100 (94.5-100)	99.8 (98.7-100)	98.5 (92.3-100)	100 (99.2-100)
	Asym	1300	9	4	1286	1	0.8	90.0 (59.6-98.2)	99.7 (99.2-99.9)	69.2 (45.6-91.7)	99.9 (99.7-100)

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

[1] Vaginal swab, PreservCyt liquid Pap, endocervical swab, male urethral swab sample results are from Clinical Study 1, symptomatic male urine sample results are from Clinical Study 2, and asymptomatic male urine sample results are from both studies.

[2] Score CI

[3] 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. Clinical Performance of the AC2 Assay on PANTHER for Detection of *Neisseria Gonorrhoeae* in Male Urine, by Study and Symptom Status

Study	Symptom Status	n	TP	FP	TN	FN	Prev (%)	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	PPV % (95% CI)[2]	NPV % (95% CI)[2]
Study 1	Asymp	320	3	2	314	1	1.3	75.0 (30.1 to 95.4)	99.4 (97.7 to 99.8)	60 (22.4 to 93.0)	99.7 (99.0 to 100.0)
Study 2	Asymp	980	6	2	972	0	0.6	100.0 (61.0 to 100.0)	99.8 (99.3 to 99.9)	75 (44.7 to 96.9)	100 (99.7 to 100.0)
	Sympt	497	66	1	430	0	13.3	100.0 (94.5 to 100.0)	99.8 (98.7 to 100.0)	98.5 (92.3 to 100.0)	100 (99.2 to 100.0)
	Total	1477	72	3	1402	0	4.9	100.0 (94.9 to 100.0)	99.8 (99.4 to 99.9)	96 (89.2 to 99.1)	100 (99.7 to 100.0)

Asympt = asymptomatic, Prev = prevalence, Sympt = symptomatic

[1]Score CI.

[2]PPV 95% CI computed from the exact 95% CI for Positive Likelihood Ratio, NPV 95% CI computed from the exact 95% CI for Negative Likelihood Ratio.

Chlamydia trachomatis Infected Status Tables

The frequency of test outcomes from reference NAAT and investigational PANTHER System testing is summarized in **Tables 10** through **12** for CT.

Table 10: Clinical Study 1. CT Infected Status for Performance Evaluation in Female Vaginal Swab, PreservCyt Solution Liquid Pap, and Endocervical Swab Samples

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 11: Clinical Study 1: CT Infected Status for Performance Evaluation in Male Urethral Swab Samples

CT Infected Status	Assay Results					Symptom Status	
	AC2 DTS		ACT TIGRIS		AC2 PANTHER		
	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, MS = male urethral swab, MU = male urine, NA = result not available, PANTHER = PANTHER System, Sym = symptomatic, TIGRIS = TIGRIS DTS System.

Table 12: Clinical Study 1 and Clinical Study 2. CT Infected Status for Performance Evaluation in Male Urine Samples

	Assay Results								
CT Infected Status	AC2[1]	ACT TIGRIS[2]			NAAT 1[3]	NAAT 2[3]	AC2 PANTHER	Symptom Status	
	MS	MU	MS	MU	MU	MU	MU	Sym	Asym
Clinical Study 1									
Infected	+	+	+	+			+		38
Infected	+	-	+	+			+		2
Infected	+	-	+	-			-		2
Clinical Study 2									
Infected	+	+			+	+	+	73	66
Infected	+	+			+	+	-	2	1
Infected	+	+			+	-	+	0	1
Infected	+	+			+	NA	+	0	1
Infected	+	+			-	+	+	3	0
Infected	+	+			-	+	-	0	1
Infected	+	-			+	+	+	4	0
Infected	+	-			+	+	-	3	0
Infected	+	=			-	+	-	0	1
Infected	-	+			+	+	+	5	4
Clinical Study 1									
Not Infected	+	+	-	-			-		1
Not Infected	+	-	-	-			-		2
Not Infected	-	-	+	-			-		2
Not Infected	-	-	-	+			+		1
Not Infected	-	-	-	-			-		273
Not Infected	NA	-	-	-			-		2
Clinical Study 2									
Not Infected	+	-			-	-	-	1	6
Not Infected	-	+			-	-	+	0	1
Not Infected	-	-			+	-	+	1	0
Not Infected	-	-			+	-	-	0	2
Not Infected	-	-			-	-	-	388	874
Not Infected	-	-			-	=	-	0	1
Not Infected	-	-			-	NA	-	10	18
Not Infected	-	-			NA	-	-	1	2
Not Infected	-	NA			-	-	-	2	0
Not Infected	NA	-			-	-	-	4	0

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

[1]Male urethral swab and male urine samples were tested with the APTIMA Combo 2 Assay on the DTS Systems in Clinical Study 1 and on the TIGRIS System in Clinical Study 2.

