May 23, 2019

Hologic, Inc.
Jeffrey Hergesheimer
Regulatory Affairs Manager
10210 Genetic Center Drive
San Diego, California 92121

Re: K190515
Trade/Device Name: Aptima Combo 2 Assay (Panther System)
Regulation Number: 21 CFR 866.3393
Regulation Name: Device to detect nucleic acids from non-viral microorganism(s) causing sexually transmitted infections and associated resistance marker(s)
Regulatory Class: Class II
Product Code: QEP, LSL, MKZ
Dated: February 28, 2019
Received: March 1, 2019

Dear Jeffrey Hergesheimer:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for

Uwe Scherf, Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

# 510(k) SUMMARY
## Aptima Combo 2 Assay (Panther System)

## I. SUBMITTER

Hologic, Inc.
10210 Genetic Center Drive
San Diego, CA 92121

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**Date Prepared:** February 28, 2019

## II. DEVICE

| | |
|---|---|
| Proprietary Name of Device: | Aptima Combo 2 Assay (Panther System) |
| Regulation Name: | Device to detect nucleic acids from non-viral microorganism(s) causing sexually transmitted infections and associated resistance marker(s) |
| Regulation Number: | 21 CFR 866.3393 |
| Regulatory Class: | Class II |
| Product Code: | QEP, LSL, MKZ |

## III. PREDICATE DEVICE

The predicate device is the Aptima Mycoplasma genitalium Assay; DEN180047, cleared January 23, 2019.

## IV. DEVICE DESCRIPTION

Clearance of this pre-market application will add extra-genital (throat and rectal) swab specimens as acceptable specimen types using the Aptima Combo 2 assay on the Panther system.

Principles of the Procedure

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.

Assay Components

The reagents required to perform the Aptima Combo 2 assay (Panther System) are available in two kit sizes (100- and 250-tests). The kits are packaged in 3 boxes containing 11 reagents which are required for sample processing. A description of the components that are required to perform the Aptima Combo 2 assay are detailed in **Table 1.** In addition, there are two ancillary kits required to run the assay (**Table 2**), and one collection kit utilized for collection of throat and rectal swab specimens (**Table 3**).

**Table 1: Reagents Required to Perform the Aptima Combo 2 Assay**

| Box | Components Description |
|---|---|
| **1** | Amplification Reagent |
| | Enzyme Reagent |
| | Probe Reagent |
| | Target Capture Reagent B |
| **2** | Amplification Reconstitution Solution |
| | Enzyme Reconstitution Solution |
| | Probe Reconstitution Solution |
| | Selection Reagent |
| | Target Capture Reagent |
| **3** | Aptima Positive Control CT/Neg Control GC |
| | Aptima Positive Control GC/Neg Control CT |

**Table 2: Ancillary Kits Required to Perform the Aptima Combo 2 Assay**

| |
|---|
| Aptima Assay Fluids Kit |
| Aptima Auto Detect Reagents Kit |

**Table 3: Specimen Collection Kit Required for Collection of Throat and Rectal Swab Specimens**

| |
|---|
| Aptima Multitest Swab Specimen Collection Kit |

Instrumentation

The Aptima Combo 2 assay has been designed for and validated on the Panther system. The Panther system is an integrated hardware and software system that together with the Aptima Combo 2 assay fully automates all the steps necessary to perform the assay from sample preparation through amplification of nucleic acid, detection, data reduction and amplicon inactivation.

## V. 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 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, throat, rectal and male urethral swab specimens, clinician-collected gynecological specimens collected in the PreservCyt® Solution, patient-collected vaginal swab specimens,[1] and female 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 Aptima Multitest Swab Specimen Collection Kit has not been evaluated for home use.

## VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

A comparison of the Aptima Combo 2 assay (Panther System) with the addition of the extra-genital specimen types to the predicate device, Aptima Mycoplasma genitalium Assay (DEN180047; January 23, 2019), is summarized in **Table 4** (similarities) and **Table 5** (differences).

