

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

K062440

B. Purpose for Submission:

The Gen-Probe APTIMA[®] Assay for *Neisseria gonorrhoeae* (AGC) is a nucleic acid amplification test (NAAT) intended for the qualitative detection of ribosomal RNA from *Neisseria gonorrhoeae* (GC) in endocervical, male urethral and vaginal swab specimens and in female and male urine specimens. The assay originally received FDA clearance in 2005 (K043144). The current application is for the additional indication of testing specimens collected and processed with the Cytoc ThinPrep 2000 System. New PreservCyt labeling for the approved ancillary liquid pap Specimen Transfer Kit is included in the current submission.

C. Measurand:

Neisseria gonorrhoeae (GC) ribosomal RNA

D. Type of Test:

NAAT

E. Applicant:

GEN-PROBE, INC.

F. Proprietary and Established Names:

GEN-PROBE[®] APTIMA[®] Assay for *Neisseria gonorrhoeae*

G. Regulatory Information:

| Product Code | Classification | Regulation Section | Panel |
|---------------------|-----------------------|---------------------------|-------------------|
| LSL | Class II | 21 CFR 866.3390 | Microbiology (83) |

H. Intended Use:

1. Intended use(s):

The APTIMA[®] Assay for *Neisseria gonorrhoeae* is a target amplification nucleic acid probe test that utilizes target capture for the in vitro qualitative detection of

ribosomal RNA (rRNA) from *Neisseria gonorrhoeae* (GC) to aid in the diagnosis of gonococcal urogenital disease. The assay may be used to test the following specimens from symptomatic individuals: clinician-collected endocervical, vaginal and male urethral swab specimens; and female and male urine specimens. The assay may be used to test the following specimens from asymptomatic individuals: clinician-collected endocervical and vaginal swab specimens; and patient-collected vaginal swab specimens¹ and female and male urine specimens. The assay is also intended for use with the testing of gynecological specimens, from both symptomatic and asymptomatic patients, collected in the PreservCyt Solution and processed with the Cytoc ThinPrep 2000 System.

¹Patient-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:

See Intended Use above.

3. Special conditions for use statement(s):

This device is for prescription use only

4. Special instrument requirements:

Gen-Probe DTS System

I. Device Description:

The GEN-PROBE[®] APTIMA[®] Assay for *Neisseria gonorrhoeae* is a nucleic acid amplification test (NAAT). See Test Principle below for more details.

J. Substantial Equivalence Information:

Addition of a PreservCyt (PC) specimen indication to the previously cleared device. Collection device and media are different, as are specimen handling and storage conditions.

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

Not Applicable

L. Test Principle:

The GEN-PROBE APTIMA Assay for *Neisseria gonorrhoeae* combines the technologies of target capture, Transcription-Mediated Amplification (TMA), and Hybridization Protection Assay (HPA). During target capture, rRNA molecules

are isolated from specimens by capture oligomers on magnetic microparticles. After target capture, the specimens are ready for TMA. The GEN-PROBE APTIMA Assay for *Neisseria gonorrhoeae* reaction replicates a specific region of the 16S rRNA from *N. gonorrhoeae* via DNA intermediates. Detection of the rRNA amplicons is achieved using a single-stranded chemiluminescent DNA probe, which is labeled with an acridinium ester molecule. The labeled DNA probe combines with amplicon to form stable RNA:DNA hybrids and light emitted from the labeled RNA:DNA hybrids is reported as Relative Light Units (RLU). Assay results are determined by a cut-off based on the RLU.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

PreservCyt specimen within-laboratory precision with the APTIMA GC Assay was determined by spiking PreservCyt vials with 20 GC CFU per vial (0.1 CFU per reaction) and 100 GC CFU per vial (0.5 CFU per reaction). Vials containing 10,000 GC CFU per vial (50 CFU per reaction) and unspiked PreservCyt vials were tested as positive and negative controls. Ten vials spiked at each CFU level and ten unspiked vials were divided between two operators. The operators vortexed the vials and then transferred 14 aliquots (1.0 mL each) per vial into 14 APTIMA Transfer Tubes as per the APTIMA Specimen Transfer Kit package insert. The operators were blinded to the samples' titers. Each of the resulting Pap-STM samples was tested once in the APTIMA GC Assay. A total of five runs were performed over a five day period for 140 results at the 0.1, 0.5, and 50 CFU level. There were 136 valid results and 4 invalid results for the negative control panel. The invalid results were due to a misplacement of a TTU in the Leader HC+. The results are summarized below:

