510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K132251

B. Purpose for Submission:

To obtain clearance for an additional specimen type, male urine on APTIMA Combo 2® Assay on the PANTHER® System

C. Measurand:

Chlamydia trachomatis and Neisseria gonorrhoeae ribosomal RNA

D. Type of Test:

Nucleic acid amplification assay

E. Applicant:

Hologic/Gen-Probe Incorporated

F. Proprietary and Established Names:

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

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3120 - Chlamydia serological reagents

   21 CFR 866.3390 - Neisseria spp. direct serological test reagents

2. Classification:

   Class II

3. Product code:

MKZ: DNA Probe, Nucleic Acid Amplification, Chlamydia
LSL: DNA-Reagents, Neisseria
NSU: Instrumentation for Clinical Multiplex Test Systems

4. Panel:

   Microbiology (83)

H. Intended Use:

1. Intended use(s):

   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.

2. Indication(s) for use:

   Same as the Intended Use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Gen-Probe PANTHER System

I. Device Description:

The APTIMA Combo 2 Assay is a nucleic acid amplification test that qualitatively detects and differentiates ribosomal RNA (rRNA) from *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC) in the following specimens:

- Clinician-collected endocervical, vaginal, and male urethral swab specimens
- Male urine specimens

- Clinician-collected PreservCyt Solution liquid Pap specimens
- Patient-collected vaginal swab specimens

The current APTIMA Combo 2 Assay is similar to the APTIMA Combo 2 Assay originally cleared (ref: K111409) for use on the Panther System. It does not introduce any changes to the original design, method of manufacture, assay procedure, principle of operation, mechanism of action, conditions of use, hardware or software of the PANTHER instrument, or to the results interpretation for the cleared APTIMA Combo 2 Assay. There are no changes to the APTIMA Combo 2 Assay (PANTHER System) catalog numbers (303094 and 302923), accessories, or ancillary kits. The existing 'APTIMA Urine Specimen Collection Kit for Male and Female Urine Specimens' (catalog number 301040) will be added to the APTIMA Combo 2 Assay (PANTHER System) package insert as an ancillary kit. This collection kit is used with the cleared APTIMA Combo 2 Assay on the DTS System (K003395) and TIGRIS System (K032194).

The APTIMA Combo 2 Assay kit is comprised of 3 boxes:

- Refrigerated Box contains the Amplification Reagent, Enzyme Reagent, Probe Reagent, and Target Capture Reagent-B
- Room Temperature Box contains Amplification Reconstitution Solution, Enzyme Reconstitution Solution, Probe Reconstitution Solution, Selection Reagent and Target Capture Reagent
- Controls Box contains the Negative and Positive Controls

The APTIMA Combo 2 Assay on PANTHER utilizes three specimen collection kits.

- APTIMA Unisex Swab Specimen Collection Kit for Endocervical and Male Urethral Swab Specimens
- APTIMA Urine Collection Kit for Male and Female Urine Specimens (APTIMA Combo 2 Assay on the PANTHER System has not been cleared for use with female urine specimens)
- APTIMA Vaginal Swab Specimen Collection Kit
- APTIMA Specimen Transfer Kit (for use with gynecologic samples collected in PreservCyt Solution)

J. Substantial Equivalence Information:

1. Predicate device name(s):

   APTIMA Combo 2® Assay (PANTHER® System)

2. Predicate 510(k) number(s):

   K111409

3. Comparison with predicate:

Item	Predicate	Device
Device Class	II	II
Regulation Specialty	Microbiology	Microbiology
Qualitative /Quantitative Assay	Qualitative	Qualitative
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, 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.	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.

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 -20oC to -70oC 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 -20oC to -70oC for up to 365 days.	ThinPrep Liquid Pap in PreservCyt: Same
	Urine not cleared.	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

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

Establishing the Performance Characteristics of In Vitro Diagnostic Devices for *Chlamydia trachomatis* and/or *Neisseria gonorrhea*: Screening and Diagnostic Testing - Draft Guidance for Industry and FDA Staff, May 11, 2011.