**Table 4: Similarities Between Predicate Device and Subject Device**

| Item | Predicate Device<br>Aptima Mycoplasma genitalium Assay<br>(DEN180047) | Subject Device<br>Aptima Combo 2 Assay (Panther) |
|---|---|---|
| Technology Principle of Operation | Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA) | Same |
| Platform | Automated Panther System | Same |
| Assay Results | Qualitative | Same |

**Table 5: Differences Between Predicate Device and Subject Device**

| Item | Aptima Mycoplasma genitalium Assay<br>(Predicate Device) | Aptima Combo 2 Assay (Panther)<br>(Subject Device) |
|---|---|---|
| Intended Use | The Aptima Mycoplasma genitalium assay is an in vitro nucleic acid amplification test (NAAT) for the qualitative detection of ribosomal RNA (rRNA) from *Mycoplasma genitalium* on the fully automated Panther system. It is intended for use as an aid in the diagnosis of *M. genitalium* urogenital infections in male and female patients suspected of *M. genitalium* infection.<br>The assay may be used to test the following specimens: clinician-collected and self-collected vaginal swabs (in a clinical setting), clinician-collected endocervical swabs, female and male urine, clinician-collected male urethral swabs, and self-collected penile meatal swabs (in | 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 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, throat, rectal and male urethral swab specimens, clinician-collected gynecological specimens collected in the PreservCyt Solution, patient-collected vaginal |

| Item | Aptima Mycoplasma genitalium Assay (Predicate Device) | Aptima Combo 2 Assay (Panther) (Subject Device) |
|---|---|---|
| | a clinical setting).<br><br>For females, a vaginal swab is the preferred specimen type due to higher clinical sensitivity for detecting *M. genitalium* than other specimen types; however, female urine or clinician-collected endocervical swabs may be used as alternative specimens when vaginal swab specimens are not available. If female urine or clinician-collected endocervical swab specimens test negative, testing with a vaginal swab may be indicated, if *M. genitalium* infection is suspected. | swab specimens, [1] and female and male urine specimens.<br>[1]Patient-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated. The Aptima Multitest Swab Specimen Collection Kit has not been evaluated for home use. |
| Specimen Types | **Female specimens**:<br>• Vaginal swab<br>• Endocervical swab<br>• Urine<br><br>**Male Specimens**:<br>• Penile meatal swab<br>• Urethral swab<br>• Urine | **Female specimens**:<br>• Vaginal swab<br>• Endocervical swab<br>• Gynecological specimens in PreservCyt solution<br>• Urine<br>• Throat swab<br>• Rectal swab<br><br>**Male Specimens**:<br>• Urethral swab<br>• Urine<br>• Throat swab<br>• Rectal swab |
| Assay Targets | *Mycoplasma genitalium* rRNA | *Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC) rRNA |
| Function | Detection of rRNA from *Mycoplasma genitalium* | Detection and differentiation of rRNA from *Chlamydia trachomatis* and *Neisseria gonorrhoeae* |

## VII. PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

### Brief Description of Analytical (Non-Clinical) Studies

The following analytical studies (non-clinical) were conducted to support the clearance of the Aptima Combo 2 assay on the Panther system with the two new clinical specimen types throat and rectal swabs.

Limit of Detection (LoD)

The 95% limit of detection for the extra-genital swabs with the Aptima Combo 2 Assay was determined for throat and rectal swabs. Two CT Serovars (E and G) and two clinical GC isolates were spiked into pools of these swabs. The panels were tested on two Panther Systems using one reagent lot in replicates of at least 20 over eight days.

The 95% limit of detection for throat and rectal swabs was 0.007 IFU/mL for CT. The 95% limit of detection for throat and rectal swabs was 0.10 CFU/mL for GC.

Cross-Reactivity

To evaluate if various non-targeted microbes, which may be found in extra-genital specimens, cross-react or interfere with the sensitivity and specificity of the AC2 assay. Results demonstrated that presence of the microorganisms in **Table 6** did not interfere with the detection of CT and GC, and did not generate a positive result in the absence of CT and GC.