Table 11. APTIMA GC Assay Within-Laboratory Precision Data for PreservCyt Using a 4-Member Precision Panel Containing 0 to 500 CFU/mL GC Cells

| Panel Member | CFU/mL PreservCyt | CFU/rxn | n | Agreed | % Agmt. | Mean RLU (x1000) | Within-Operator | | Between-Day | | Between-Operator | | Total | |
|--------------|-------------------|---------|------|--------|---------|------------------|-----------------|--------|-------------|--------|------------------|--------|------------|--------|
| | | | | | | | SD (x1000) | CV (%) | SD (x1000) | CV (%) | SD (x1000) | CV (%) | SD (x1000) | CV (%) |
| A | 1 | 0.1 | 140 | 39 | 27.9 | 313.7 | 758.3 | 241.7 | 132.5 | 42.2 | 0.0 | 0.0 | 769.8 | 245.4 |
| B | 5 | 0.5 | 140 | 113 | 80.7 | 1211.1 | 1031.3 | 85.2 | 169.8 | 14.0 | 150.4 | 12.4 | 1056.0 | 87.2 |
| C | 500 | 50 | 140 | 140 | 100 | 5638.8 | 220.7 | 3.9 | 135.7 | 2.4 | 0.0 | 0.0 | 259.1 | 4.6 |
| D | 0 | 0 | 136* | 136 | 100 | 1.2 | 0.5 | N/A | 0 | N/A | 0.3 | N/A | 0.6 | N/A |

* There were four invalid results due to a misplaced TTU in the Leader HC+.

Note: Variability from some factors may be numerically negative, which can occur if the variability due to those factors is small. When this occurs, the variability as measured with SD and %CV is set to zero (12). N/A = Not applicable for negative panel members. Operator = Run. Samples with discordant results were included in the signal variability analysis.

b. *Linearity/assay reportable range:*

Not Applicable

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

Not Applicable

d. *Detection limit:*

A study was performed that showed the AGC Assay detected GC cells at the analytical sensitivity claim (50 CFU/assay) for 3 replicates of each of 20 GC clinical isolates tested in PC media. See results below:

Table 18.8-01: PreservCyt Analytical Sensitivity for Detection of GC

| GP Cl# | GC Cells Per Assay | Replicate 1 | | Replicate 2 | | Replicate 3 | |
|--------|--------------------|-------------|--------|-------------|--------|-------------|--------|
| | | RLU | Result | RLU | Result | RLU | Result |
| 760 | 500 | 5,659,000 | GC+ | 5,804,000 | GC+ | 5,665,000 | GC+ |
| | 50 | 3,657,000 | GC+ | 3,223,000 | GC+ | 2,820,000 | GC+ |
| | 5 | 541,000 | GC+ | 559,000 | GC+ | 621,000 | GC+ |
| | 0.5 | 49,000 | GC- | 70,000 | GCe | 140,000 | GC+ |
| 764 | 500 | 5,922,000 | GC+ | 5,884,000 | GC+ | 6,229,000 | GC+ |
| | 50 | 4,046,000 | GC+ | 4,313,000 | GC+ | 4,559,000 | GC+ |
| | 5 | 949,000 | GC+ | 888,000 | GC+ | 1,005,000 | GC+ |
| | 0.5 | 63,000 | GCe | 83,000 | GCe | 52,000 | GCe |
| 772 | 500 | 5,775,000 | GC+ | 5,844,000 | GC+ | 5,883,000 | GC+ |
| | 50 | 2,999,000 | GC+ | 2,772,000 | GC+ | 3,153,000 | GC+ |
| | 5 | 555,000 | GC+ | 598,000 | GC+ | 572,000 | GC+ |
| | 0.5 | 35,000 | GC- | 27,000 | GC- | 29,000 | GC- |
| 783 | 500 | 5,313,000 | GC+ | 5,218,000 | GC+ | 5,165,000 | GC+ |
| | 50 | 4,776,000 | GC+ | 4,738,000 | GC+ | 4,683,000 | GC+ |
| | 5 | 2,453,000 | GC+ | 1,909,000 | GC+ | 2,400,000 | GC+ |
| | 0.5 | 422,000 | GC+ | 607,000 | GC+ | 716,000 | GC+ |
| 787 | 500 | 4,597,000 | GC+ | 4,904,000 | GC+ | 4,893,000 | GC+ |
| | 50 | 2,712,000 | GC+ | 2,242,000 | GC+ | 2,165,000 | GC+ |
| | 5 | 327,000 | GC+ | 383,000 | GC+ | 623,000 | GC+ |
| | 0.5 | 48,000 | GC- | 24,000 | GC- | 41,000 | GC- |
| 789 | 500 | 5,833,000 | GC+ | 5,984,000 | GC+ | 6,111,000 | GC+ |
| | 50 | 3,402,000 | GC+ | 3,492,000 | GC+ | 2,688,000 | GC+ |
| | 5 | 409,000 | GC+ | 525,000 | GC+ | 516,000 | GC+ |
| | 0.5 | 70,000 | GCe | 41,000 | GC- | 96,000 | GCe |
| 790 | 500 | 4,431,000 | GC+ | 4,385,000 | GC+ | 4,370,000 | GC+ |
| | 50 | 2,097,000 | GC+ | 2,032,000 | GC+ | 2,369,000 | GC+ |
| | 5 | 313,000 | GC+ | 313,000 | GC+ | 200,000 | GC+ |
| | 0.5 | 30,000 | GC- | 7,000 | GC- | 10,000 | GC- |
| 793 | 500 | 6,081,000 | GC+ | 5,966,000 | GC+ | 5,814,000 | GC+ |
| | 50 | 5,319,000 | GC+ | 5,032,000 | GC+ | 5,180,000 | GC+ |
| | 5 | 2,347,000 | GC+ | 1,805,000 | GC+ | 1,824,000 | GC+ |
| | 0.5 | 138,000 | GC+ | 499,000 | GC+ | 436,000 | GC+ |
| 794 | 500 | 6,259,000 | GC+ | 6,424,000 | GC+ | 6,444,000 | GC+ |
| | 50 | 6,352,000 | GC+ | 5,261,000 | GC+ | 5,328,000 | GC+ |
| | 5 | 1,753,000 | GC+ | 1,617,000 | GC+ | 1,465,000 | GC+ |
| | 0.5 | 128,000 | GC+ | 175,000 | GC+ | 204,000 | GC+ |
| 795 | 500 | 5,104,000 | GC+ | 4,990,000 | GC+ | 4,851,000 | GC+ |
| | 50 | 3,787,000 | GC+ | 3,778,000 | GC+ | 4,110,000 | GC+ |
| | 5 | 953,000 | GC+ | 1,266,000 | GC+ | 1,290,000 | GC+ |
| | 0.5 | 141,000 | GC+ | 138,000 | GC+ | 123,000 | GC+ |