EP5-A2, 2004 – Evaluation of Precision Performance of Quantitative Measurement Methods, CLSI Approved Guideline

EP15-A2, 2006 – User Verification of Performance for Precision and Trueness, CLSI Approved Guideline

L. Test Principle:

The APTIMA Combo 2 Assay involves 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 *Chlamydia trachomatis* (CT) and a specific region of the 16S rRNA from *Neisseria gonorrhea* (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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Within-Laboratory Repeatability:
   Within-laboratory repeatability was conducted previously to support the clearance of K111409. Please refer to decision summary of K111049.

   Reproducibility:
   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 One and using panel members created with clinical urine specimens in Reproducibility Study Two.

   Reproducibility Study One
   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. The table below 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.

Reproducibility Study One Data

Target Concentration		Agreed/N	Agmt (%)	Mean RLU (x1000)	Between-Sites		Between-Operators		Between-Days		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 (%)	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 Two

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 create panel members with the expected targeted concentrations. 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 are shown in the table below. Percent

agreement with expected results is also shown. Only samples with valid results were included in the analyses.

Reproducibility Study Two Data

Target Concentration		Agreed/N	Agmt (%)	Mean RLU (x1000)	Between-Sites		Between-Operators		Between-Days		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 (%)	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.

b. Linearity/assay reportable range:

Not Applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Freeze-Thaw Stability

The purpose of this study was to evaluate the sensitivity and specificity of the APTIMA Combo 2 Assay on the PANTHER System using urine samples that were frozen and thawed prior to testing. Paired fresh (non-frozen) and frozen urine samples were evaluated. The urine specimens were diluted 1:1 with urine transport

medium (UTM) and then split into two aliquots to generate negative and positive samples:

1. One aliquot was left un-spiked (negative sample).
2. One aliquot was spiked with 0.25 IFU/mL of cultured CT serovar E and 12.5 CFU/mL of cultured GC strain 49226 (CT/GC-positive sample).

The un-spiked and spiked urine samples were split into two aliquots to test fresh (non-frozen) and frozen sample storage conditions:

1. Fresh samples: One spiked and one un-spiked aliquot of each urine sample was stored at 2˚C to 30°C until tested.
2. Frozen samples: One spiked and one un-spiked aliquot of each sample was frozen and stored at ≤ -20˚C for at least 72 hours (to ensure samples were completely frozen) until tested.

The results from this study demonstrate equivalency between urine samples tested fresh and paired samples tested after being frozen and thawed.

Quality Control Results and Acceptability

The Positive Control, CT / Negative Control, GC and the Positive Control, GC / Negative Control, CT act as controls for the target capture, amplification, and detection steps of the assay. The Positive Control, CT / Negative Control, GC serves as the negative control for the GC test results. The Positive Control, GC / Negative Control, CT serves as the negative control for the CT test results. If desired, a dual negative control furnished by the user can be added to monitor assay background. Correct preparation of specimens is confirmed visually by the presence of a single APTIMA collection swab in a swab specimen transport tube or the absence of a swab in an APTIMA specimen transfer tube for PreservCyt liquid Pap specimens.

The APTIMA Combo 2 Assay Controls must produce the following test results:

Control	Total RLU (x1000)	CT Result	GC Result
Positive Control, CT /Negative Control, GC	≥ 100 and < 3,000	Positive	Negative
Positive Control, GC /Negative Control, CT	≥ 150 and < 3,000	Negative	Positive

d. Detection limit:

The Limit of Detection (LoD) study included a series of dilution panels of CT (serovars E and G) and GC (ATCC strain 49226 and 19424) prepared in urine and in specimen transport medium (STM) to achieve several test concentrations. The positivity, with the two-sided 95% Score confidence interval, was calculated for each test concentration of each panel. Probit analysis was performed on the positivity results of each panel to determine the predicted 95% detection limit. The LoDs in both STM and urine sample matrices are well below the assay sensitivity claims for CT (1 IFU/assay) and GC (50 cells/assay).

