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

A. 510(k) Number:
K032554

B. Analyte:
Chlamydia trachomatis and *Neisseria gonorrhoeae* rRNA

C. Type of Test:
Nucleic acid amplification method for direct detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* rRNA in endocervical, urethral, and vaginal swabs; also urine

D. Applicant:
Gen-Probe, Inc.

E. Proprietary and Established Names:
Aptima® Combo 2 Assay

F. Regulatory Information:

1. Regulation section: 21 CFR Part 866.3390 and 866.3120, Chlamydia Serological Reagents and Neisseria spp. Direct Serological Test Reagents
2. Classification: Class II
3. Product Code: LSL and MKZ
4. Panel: 83

G. 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 ribonucleic acid (rRNA) from *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* in clinician-collected endocervical, vaginal, and male urethral swab specimens, patient-collected vaginal swab specimens* and male and female urine specimens. The assay may be used to test specimens from symptomatic and asymptomatic individuals to aid in the diagnosis of gonococcal and/or chlamydial urogenital disease.
*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.

An additional component with its own labeling was included with this submission:

The APTIMA Vaginal Swab Specimen Collection Kit is for use with the APTIMA Assays for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. The APTIMA Vaginal Swab Specimen Collection Kit is intended to be used for clinician and patient collection of vaginal swab specimens according to the instructions provided. Patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated. The APTIMA Vaginal Swab Specimen Collection Kit is not for home use.

1. Indication(s) for use:
   Patient- and clinician- collected vaginal swabs
2. Special condition for use statement(s):
   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.
3. Special instrument Requirements: NA

H. Device Description:

The APTIMA Vaginal Swab Specimen Collection Kit contains a specimen collection swab that is identical in design to the PACE endocervical collection swab (original 510(k) unknown;note: the first reference to an endocervical collection kit for use with PACE is in K881277). The bud of this swab is softer than the Unisex Swab currently used with the Aptima Combo2, and is sterile. The transport tube included in the kit is identical in composition and formulation to that included in the Aptima Unisex Swab Specimen Collection kit (K003395).

The Collection Kit also contains instructions for a woman to follow when the patient-collected specimen is an option, along with a specimen transport and collection tube that is identical to the tube used for other Aptima swab collection transfers. The specimen may also be collected by clinicians during a patient examination. The instructions for self-collection are new and have not been used by other commercially available collection kits.

The APTIMA Combo 2 Assay is unchanged otherwise. The indications for use for this assay system has been changed to add an additional specimen type to the intended use.

I. Substantial Equivalence Information:

1. Predicate device name(s): Aptima Combo 2 Assay (AC2) and PACE2 collection
2. Predicate K number(s): k003395 and k881277
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	Detection of CT and GC rRNA	Same
Aptima Combo 2 reagents and procedure	Same	Same
Collection Swab	Same	sterile
Transport media	Same	3.9 mL
Differences		
Item	**Device**	**Predicate**
Indicated	Additionally, vaginal swabs	Urethral and endocervical

Specimen type		swabs; urine (male and female)
Swab bud	softer – female only	Unisex
Collection	patient- and clinician-collection instructions	clinician

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

K. Test Principle: Following lysis of cells and stabilization of nucleases in transport medium, target rRNA (23S rRNA from *C. trachomatis* and 16S rRNA from *N. gonorrhoeae*) is captured by oligomers complementary to sequences in the target region. Target:oligomer complexes hybridize to poly-deoxythymidine molecules covalently bound to magnetic microparticles that are washed to remove potential inhibitors from the specimen. Two primer sets, reverse transcriptase and RNA polymerase complete target amplification followed by hybridization of single-stranded chemiluminescent probes labeled with two different acridium ester molecules to a region within each amplicon type. *C. trachomatis* DNA probes are labeled with a rapidly emitting acridium ester, while *N. gonorrhoeae* is labeled with a slowly emitting acridium ester. Hybridized probe is differentiated from unhybridized probe by protection with secondary complex structure. Emitted light from labeled RNA:DNA hybrids is measured in a luminometer over a preset read time, using dual kinetic assay (DKA) software that applies a mathematical algorithm to distinguish *C. trachomatis* from *N. gonorrhoeae* emission patterns. Assay results are determined by total RLU and the kinetic curve type.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