**Table 6: Cross-Reactivity Microorganisms for Throat and Rectal Specimens**

| **Organism** | **Organism** | **Organism** |
|---|---|---|
| Adenovirus | *Eggerthella lenta* | Metapneumo virus |
| *Anaercoccus spp.* | *Entamoeba histolytica* | *Moraxella catarrhalis* |
| *Arcanobacterium haemolyticum* | Enterovirus | *Mycoplasma pneumoniae* |
| *Bacteroides oralis* | Epstein-Barr Virus | Norovirus |
| *Bordetella parapertussis* | *Fusobacterium necrophorum* | *Peptostreptococcus micros* |
| *Bordetella pertussis* | *Giardia lamblia* | *Prevotella spp.* |
| *Burkholderia cepacia* | *Haemophilus parahaemolyticus* | Respiratory syncytial virus |
| *Campylobacter rectus* | *Haemophilus parainfluenzae* | Rhinovirus |
| *Citrobacter koseri* | *Helicobacter pylori* | *Shigella dysenteriae* |
| *Clostridioides difficile* | Hepatitis B Virus | *Shigella flexneri* |
| Coronavirus | Hepatitis C Virus | *Shigella sonnei* |
| *Corynebacterium diphtheriae* | Human influenza virus A | *Stenotrophomonas maltophilia* |
| *Corynebacterium pseudodiphtheriticum* | Human influenza virus B | *Streptococcus anginosus group* |
| Coxsackie Virus | *Legionella jordanis* | *Veillonella parvula* |
| Echovirus | *Legionella micdadei* | |

Interfering Substances

The following interfering substances were individually spiked into STM and tested on the Panther System: cold sore medication, lip balm, hemorrhoidal cream, human feces, cough suppressant, toothpaste, mouthwash, laxative suppository, anti-diarrheal medication, and antacid. All were tested for potential assay interference in the absence and presence of CT and GC slightly above the limit of detection.

**Brief Description of Clinical Study**

Clinical testing of the Aptima Combo 2 assay on the Panther system included performance testing in rectal swab and throat swab specimens.

A multicenter study was conducted using prospectively-collected rectal swab and throat swab samples from adult (≥18 years) participants seeking STI testing, with or without symptoms of STIs, who were attending participating US medical facilities. Nine (9) participating US STI screening and management, family planning, student health, women's health, and HIV management clinics, and clinics focusing on the lesbian, gay, bisexual, and transgender (LGBT) population enrolled 2767 symptomatic and asymptomatic men and women.

Up to eight specimens were collected by the clinician from each subject: 4 rectal swabs and 4 throat swabs, collected in a randomized order. One swab of each specimen type was tested with the Aptima Combo 2 assay. The remaining rectal swab and throat swab specimens were tested with up to three reference NAATs – cleared for the detection of urogenital CT/GC infection and validated for use in rectal swab and throat swab specimens – to establish the anatomic site infected status (ASIS) for each specimen type-organism combination for each subject. The ASIS was determined based on results from testing the same sample type. Subjects were categorized as infected if a positive result occurred in at least two reference NAATs, and as not infected if at least 2 of the reference results were negative; the third (tie-breaker) reference was only required if the first 2 reference results were discordant.

The clinical performance of the Aptima Combo 2 assay was evaluated against the ASIS for each specimen type-organism combination; sensitivity and specificity were calculated for each specimen type for CT and GC separately, along with corresponding 2-sided 95% CIs.

Of the 2767 subjects enrolled, 8 did not complete the collection visit and had no specimens sent for testing, 167 had samples tested but were excluded due to temperature excursions that compromised specimen integrity, and 1 had no samples tested in error. Of the 2591 non-excluded subjects that had at least one sample type tested, the following samples were excluded from performance analyses: 6 throat samples were excluded from evaluations of CT

performance, 12 throat samples were excluded from evaluations of GC performance, 29 rectal samples were excluded from evaluations of CT performance, and 22 rectal swab samples were excluded from evaluations of GC performance. **Table 7** shows the demographic of evaluable subjects.

**Table 7: Summary of Demographics of Evaluable Subjects**

| | |
|---|---|
| **Total, N** | 2591 |
| **Age, years** | |
| Mean ± SD | 33.8 ± 11.74 |
| Median | 30.0 |
| Range | 18-76 |
| **Age category (years), n (%)** | |
| 18-20 | 181 (7.0) |
| 21-25 | 565 (21.8) |
| >25 | 1845 (71.2 |
| **Sex, n (%)** | |
| Female | 538 (20.8) |
| Male | 2053 (79.2) |
| **Symptom Status (Rectal), n (%)** | |
| Asymptomatic | 2396 (92.5) |
| Symptomatic | 195 (7.5) |
| **Symptom Status (Throat), n (%)** | |
| Asymptomatic | 2285 (88.2) |
| Symptomatic | 306 (11.8) |

The CT+/GC-, CT-/GC+, and CT+/GC+ positivity rates were calculated for each anatomic site for subjects with valid, non-equivocal Aptima Combo 2 assay results for each specimen type (see **Table 8** and **Table 9)**. Performance characteristics were calculated overall and by symptom status for CT (see **Table 10**) and GC (see **Table 11**).