The LoD of the APTIMA Combo 2 Assay on the PANTHER system in both urine and STM sample matrices was verified for 12 serovars of CT and 30 strains of GC. Dilutions of less than 2.5 IFU/mL tested positive in the APTIMA Combo 2 Assay for the following 12 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). Dilutions of less than 125 CFU/mL 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 cells/mL).

e. Analytical specificity:

Please refer to the decision summary of K111049 for cross reactivity data.

f. Interference:

Please refer to the decision summary of K111049.

g. Carryover Study:

The purpose of this study was to determine the carryover rate of the APTIMA Combo 2 Assay on the PANTHER System when high titer positive samples were alternately processed with negative samples in a checkerboard format. Six runs were performed on one PANTHER instrument using one reagent lot for three days. The first run comprised of 135 negative samples was performed to establish the baseline false positive rate. The five subsequent runs were comprised of 54 samples (GC-positive and GC-negative samples) alternated in checkerboard format. High titer positive samples for this study were made by spiking GC rRNA into specimen transport media (STM) to give a final concentration equivalent to ~ 2×10^5 cells/mL. The false positive rate from the baseline run without any positive samples (Run 1) was 0% (0/135; 100% specificity). The false positive rate from the runs with positive samples in the checkerboard design (Runs 2-6) was 0.74% (1/135; 99.26% specificity). The carryover rate was 0.74% with a 95% CI of -2.03 to 4.10.

h. Assay cut-off:

Assay test results are automatically interpreted by the APTIMA Assay software, using the APTIMA Combo 2 protocol. A test result may be a negative, equivocal, positive, or invalid as determined by the kinetic type and total RLU in the detection step. A test result may be invalid due to a parameter outside the normal expected ranges. Initial equivocal and invalid test results should be retested.

Kinetic Type	Total RLU (x1000) to give CT Result		
	Negative	**Equivocal**	**Positive**
CT only	1 to < 25	25 to < 100	100 to < 4,500
CT and GC	1 to < 85	85 to < 250	250 to < 4,500
CT indeterminate	1 to < 85	85 to < 4,500	N/A

Kinetic Type	Total RLU (x1000) to give GC Result		
	Negative	**Equivocal**	**Positive**
GC only	1 to < 60	60 to < 150	150 to < 4,500
GC and CT	1 to < 85	85 to < 250	250 to < 4,500
GC indeterminate	1 to < 85	85 to < 4,500	N/A

2. Comparison studies:

a. Method comparison with predicate device:

The comparison studies were conducted in two clinical studies with prospectively collected samples (see the Clinical studies section below).

b. Matrix comparison:

Not applicable

3. Clinical studies:

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 One, and with male urine specimens in Clinical Study Two.

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

A prospective, multi-center 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 seven 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 two specimens were collected from each male subject (one urethral swab and one first-catch urine, in that order) and up to four specimens were collected from each female subject (one first-catch urine, one vaginal swab, one PreservCyt Solution liquid Pap specimen, and one 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 instructions. The samples were split among 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, one 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 one endocervical swab had final CT equivocal results and one PreservCyt Solution liquid Pap sample, and one 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 8, 9, 11, and 12 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 Two: Male Urine Specimen Clinical Study

A prospective, multi-center 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 (one urethral swab and one 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 10 and 13 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. Performance was calculated by comparing PANTHER System results to an infected status algorithm, which differed between the two clinical studies (see Tables 8 through 10 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 Solution liquid Pap, and endocervical swab sample results are from Clinical Study One, symptomatic male urine sample results are from Clinical Study Two, 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 Charatcteristics 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 Solution liquid Pap, and endocervical swab sample results are from Clinical Study One, symptomatic male urine sample results are from Clinical Study Two, 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.

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 6 and 7 combining data from the two clinical studies. The infected status algorithm differed between the two clinical studies (see Tables 11 through 13 for the GC infected status algorithms). Table 6 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 6: 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 Solution liquid Pap, endocervical swab, and male urethral swab sample results are from Clinical Study One, symptomatic male urine sample results are from Clinical Study Two, 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 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 by symptom status. GC prevalence was higher in symptomatic men but similar in symptomatic and asymptomatic women.

Table 7: 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 Solution liquid Pap, endocervical swab, and male urethral swab sample results are from Clinical Study One, symptomatic male urine sample results are from Clinical Study Two, 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.

Chlamydia trachomatis Infected Status Tables

The frequency of test outcomes from reference NAAT and investigational PANTHER System testing is summarized in Tables 8 through 10 for CT.