| | | | | | | | |
|-----|-----|-----------|-----|-----------|-----|-----------|-----|
| 799 | 500 | 6,031,000 | GC+ | 5,852,000 | GC+ | 5,962,000 | GC+ |
| | 50 | 3,781,000 | GC+ | 4,310,000 | GC+ | 4,293,000 | GC+ |
| | 5 | 820,000 | GC+ | 936,000 | GC+ | 1,053,000 | GC+ |
| | 0.5 | 52,000 | GCe | 65,000 | GCe | 102,000 | GC+ |
| 800 | 500 | 6,080,000 | GC+ | 6,221,000 | GC+ | 6,182,000 | GC+ |
| | 50 | 4,931,000 | GC+ | 4,733,000 | GC+ | 5,191,000 | GC+ |
| | 5 | 1,748,000 | GC+ | 1,992,000 | GC+ | 1,962,000 | GC+ |
| | 0.5 | 229,000 | GC+ | 198,000 | GC+ | 202,000 | GC+ |
| 801 | 500 | 5,485,000 | GC+ | 5,524,000 | GC+ | 5,834,000 | GC+ |
| | 50 | 3,570,000 | GC+ | 3,765,000 | GC+ | 3,909,000 | GC+ |
| | 5 | 504,000 | GC+ | 445,000 | GC+ | 444,000 | GC+ |
| | 0.5 | 44,000 | GC- | 94,000 | GCe | 28,000 | GC- |
| 802 | 500 | 5,911,000 | GC+ | 5,916,000 | GC+ | 6,050,000 | GC+ |
| | 50 | 4,350,000 | GC+ | 4,248,000 | GC+ | 4,107,000 | GC+ |
| | 5 | 987,000 | GC+ | 870,000 | GC+ | 957,000 | GC+ |
| | 0.5 | 65,000 | GCe | 49,000 | GC- | 127,000 | GC+ |
| 806 | 500 | 5,071,000 | GC+ | 5,194,000 | GC+ | 5,150,000 | GC+ |
| | 50 | 2,710,000 | GC+ | 2,408,000 | GC+ | 2,178,000 | GC+ |
| | 5 | 242,000 | GC+ | 178,000 | GC+ | 148,000 | GC+ |
| | 0.5 | 16,000 | GC- | 15,000 | GC- | 26,000 | GC- |
| 813 | 500 | 5,864,000 | GC+ | 5,841,000 | GC+ | 5,664,000 | GC+ |
| | 50 | 4,117,000 | GC+ | 4,345,000 | GC+ | 4,650,000 | GC+ |
| | 5 | 1,184,000 | GC+ | 1,343,000 | GC+ | 1,151,000 | GC+ |
| | 0.5 | 81,000 | GCe | 127,000 | GC+ | 130,000 | GC+ |
| 827 | 500 | 6,228,000 | GC+ | 6,145,000 | GC+ | 5,946,000 | GC+ |
| | 50 | 4,764,000 | GC+ | 4,781,000 | GC+ | 4,503,000 | GC+ |
| | 5 | 1,373,000 | GC+ | 1,341,000 | GC+ | 1,059,000 | GC+ |
| | 0.5 | 152,000 | GC+ | 117,000 | GC+ | 115,000 | GC+ |

| | | | | | | | |
|------|-----|-----------|-----|-----------|-----|-----------|-----|
| 3043 | 500 | 6,164,000 | GC+ | 6,263,000 | GC+ | 6,319,000 | GC+ |
| | 50 | 4,122,000 | GC+ | 3,313,000 | GC+ | 3,431,000 | GC+ |
| | 5 | 488,000 | GC+ | 527,000 | GC+ | 571,000 | GC+ |
| | 0.5 | 60,000 | GCe | 107,000 | GC+ | 91,000 | GCe |
| 3045 | 500 | 6,041,000 | GC+ | 6,239,000 | GC+ | 6,297,000 | GC+ |
| | 50 | 4,550,000 | GC+ | 4,539,000 | GC+ | 4,307,000 | GC+ |
| | 5 | 605,000 | GC+ | 942,000 | GC+ | 891,000 | GC+ |
| | 0.5 | 83,000 | GCe | 117,000 | GC+ | 145,000 | GC+ |
| 3047 | 500 | 6,534,000 | GC+ | 6,466,000 | GC+ | 6,483,000 | GC+ |
| | 50 | 5,214,000 | GC+ | 6,324,000 | GC+ | 5,122,000 | GC+ |
| | 5 | 1,618,000 | GC+ | 1,417,000 | GC+ | 1,685,000 | GC+ |
| | 0.5 | 89,000 | GCe | 124,000 | GC+ | 118,000 | GC+ |

e = Equivocal Result

e. Analytical specificity:

Neisseria species were used to evaluate the analytical specificity of the AGC Assay. A total of 47 culture isolates were tested in the liquid Pap media.

None of the culture isolates produced a positive result in the AGC Assay. See results below:

Table 18.9-01: Specificity of the AGC Assay with PreservCyt Samples

| <i>Specimen ID</i> | Gen-Probe Number | ATCC Number | Concentration Tested/Assay | Rep # | PreserCyt Results RLU |
|---|------------------|-------------|----------------------------|--------|-----------------------|
| <i>Neisseria cinerea</i> | 761 | 14685 | 1.6 x 10 ⁹ | 1 2 | 3,000 3,000 |
| <i>Neisseria cinerea</i> | CI3051 | | 2.9 x 10 ⁸ | 1 2 | 3,000 3,000 |
| <i>Neisseria cinerea</i> | CI4543 | | 1.3 x 10 ⁸ | 1 2 | 3,000 3,000 |
| <i>Neisseria cinerea</i> | CI4546 | | 4.9 x 10 ⁸ | 1 2 | 3,000 3,000 |
| <i>Neisseria dentrificans</i> | 763 | 14686 | 3.0 x 10 ⁸ | 1 2 | 3,000 3,000 |
| <i>Neisseria elongata</i> | CI1502 | 49377 | 1.2 x 10 ⁹ | 1 2 | 22,000 22,000 |
| <i>Neisseria elongata</i> | CI1503 | 49378 | 1.2 x 10 ⁸ | 1 2 | 22,000 23,000 |
| <i>Neisseria elongata</i> | CI1504 | 49379 | 1.8 x 10 ⁸ | 1 2 | 22,000 21,000 |
| <i>Neisseria flava</i> | 1558 | 14221 | 2.5 x 10 ⁹ | 1 2 | 3,000 3,000 |
| <i>Neisseria flavescens</i> | CI812 | | 5.0 x 10 ⁶ | 1 2 | 3,000 3,000 |
| <i>Neisseria lactamica</i> | 760 | 23970 | 1.1 x 10 ⁹ | 1 2 | 3,000 3,000 |
| <i>Neisseria lactamica</i> | CI3013 | | 9.5 x 10 ⁸ | 1 2 | 3,000 4,000 |
| <i>Neisseria lactamica</i> | CI3018 | | 1.5 x 10 ⁸ | 1 2 | 3,000 3,000 |
| <i>Neisseria lactamica</i> | CI3021 | | 5.0 x 10 ⁹ | 1 2 | 22,000 22,000 |
| <i>Neisseria lactamica</i> | CI3022 | | 9.4 x 10 ⁹ | 1 2 | 3,000 3,000 |
| <i>Neisseria lactamica</i> | CI3049 | | 2.3 x 10 ¹⁰ | 1 2 | 23,000 22,000 |
| <i>Neisseria lactamica</i> | CI3065 | | 1.5 x 10 ¹⁰ | 1 2 | 21,000 22,000 |
| <i>Neisseria lactamica</i> | CI3067 | | 2.9 x 10 ¹⁰ | 1 2 | 21,000 21,000 |
| <i>Neisseria lactamica</i> | CI834 | | 6.0 x 10 ⁹ | 1 2 | 22,000 22,000 |
| <i>Neisseria meningitidis</i> Serogroup A | 755 | 13077 | 4.0 x 10 ¹⁰ | 1 2 | 20,000 19,000 |
| <i>Neisseria meningitidis</i> Serogroup B | 756 | 13090 | 3.1 x 10 ⁶ | 1 2 | 3,000 3,000 |
| <i>Neisseria meningitidis</i> Serogroup C | 757 | 13102 | 5.0 x 10 ⁸ | 1 2 | 3,000 3,000 |
| <i>Neisseria meningitidis</i> Serogroup C | 1388 | 13109 | 2.9 x 10 ¹¹ | 1 2 | 3,000 7,000 |
| <i>Neisseria meningitidis</i> Serogroup C | 1389 | 13100 | 8.0 x 10 ¹⁰ | 1 2 | 3,000 3,000 |