**Table 8: Aptima Combo 2 Assay Positivity in Rectal Swab Specimens**

| Collection Site | % Positivity (# positive/# tested) | | |
|---|---|---|---|
| | CT+/GC+ | CT+/GC- | CT-/GC+ |
| All | 2.3 (59/2562) | 6.3 (161/2562) | 5.8 (148/2562) |
| 1 | 2.1 (3/141) | 10.6 (15/141) | 6.4 (9/141) |
| 2 | 0.4 (1/223) | 6.3 (14/223) | 1.3 (3/223) |
| 3 | 3.4 (12/357) | 4.5 (16/357) | 4.5 (16/357) |
| 4 | 0.0 (0/110) | 1.8 (2/110) | 0.9 (1/110) |
| 5 | 2.4 (8/332) | 4.2 (14/332) | 3.6 (12/332) |
| 6 | 0.8 (3/395) | 2.5 (10/395) | 5.8 (23/395) |
| 7 | 3.4 (10/290) | 5.5 (16/290) | 5.5 (16/290) |
| 8 | 1.6 (6/366) | 10.9 (40/366) | 6.3 (23/366) |
| 9 | 4.6 (16/348) | 9.8 (34/348) | 12.9 (45/348) |

CT = *Chlamydia trachomatis*, GC = *Neisseria gonorrhoeae*.

**Table 9: Aptima Combo 2 Assay Positivity in Throat Swab Specimens**

| Collection Site | % Positivity (# positive/# tested) | | |
|---|---|---|---|
| | CT+/GC+ | CT+/GC- | CT-/GC+ |
| All | 0.3 (9/2584) | 1.7 (44/2584) | 8.2 (212/2584) |
| 1 | 0.0 (0/143) | 2.8 (4/143) | 9.8 (14/143) |
| 2 | 0.0 (0/225) | 0.4 (1/225) | 1.3 (3/225) |
| 3 | 0.3 (1/363) | 0.8 (3/363) | 5.5 (20/363) |
| 4 | 0.0 (0/112) | 0.9 (1/112) | 1.8 (2/112) |
| 5 | 0.6 (2/333) | 1.5 (5/333) | 4.5 (15/333) |
| 6 | 0.3 (1/398) | 1.0 (4/398) | 7.8 (31/398) |
| 7 | 0.3 (1/288) | 1.7 (5/288) | 9.7 (28/288) |
| 8 | 0.3 (1/367) | 4.1 (15/367) | 10.4 (38/367) |
| 9 | 0.8 (3/355) | 1.7 (6/355) | 17.2 (61/355) |

CT = *Chlamydia trachomatis*, GC = *Neisseria gonorrhoeae*.

**Table 10: Aptima Combo 2 Assay Performance Compared to ASIS for Detection of *Chlamydia trachomatis***

| Specimen Type | Symptom Status | n | TP | FP | TN | FN | Prev (%) | Sensitivity % (95% CI)[1] | Specificity % (95% CI)[1] |
|---|---|---|---|---|---|---|---|---|---|
| Throat | All | 2585 | 45 | 8 | 2526 | 6 | 2.0 | 88.2 (76.6-94.5) | 99.7 (99.4-99.8) |
| | Symptomatic | 306 | 9 | 1 | 296 | 0 | 2.9 | 100 (70.1-100) | 99.7 (98.1-99.9) |
| | Asymptomatic | 2279 | 36 | 7 | 2230 | 6 | 1.8 | 85.7 (72.2-93.3) | 99.7 (99.4-99.8) |
| Rectal | All | 2562 | 197 | 25 | 2322 | 18 | 8.4 | 91.6[2] (87.2-94.6) | 98.9[2] (98.4-99.3) |
| | Symptomatic | 190 | 23 | 2 | 164 | 1 | 12.6 | 95.8[3] (79.8-99.3) | 98.8[3] (95.7-99.7) |
| | Asymptomatic | 2372 | 174 | 23 | 2158 | 17 | 8.1 | 91.1[4] (86.2-94.4) | 98.9[4] (98.4-99.3) |

ASIS = anatomic site infected status, Prev = prevalence

Note: Symptomatic status refers to the anatomic site-specific symptomatic status.