[2]Male urethral swab and male urine samples were tested with the APTIMA CT Assay on the TIGRIS DTS Systems in Clinical Study 1.

[3]Male urine samples were tested with two FDA-cleared CT NAATs in Clinical Study 2.

Note: Data from asymptomatic men in Clinical Study 1 are combined with data from Clinical Study 2.

Neisseria gonorrhoeae Infected Status Tables

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

Table 13: Clinical Study 1. GC Infected Status for Performance Evaluation in Female Vaginal Swab, PreservCyt Solution Liquid Pap, and Endocervical Swab

GC Infected Status	Assay Results							Symptom Status	
	AC2 TIGRIS		AGC TIGRIS		AC2 PANTHER				
	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, AGC = APTIMA GC 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.

Table 14: Clinical Study 1. GC Infected Status for Performance Evaluation in Male Urethral Swab Samples

GC Infected Status	Assay Results					Symptom Status	
	AC2 DTS		AGC DTS		AC2 PANTHER		
	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.

Table 15. Clinical Study 1 and Clinical Study 2. GC Infected Status for Performance Evaluation in Male Urine Samples

GC Infected Status	Assay Results							Symptom Status	
	AC2[1]	AGC DTS[2]			NAAT 1[3]	NAAT 2[3]	AC2 PANTHER		
	MS	MU	MS	MU	MU	MU	MU	Sym	Asym
Clinical Study 1									
Infected	+	+	+	+			+		3
Infected	+	-	+	-			-		1
Clinical Study 2									
Infected	+	+			+	+	+	63	4
Infected	+	+			+	NA	+	1	1
Infected	-	+			+	-	+	0	1
Infected	NA	+			+	+	+	2	0
Clinical Study 1									
Not Infected	-	-	NA	NA			+		2
Not Infected	-	-	NA	NA			-		314
Clinical Study 2									
Not Infected	+	-			-	-	-	2	4
Not Infected	-	+			-	-	+	0	1
Not Infected	-	-			+	-	-	6	2
Not Infected	-	-			-	+	-	1	0
Not Infected	-	-			-	-	+	1	1
Not Infected	-	-			-	-	-	407	945
Not Infected	-	-			-	NA	-	9	19
Not Infected	-	-			NA	-	-	1	2
Not Infected	-	NA			-	-	-	2	0
Not Infected	NA	-			-	-	-	2	0

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

[1]Male urethral swab and male urine samples were tested with the APTIMA Combo 2 Assay on the DTS Systems in Clinical Study 1 and on the TIGRIS System in Clinical Study 2.

[2]Male urethral swab and male urine samples were tested with the APTIMA CT Assay on the DTS Systems in Clinical Study 1.

[3]Male urine samples were tested with two FDA-cleared GC NAATs in Clinical Study 2.

Note: Data from asymptomatic men in Clinical Study 1 are combined with data from Clinical Study 2.

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 Clinical Study 1 and Clinical Study 2.

Table 16: Clinical Study 1 and Clinical Study 2. RLU Distribution of APTIMA Combo 2 Controls

Control	Statistic	Total RLU (x1000)	
		Clinical Study 1	Clinical Study 2
Positive Control, CT/ Negative Control, GC	N	66	23
	Maximum	1335	1258
	Median	1081.5	1135.0
	Minimum	624	910
	CV%	11.2	7.5
Positive Control, GC/ Negative Control, CT	N	66	23
	Maximum	1241	1311
	Median	1172.0	1174.0
	Minimum	1063	1082
	CV%	3.2	4.9

Reproducibility Studies

Reproducibility of the APTIMA Combo 2 Assay on the PANTHER System was evaluated in two different studies using panel members created with Specimen Transport Medium in Reproducibility Study 1 and using panel members created with clinical urine specimens in Reproducibility Study 2.

Reproducibility Study 1

APTIMA Combo 2 Assay reproducibility was evaluated with panel members created using Specimen Transport Medium at three external US laboratories using the PANTHER System. Testing was performed using one lot of assay reagents and a total of six operators (two at each site). Testing was performed over at least 10 days at each site. The negative panel member consisted of Specimen Transport Medium and positive panel members were created by spiking Specimen Transport Medium with lysate from 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 and the mean, standard deviation (SD), and coefficient of variation (CV) of the RLU data for each panel member between-sites, between-operators, between-days, between-runs, within-runs, and overall. Percent agreement with expected results is also shown. Only samples with valid results were included in the analyses.