| | | | | | |
|--|--------|-------|----------------------|--------|------------------|
| <i>Neisseria meningitidis</i> Serogroup C | 1390 | 13112 | 2.7×10^6 | 1 2 | 3,000 3,000 |
| <i>Neisseria meningitidis</i> Serogroup D | 401 | 13113 | 1.7×10^{11} | 1 2 | 3,000 2,000 |
| <i>Neisseria meningitidis</i> Serogroup W135 | 1387 | 43744 | 1.6×10^8 | 1 2 | 3,000 3,000 |
| <i>Neisseria meningitidis</i> Serogroup Y | 787 | 35561 | 3.0×10^{10} | 1 2 | 3,000 3,000 |
| <i>Neisseria mucosa</i> | 190 | 19696 | 2.4×10^8 | 1 2 | 20,000 21,000 |
| <i>Neisseria mucosa</i> | 791 | 25999 | 1.3×10^8 | 1 2 | 4,000 3,000 |
| <i>Neisseria perflava</i> | 1559 | 10555 | 1.0×10^8 | 1 2 | 3,000 3,000 |
| <i>Neisseria polysaccharea</i> | 1489 | 43768 | 3.0×10^9 | 1 2 | 20,000 19,000 |
| <i>Neisseria sicca</i> | 272 | 9913 | 5.9×10^8 | 1 2 | 3,000 3,000 |
| <i>Neisseria sicca</i> | 762 | 29193 | 7.2×10^7 | 1 2 | 3,000 3,000 |
| <i>Neisseria subflava</i> | CI3113 | | 4.5×10^7 | 1 2 | 3,000 3,000 |
| <i>Neisseria subflava</i> | NH1 | | 2.2×10^7 | 1 2 | 21,000 20,000 |
| <i>Neisseria subflava</i> | NH5 | | 2.4×10^7 | 1 2 | 3,000 3,000 |
| <i>Neisseria subflava</i> | NH6 | | 2.7×10^8 | 1 2 | 3,000 3,000 |
| <i>Neisseria subflava</i> | NH7 | | 1.2×10^9 | 1 2 | 3,000 3,000 |
| <i>Neisseria subflava</i> | NH8 | | 4.7×10^8 | 1 2 | 3,000 3,000 |
| <i>Neisseria subflava</i> | NH11 | | 1.0×10^9 | 1 2 | 3,000 3,000 |
| <i>Neisseria subflava</i> | NH13 | | 3.0×10^7 | 1 2 | 22,000 20,000 |
| <i>Neisseria subflava</i> | NH14 | | 4.5×10^7 | 1 2 | 21,000 20,000 |
| <i>Neisseria subflava</i> | NH15 | | 8.7×10^7 | 1 2 | 21,000 20,000 |
| <i>Neisseria subflava</i> | NH17 | | 1.1×10^9 | 1 2 | 21,000 21,000 |
| <i>Neisseria subflava</i> | NH18 | | 5.7×10^7 | 1 2 | 21,000 21,000 |
| <i>Neisseria subflava</i> | NH20 | | 2.1×10^8 | 1 2 | 22,000 21,000 |

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Not Applicable

3. Clinical studies:

A prospective multi-center clinical study was conducted to evaluate the use of the PreservCyt transport medium (a component of the ThinPrep 2000 System) as an alternative medium for gynecological specimens for the detection of *N. gonorrhoeae* by the APTIMA GC Assay. One thousand six hundred forty-seven (1,647) symptomatic and asymptomatic subjects attending OB/GYN, family planning, public health, women's, and STD clinics were enrolled and evaluated in the clinical study. Of these subjects, 1,288 were asymptomatic subjects and 359 were symptomatic subjects (Table 5b). Subjects were enrolled from sites with GC prevalence that ranged from 0.0% to 5.0% (Table 6b).

Two specimens were collected from each eligible subject: one PreservCyt liquid Pap specimen and one endocervical swab specimen. PreservCyt liquid Pap specimens were collected with the spatula/cyto-brush or a broom-like brush cervical sampling device. The distribution of cervical sampling devices is summarized in Table 4 by specimen collection site and overall.

PreservCyt liquid Pap specimens were processed in accordance with the ThinPrep 2000 Processor Operator's Manual and APTIMA Specimen Transfer Kit package insert. After processing the PreservCyt liquid Pap specimen with the ThinPrep 2000 Processor, the specimen was transferred into the APTIMA Specimen Transfer Kit for testing with the APTIMA GC Assay.

Sensitivity and specificity of the APTIMA GC Assay in PreservCyt liquid Pap specimens were calculated by comparing results to the patient infected status. The algorithm included APTIMA Combo 2 Assay and APTIMA GC Assay results in endocervical swab specimens. Both reference NAATs were required to be positive to establish an infected patient status. At least one reference NAAT was required to be negative to establish a non-infected patient status. The one equivocal result that was obtained from a reference NAAT was considered to be discordant with the investigative assay for the purpose of calculating performance, and thus the patient infected status was categorized as non-infected (n=1). Table 8 summarizes the frequency of test outcomes for the endocervical swab specimens tested with the APTIMA Combo 2 Assay and APTIMA GC Assay.