[1] Score CI.

[2] Equivocal results excluded; the percent of equivocal results is 0.4% (10/2572). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 89.5% (197/220), 95% CI: 84.8% - 92.9% and Specificity = 98.7% (2322/2352), 95% CI: 98.2% - 99.1%.

[3] Equivocal results excluded; the percent of equivocal results is 0.5% (1/191). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 95.8% (23/24), 95% CI: 79.8% - 99.3% and Specificity = 98.2% (164/167), 95% CI: 94.9% - 99.4%.

[4] Equivocal results excluded; the percent of equivocal results is 0.4% (9/2381). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 88.8% (174/196), 95% CI: 83.6% - 92.5% and Specificity = 98.8% (2158/2185), 95% CI: 98.2% - 99.1%.

**Table 11: Aptima Combo 2 Assay Performance Compared to ASIS for Detection of *Neisseria gonorrhoeae***

| Specimen Type | Symptom Status | n | TP | FP | TN | FN | Prev (%) | Sensitivity % (95% CI)[1] | Specificity % (95% CI)[1] |
|---|---|---|---|---|---|---|---|---|---|
| Throat | All | 2579 | 195 | 25 | 2351 | 8 | 7.9 | 96.1[2] (92.4-98.0) | 98.9[2] (98.5-99.3) |
| | Symptomatic | 303 | 39 | 2 | 262 | 0 | 12.9 | 100[3] (91.0-100) | 99.2[3] (97.3-99.8) |
| | Asymptomatic | 2276 | 156 | 23 | 2089 | 8 | 7.2 | 95.1[4] (90.7-97.5) | 98.9[4] (98.4-99.3) |
| Rectal | All | 2569 | 192 | 13 | 2359 | 5 | 7.7 | 97.5[5] (94.2-98.9) | 99.5[5] (99.1-99.7) |
| | Symptomatic | 192 | 38 | 0 | 154 | 0 | 19.8 | 100[6] (90.8-100) | 100[6] (97.6-100) |
| | Asymptomatic | 2377 | 154 | 13 | 2205 | 5 | 6.7 | 96.9[7] (92.9-98.6) | 99.4[7] (99.0-99.7) |

ASIS = anatomic site infected status, Prev = prevalence

Note: Symptomatic status refers to the anatomic site-specific symptomatic status.

[1] Score CI.

[2] Equivocal results excluded; the percent of equivocal results is 0.1% (3/2582). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 96.1% (195/203), 95% CI: 92.4% - 98.0% and Specificity = 98.8% (2351/2379), 95% CI: 98.3% - 99.2%.

[3] Equivocal results excluded; the percent of equivocal results is 0.7% (2/305). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 100% (39/39), 95% CI: 91.0% - 100% and Specificity = 98.5% (262/266), 95% CI: 96.2% - 99.4%.

[4] Equivocal results excluded; the percent of equivocal results is 0.04% (1/2277). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 95.1% (156/164), 95% CI: 90.7% - 97.5% and Specificity = 98.9% (2089/2113), 95% CI: 98.3% - 99.2%.

[5] Equivocal results excluded; the percent of equivocal results is 0.2% (5/2574). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 96.5% (192/199), 95% CI: 92.9% - 98.3% and Specificity = 99.3% (2359/2375), 95% CI: 98.9% - 99.6%.

[6] Equivocal results excluded; the percent of equivocal results is 0.5% (1/193). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 97.4% (38/39), 95% CI: 86.8% - 99.5% and Specificity = 100% (154/154), 95% CI: 97.6% - 100%.

[7] Equivocal results excluded; the percent of equivocal results is 0.2% (4/2381). If all equivocal results are considered discordant results (e.g., false positive or false negative), Sensitivity = 96.3% (154/160), 95% CI: 92.1% - 98.3% and Specificity = 99.3% (2205/2221), 95% CI: 98.8% - 99.6%.

## VIII. CONCLUSIONS

The analytical and clinical study results demonstrate that the Aptima Combo 2 assay on the Panther system performs comparably to the predicate device in detecting non-viral microorganisms that cause sexually transmitted infections and support a substantial equivalence decision.