Table 17: Reproducibility Study 1 Data

Target Concentration					Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
CT (IFU/mL)	GC (CFU/mL)	Agreed/N	Agmt (%)	Mean RLU (x1000)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)	SD (x1000)	CV (%)
0	0	180/180	100	6	1.0	17.5	0.5	8.1	0.2	3.7	0.5	8.2	1.5	24.4	1.9	32.4
0.25	0	180/180	100	1207	45.0	3.7	17.3	1.4	0.0	0.0	35.1	2.9	66.9	5.5	89.7	7.4
2.5	0	180/180	100	1272	41.3	3.2	19.2	1.5	0.0	0.0	31.0	2.4	36.8	2.9	66.3	5.2
25	0	180/180	100	1292	43.7	3.4	14.9	1.2	7.7	0.6	35.1	2.7	36.3	2.8	68.8	5.3
1000	0	180/180	100	1294	48.1	3.7	14.3	1.1	26.8	2.1	29.6	2.3	34.8	2.7	73.0	5.6
0	0.25	180/180	100	589	92.2	15.7	19.9	3.4	28.1	4.8	21.2	3.6	44.8	7.6	110.2	18.7
0	12.5	179/179	100	1251	163.5	13.1	0.0	0.0	15.1	1.2	31.5	2.5	29.8	2.4	169.8	13.6
0	125	180/180	100	1295	168.3	13.0	6.7	0.5	33.4	2.6	21.1	1.6	33.3	2.6	176.2	13.6
0	1250	180/180	100	1309	166.5	12.7	0.0	0.0	28.4	2.2	27.6	2.1	31.2	2.4	173.9	13.3
0	2500	179/179	100	1305	170.9	13.1	11.4	0.9	30.4	2.3	15.2	1.2	32.2	2.5	177.5	13.6
2.5	125	178/178	100	2513	123.9	4.9	24.6	1.0	24.0	1.0	57.5	2.3	52.4	2.1	150.3	6.0
2.5	2500	180/180	100	2515	123.5	4.9	6.5	0.3	33.8	1.3	39.3	1.6	59.4	2.4	146.6	5.8
1000	125	179/179	100	2524	117.4	4.6	35.2	1.4	52.1	2.1	28.9	1.1	54.7	2.2	146.8	5.8
1000	2500	180/180	100	2525	118.2	4.7	21.6	0.9	38.7	1.5	54.8	2.2	48.5	1.9	145.9	5.8

Agmt = agreement, CFU = colony-forming unit, CV = coefficient of variation, IFU = inclusion-forming unit, 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.

Reproducibility Study 2

APTIMA Combo 2 Assay reproducibility was evaluated with panel members created using clinical urine specimens at two external US laboratories and in-house using the PANTHER System. Testing was performed using one lot of assay reagents and a total of six operators (two at each site). Testing was performed over at least 10 days at each site. The negative panel member consisted of negative urine and the positive panel members were created by spiking negative urine with lysate from CT and/or GC organisms to result in panel members with expected targeted concentrations. **Table 18** shows the CT and GC concentrations for each panel member and the mean, SD, and CV of the RLU data for each panel member between-sites, between-operators, between-days, between-runs, within-runs, and overall. Percent agreement with expected results is also shown. Only samples with valid results were included in the analyses.

Table 18: Reproducibility Study 2 Data

Target Concentration					Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
CT (IFU/mL)	GC (CFU/mL)	Agreed/N	Agmt (%)	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	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	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	1185	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	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	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	422	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	1142	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	1224	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	1263	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	1309	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	2468	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	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	2504	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	79.1	3.4	0.0	0.0	0.0	0.0	74.2	3.1	55.2	2.3	121.7	5.2

Agmt = agreement, CFU = colony-forming unit, CV = coefficient of variation, IFU = inclusion-forming unit, 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

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

October 17, 2013

Hologic/Gen-Probe Incorporated
Jody J. Fleming, MBA, RAC
Regulatory Affairs Manager
10210 Genetic Center Drive
San Diego, CA, 92121

Re: K132251

Trade/Device Name: APTIMA Combo 2® Assay (on the PANTHER® System)
Regulation Number: 21 CFR 866.3120
21 CFR 866.3390
Regulation Name: Chlamydia serological reagents
Neisseria spp. direct serological test reagents
Regulatory Class: II
Product Code: MKZ, LSL, NSU
Dated: July 22, 2013
Received: July 23, 2013

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

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact 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/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Sally A. Hojvat -S

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013

Indications for Use

510(k) Number (if known): K132251

Device Name: APTIMA Combo 2® Assay

Indications For 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, patient-collected vaginal swab specimens,[1] and male urine 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 Center for Devices and Radiological Health (CDRH)

Kathleen A. Simon -S
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