The analytical performance of the assay has not changed

2. Comparison studies:
    a. *Method comparison with predicate device: NA*
    b. *Matrix comparison:* NA

3. Clinical studies:
    a. *Clinical sensitivity:*
    Overall, sensitivity with vaginal swabs was >95% (and lower 95% CI >90%) for females identified as infected by an endocervical swab or a urine specimen that was positive by AC2 and also positive by another nucleic acid amplification assay that identifies a different target (plasmid DNA vs 23S rRNA) and uses a different test principle (Strand Displacement vs. Transcription-mediated amplification). Reduced sensitivity was noted for women >25 y with overt symptoms. Additional warnings are included in the labeling and in patient instructions about use of vaginal swabs (or urine specimens) when a pelvic exam is warranted by virtue of patient-described symptoms.

C. trachomatis Sensitivity and Specificity: APTIMA Combo 2 Assay Vaginal Swab Specimens vs. Patient Infected Status

Specimen	Symptom Status	N	TP	FP	TN	FN	Sensitivity	(95% C.I.)	Specificity	(95% C.I.)
Patient-Collected Vaginal Swab	Asymptomatic	628	62	16	549	1	98.4	(91.5 - 100)	97.2	(95.4 - 98.4)
	All	1423	172	28	1217	6	96.6	(92.8 - 98.8)	97.8	(96.8 - 98.5)
Clinician-Collected Vaginal Swab	Symptomatic	809	113	23	669	4	96.6	(91.5 - 99.1)	96.7	(95.1 - 97.9)
	Asymptomatic	636	61	14	559	2	96.8	(89.0 - 99.6)	97.6	(95.9 - 98.7)
	All	1445	174	37	1228	6	96.7	(92.9 - 98.8)	97.1	(96.0 - 97.9)

N. gonorrhoeae Sensitivity and Specificity: APTIMA Combo 2 Assay Vaginal Swab Specimens vs. Patient Infected Status

Specimen	Symptom Status	N	TP	FP	TN	FN	Sensitivity	(95% C.I.)	Specificity	(95% C.I.)
Patient-Collected Vaginal Swab	Asymptomatic	629	22	2	605	0	100	(84.6 - 100)	99.7	(98.8 - 100)
	All	1423	76	6	1340	1	98.7	(93.0 - 100)	99.6	(99.0 - 99.8)
Clinician-Collected Vaginal Swab	Symptomatic	807	53	5	747	2	96.4	(87.5 - 99.6)	99.3	(98.5 - 99.8)
	Asymptomatic	637	22	3	611	1	95.7	(78.1 - 99.9)	99.5	(98.6 - 99.9)
	All	1444	75	8	1358	3	96.2	(89.2 - 99.2)	99.4	(98.8 - 99.7)

b. *Clinical specificity:* With the clinical evaluation performed, 28/1245 (97.2%) and 5/752 (98.7%) self-collected vaginal swab specimens were positive when infection was not detected by two other tests in one or more of the specimen types evaluated (endocervical swab and urine). Overall, 28/200 (14.0%) of positive self-collected vaginal swabs were probable false positive for *C. trachomatis*. Warnings in the package insert advise that positive results should be considered presumptive and confirmed by another nucleic acid amplification assay (or culture in the case of N. gonorrhoeae). Clinician-collected vaginal swabs had higher FP rates for C. trachomatis. An additional warning was included for clinicians to avoid sampling the vaginal fornix area which could contribute to lower specificity.

c. *Other clinical supportive data (when a and b are not applicable):* Each participant in the clinical evaluation provided feedback on the self-collection procedure; approx. 5-10% in the junior high and high school groups did not find the procedure easy to use, or the instructions easy to read and follow. Notably, the percentages increased when a nurse was present. Other recently published information was used to assess the safety of self-collection using a similar collection device. In these reports, up to 25-30% of participants preferred not to collect their own vaginal specimen.