Table 5b shows the sensitivities and specificities of the APTIMA GC Assay by symptom status and overall. Overall sensitivity was 92.3% (12/13). In symptomatic and asymptomatic subjects, sensitivities were 100% (7/7) and 83.3% (5/6), respectively. Overall specificity was 99.8% (1630/1634). In symptomatic and asymptomatic subjects, specificities were 99.4% (350/352) and 99.8% (1280/1282), respectively.

Table 6b shows the sensitivities and specificities of the APTIMA GC Assay by specimen collection site and overall. Sensitivities ranged from 80.0% to 100%. Specificities ranged from 99.0% to 100%.

Table 4. Distribution of Cervical Sampling Device Used for PreservCyt Solution Liquid Pap Specimens

| Cervical Sampling Device Used | Clinical Collection Site | | | | | | Total |
|-------------------------------|--------------------------|-----|-----|-----|-----|-----|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | |
| Spatula/Cytobrush | 0 | 124 | 475 | 287 | 57 | 364 | 1307 |
| Broom-Type Device | 100 | 0 | 0 | 0 | 240 | 0 | 340 |

Table 8. PreservCyt Solution Liquid Pap Specimen Analysis for Patient Infected Status

| Patient Infected Status | Endocervical Swab | | Symptom Status | |
|-------------------------|----------------------|-----------------|----------------|--------------|
| | APTIMA COMBO 2 Assay | APTIMA GC Assay | Symptomatic | Asymptomatic |
| Infected | Positive | Positive | 7 | 6 |
| Non-Infected | Negative | Negative | 352 | 1276 |
| Non-Infected | Negative | Positive | 0 | 5 |
| Non-Infected | Equivocal | Positive | 0 | 1 |
| Total | | | 359 | 1288 |

Table 5b. Sensitivity and Specificity of the APTIMA GC Assay Relative to Patient Infected Status by Symptom Status and Overall for PreservCyt Solution Liquid Pap Specimen

| | APTIMA GC PreservCyt Solution Result | +/+ | +/- | -/+ | -/- | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) |
|--------------|--------------------------------------|-----|-----|----------------|------|-------------------------------|-----------------------------------|
| Symptomatic | Positive | 7 | 0 | 0 | 2 | 100 (7/7) (59.0 – 100) | 99.4 (350/352) (98.0 – 99.9) |
| | Negative | 0 | 0 | 0 | 350 | | |
| | Total | 7 | 0 | 0 | 352 | | |
| Asymptomatic | Positive | 5 | 0 | 1 ¹ | 1 | 83.3 (5/6) (35.9 – 99.6) | 99.8 (1280/1282) (99.4 – 100) |
| | Negative | 1 | 0 | 5 | 1275 | | |
| | Total | 6 | 0 | 6 | 1276 | | |
| All | Positive | 12 | 0 | 1 | 3 | 92.3 (12/13) (64.0 – 99.8) | 99.8 (1630/1634) (99.4 – 99.9) |
| | Negative | 1 | 0 | 5 | 1625 | | |
| | Total | 13 | 0 | 6 | 1628 | | |

+/+ = Positive endocervical swab specimen result in the APTIMA COMBO 2 Assay/Positive endocervical swab specimen result in the APTIMA GC Assay
 +/- = Positive endocervical swab specimen result in the APTIMA COMBO 2 Assay/Negative endocervical swab specimen result in the APTIMA GC Assay
 -/+ = Negative endocervical swab specimen result in the APTIMA COMBO 2 Assay/Positive endocervical swab specimen result in the APTIMA GC Assay
 -/- = Negative endocervical swab specimen result in the APTIMA COMBO 2 Assay/Negative endocervical swab specimen result in the APTIMA GC Assay
¹One specimen had a discordant result: Equivocal endocervical swab specimen result in the APTIMA COMBO 2 Assay/Positive endocervical swab specimen result in the APTIMA GC Assay.