Table 8: Clinical Study One. 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 Assay, 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 9: Clinical Study One. 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 Assay, 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 10: Clinical Study One and Clinical Study Two. CT Infected Status for Performance Evaluation in Male Urine Samples

CT Infected Status	Assay Results							Symptom Status	
	AC2[1]		ACT TIGRIS[2]		NAAT 1[3]	NAAT 2[3]	AC2 PANTHER		
	MS	MU	MS	MU	MU	MU	MU	Sym	Asym
Clinical Study One									
Infected	+	+	+	+			+		38
Infected	+	-	+	+			+		2
Infected	+	-	+	-			-		2
Clinical Study Two									
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 One									
Not Infected	+	+	-	-			-		1
Not Infected	+	-	-	-			-		2
Not Infected	-	-	+	-			-		2
Not Infected	-	-	-	+			+		1

Not Infected	-	-	-	-			-		273
Not Infected	NA	-	-	-			-		2
Clinical Study Two									
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, MS = male urethral swab, MU = male urine, NA = result not available, PANTHER = PANTHER System, Sym = symptomatic, TIGRIS = TIGRIS DTS System.

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

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

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

Note. Data from asymptomatic men in Clinical Study One are combined with data from Clinical Study Two.

Neisseria gonorrhoeae Infected Status Tables

The frequency of test outcomes from reference NAAT and investigational PANTHER System testing is summarized in Tables 11 through 13 for GC.

Table 11: Clinical Study One. 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 Assay, 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 12: Clinical Study One. 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 Assay, 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 13: Clinical Study One and Clinical Study Two. 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 One									
Infected	+	+	+	+			+		3
Infected	+	-	+	-			-		1
Clinical Study Two									
Infected	+	+			+	+	+	63	4
Infected	+	+			+	NA	+	1	1
Infected	-	+			+	-	+	0	1
Infected	NA	+			+	+	+	2	0
Clinical Study One									
Not Infected	-	-	NA	NA			+		2
Not Infected	-	-	NA	NA			-		314
Clinical Study Two									
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, MU = male urine, 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 One and on the TIGRIS DTS System in Clinical Study Two.

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

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

Note. Data from asymptomatic men in Clinical Study One are combined with data from Clinical Study Two.

RLU Distribution of APTIMA Combo 2 Controls

The distribution of the RLU values for the APTIMA Combo 2 controls is presented in Table 14 for all valid PANTHER System runs performed during Clinical Study One and Clinical Study Two.

Table 14: *Clinical Study One and Clinical Study Two. RLU Distribution of APTIMA* Combo 2 Controls

Control	Statistic	Total RLU (x1000)	
		Clinical Study One	Clinical Study Two
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

4. Clinical cut-off**:**

Not Applicable

5. Expected values/Reference range:

A summary of the prevalence of CT and GC, by specimen type, as determined by the APTIMA Combo 2 Assay on the PANTHER System for two multi-center clinical studies is shown in the following tables.

Clinical Study One: 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)											
Site	MS			CVS/PVS			PCyt			FS		
	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.

Clinical Study One and Clinical Study Two. 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 Two and asymptomatic male urine samples from both studies.

N. Instrument Name:

The PANTHER System

O. System Descriptions:

1. Modes of Operation:

   Batch, random access

2. Software:

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

   Yes ____X____ or No _____

3. Specimen Identification:

   By hand-held barcode reader and positional checks

4. Specimen Sampling and Handling:

   Fully automated

5. Calibration:

   Gen-Probe Field Service Engineers perform a luminometer calibration on the PANTHER System every 12 months as part of the Preventive Maintenance. Also, there are process

controls and calibration checks on all of the dispensers, thermal devices, and the vacuum system.

6. Quality Control:

   In addition to the assay controls that are specific to each assay, the PANTHER System contains process controls that employ both hardware and software components. The process controls include, but are not limited to:

   - Verification that the sequence of assay processing steps is correct for each reaction.
   - Verification that the reaction incubation times and temperatures are correct.
   - Verification that reagents and fluids are appropriately dispensed.

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

Not Applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.