The vaginal collection kit now contains information for women on the procedure, so each woman can know ahead of time what instructions she would need to follow and assess whether she would be comfortable and able to perform the procedure. The instructions were edited to provide greater clarity and readability.

Schachter, et al. Vaginal Swabs are appropriate specimens for diagnosis of genital tract infection with Chlamydia trachomatis. J Clin Microb 2003, 41:3784-3789.

Shafer et al. Comparing first-void urine specimens, self-collected vaginal swabs, and endocervical specimens to detect Chlamydia trachomatis and Neisseria gonorrhoeae by a nucleic acid amplification test. J Clin Microbiol 2003, 41:4395-4399.

Polaneczky et al. Use of self-collected vaginal specimens for detection of Chlamydia trachomatis infection. Obstetrics & Gynecology 1998, 91: 375-378

Richardson et al. Prevalence of Chlamydia trachomatis infections and specimen collection preference among women, using self-collected vaginal swabs in community settings. Sexually Transmitted Diseases, 2003, 30:880-885.

4. Clinical cut-off: NA

5. Expected values/Reference range: The presence of *C. trachomatis and N. gonorrhoeae* are assayed qualitatively. The presence of one or more organisms is considered evidence of infection. Asymptomatic individuals may have fewer organisms collected in a swab or urine specimen. *N. gonorrhoeae* prevalence is rare (<1%) in many female sample populations, however, prevalence increases in targeted populations (younger females from communities with higher STD rates). Prevalence of *C. trachomatis* is uniformly highest in younger females (<25 y) across most population samples. In the clinical evaluation, prevalences with the vaginal swab assays were as follows:

Prevalence of *C. trachomatis* and/or *N. gonorrhoeae* Disease by the APTIMA Combo 2 Assay Results by Clinical Site

Site	Patient-Collected Vaginal Swab, % Prevalence (# positive/# tested)					
	CT+/GC+		CT+/GC-		CT-/GC+	
1	1.8	(4/220)	16.4	(36/220)	4.1	(9/220)
2	9.6	(19/198)	18.7	(37/198)	6.6	(13/198)
3	0.9	(1/111)	9	(10/111)	2.7	(3/111)
4	0.4	(1/266)	9	(24/266)	1.9	(5/266)
5	0.5	(1/199)	7.5	(15/199)	0.5	(1/199)
6	2.8	(8/290)	10	(29/290)	5.5	(16/290)
7	0	(0/102)	11.8	(12/102)	0	(0/102)
8	0	(0/48)	8.3	(4/48)	2.1	(1/48)
All	2.4	(34/1434)	11.6	(167/1434)	3.3	(48/1434)

Clinician-Collected Vaginal Swab, % Prevalence (# positive/# tested)

Site	CT+/GC+		CT+/GC-		CT-/GC+	
	3	(7/230)	15.7	(36/230)	3.5	(8/230)
1	9.5	(19/199)	18.1	(36/199)	7	(14/199)
2	0.9	(1/113)	9.7	(11/113)	1.8	(2/113)
3	0.4	(1/267)	11.2	(30/267)	2.2	(6/267)
4	0.5	(1/199)	7	(14/199)	0.5	(1/199)
5	2	(6/296)	12.2	(36/296)	5.4	(16/296)
6	0	(0/102)	9.8	(10/102)	0	(0/102)
7	0	(0/51)	7.8	(4/51)	2	(1/51)
8	2.4	(35/1457)	12.1	(177/1457)	3.3	(48/1457)

M. Conclusion: The APTIMA Vaginal Swab Specimen Collection Kit is substantially equivalent to the APTIMA unisex swab for use with the APTIMA Combo 2 Assay for detection and differentiation of ribosomal ribonucleic acid (rRNA) from ***Chlamydia*** *trachomatis* and/or ***Neisseria gonorrhoeae*** in symptomatic and asymptomatic females to aid in the diagnosis of urogenital infection.