Table 6b. Sensitivity, Specificity and Predictive Values of the APTIMA GC Assay Relative to Patient Infected Status by Clinical Site and Overall for PreservCyt Solution Liquid Pap Specimens

| Site | APTIMA GC PreservCyt Solution Result | +/+ | +/- | -/+ | -/- | Prev (%) | Sensitivity (%) (95% C.I.) | Specificity (%) (95% C.I.) | PPV(%) | NPV(%) |
|------|--------------------------------------|-----|-----|----------------|------|----------|-------------------------------|-----------------------------------|--------|--------|
| 1 | Positive | 5 | 0 | 0 | 0 | 5.0 | 100 (5/5) (47.8 – 100) | 100 (95/95) (96.2 – 100) | 100 | 100 |
| | Negative | 0 | 0 | 0 | 95 | | | | | |
| | Total | 5 | 0 | 0 | 95 | | | | | |
| 2 | Positive | 1 | 0 | 0 | 0 | 0.8 | 100 (1/1) (2.5 – 100) | 100 (123/123) (97.0 – 100) | 100 | 100 |
| | Negative | 0 | 0 | 0 | 123 | | | | | |
| | Total | 1 | 0 | 0 | 123 | | | | | |
| 3 | Positive | 4 | 0 | 0 | 0 | 1.1 | 80.0 (4/5) (28.4 – 99.5) | 100 (470/470) (99.2 – 100) | 100 | 99.8 |
| | Negative | 1 | 0 | 0 | 470 | | | | | |
| | Total | 5 | 0 | 0 | 470 | | | | | |
| 4 | Positive | 1 | 0 | 0 | 3 | 0.3 | 100 (1/1) (2.5 – 100) | 99.0 (283/286) (97.0 – 99.8) | 25.0 | 100 |
| | Negative | 0 | 0 | 3 | 280 | | | | | |
| | Total | 1 | 0 | 3 | 283 | | | | | |
| 5 | Positive | 0 | 0 | 0 | 0 | 0.0 | N/A | 100 (297/297) (98.8 – 100) | N/A | 100 |
| | Negative | 0 | 0 | 0 | 297 | | | | | |
| | Total | 0 | 0 | 0 | 297 | | | | | |
| 6 | Positive | 1 | 0 | 1 ¹ | 0 | 0.3 | 100 (1/1) (2.5 – 100) | 99.7 (362/363) (98.5 – 100) | 50.0 | 100 |
| | Negative | 0 | 0 | 2 | 360 | | | | | |
| | Total | 1 | 0 | 3 | 360 | | | | | |
| ALL | Positive | 12 | 0 | 1 | 3 | 0.8 | 92.3 (12/13) (64.0 – 99.8) | 99.8 (1630/1634) (99.4 – 99.9) | 75.0 | 99.9 |
| | Negative | 1 | 0 | 5 | 1625 | | | | | |
| | Total | 13 | 0 | 6 | 1628 | | | | | |

N/A = not applicable

+/+ = Positive endocervical swab specimen result in the APTIMA COMBO 2 Assay/Positive endocervical swab specimen result in the APTIMA GC Assay

+/- = Positive endocervical swab specimen result in the APTIMA COMBO 2 Assay/Negative endocervical swab specimen result in the APTIMA GC Assay

-/+ = Negative endocervical swab specimen result in the APTIMA COMBO 2 Assay/Positive endocervical swab specimen result in the APTIMA GC Assay

-/- = Negative endocervical swab specimen result in the APTIMA COMBO 2 Assay/Negative endocervical swab specimen result in the APTIMA GC Assay

¹One specimen had a discordant result: Equivocal endocervical swab specimen result in the APTIMA COMBO 2 Assay/Positive endocervical swab specimen result in the APTIMA GC Assay.

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The prevalence of *N. gonorrhoeae* disease in patient populations depends on risk factors such as age, gender, the presence of symptoms, the type of clinic, and the test method. A summary of the prevalence of *N. gonorrhoeae* as determined by the

APTIMA[®] Assay for *Neisseria gonorrhoeae* (AGC) results on PreservCyt liquid Pap specimens is shown below by clinical site and overall.

Table 1b. Prevalence of *N. gonorrhoeae* by Clinical Site and Overall as Determined by APTIMA GC Assay Results Using PreservCyt Liquid Pap Specimens

| Site | % (#positive/#tested) | |
|------|-----------------------|-----------|
| 1 | 5.0 | (5/100) |
| 2 | 0.8 | (1/124) |
| 3 | 0.8 | (4/475) |
| 4 | 1.4 | (4/287) |
| 5 | 0.0 | (0/297) |
| 6 | 0.5 | (2/364) |
| All | 1.0 | (16/1647) |

N. Proposed Labeling:

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

O. Conclusion:

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