June 3, 2022

Hologic, Inc.
Jill Wyland
Director, Regulatory Affairs
10210 Genetic Center Drive
San Diego, California 92121

Re: K220321
Trade/Device Name: Aptima Combo 2 Assay (250 test kit) Panther, Aptima Combo 2 Assay (250 test kit) Tigris, Aptima Trichomonas Vaginalis Assay (250 test kit) Panther, Aptima Trichomonas Vaginalis Assay (250 test kit) Tigris
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, OUY, MKZ
Dated: February 2, 2022
Received: February 3, 2022

Dear Jill Wyland:

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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Himani Bisht, Ph.D.
Assistant Director
Viral Respiratory and HPV Branch
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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

Device Name

Indications for Use *(Describe)*

Type of Use *(Select one or both, as applicable)*

☐ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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HOLOGIC®

510(k) SUMMARY

Aptima Combo 2 Assay (Panther and Tigris System)
Aptima Trichomonas Vaginalis Assay (Panther and Tigris System)

I. SUBMITTER

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

Contact Information:

Jill Wyland
Director of Regulatory & Quality
Phone: 858-410-8487
Email: jill.wyland@hologic.com

Date Prepared: February 2, 2022

II. DEVICES

Proprietary Name:	Aptima Combo 2® Assay (Panther System)
Classification Name:	Nucleic Acid Detection System for Non-Viral Microorganism(s) Causing Sexually Transmitted Infections
Regulation Number:	866.3393
Regulatory Class:	Class II
Product Code:	QEP
Subsequent Product Code:	MKZ, LSL

Proprietary Name:	Aptima Combo 2® Assay (Tigris System)
Classification Name:	Nucleic Acid Detection System for Non-Viral Microorganism(s) Causing Sexually Transmitted Infections
Regulation Number:	866.3393
Regulatory Class:	Class II
Product Code:	QEP
Subsequent Product Code:	MKZ, LSL

Proprietary Name:	Aptima Trichomonas Vaginalis® Assay (Panther System)
Classification Name:	Trichomonas Vaginalis Nucleic Acid Amplification Test System
Regulation Number:	866.3860
Regulatory Class:	Class II
Product Code:	OUY

Proprietary Name:	Aptima Trichomonas Vaginalis® Assay (Tigris System)
Classification Name:	Trichomonas Vaginalis Nucleic Acid Amplification Test System
Regulation Number:	866.3860
Regulatory Class:	Class II
Product Code:	OUY

III. PREDICATE DEVICES

The predicate devices are the following:

- Aptima Combo 2 Assay (Panther System): K200866; cleared 05/17/2020)
- Aptima Combo 2 Assay (Tigris System): K200866; cleared 05/17/2020)
- Aptima Trichomonas Vaginalis Assay (Panther System): K122062; cleared 01/09/2013)
- Aptima Trichomonas Vaginalis Assay (Tigris System): K102911; cleared 04/19/2011)

These predicate devices have not been subject to a design-related recall.

IV. DEVICE DESCRIPTIONS

Aptima Combo 2 Assay

The Aptima Combo 2 Assay (AC2) combines the technologies of target capture, TMA, and 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 nucleic acid chemiluminescent probes, which are complementary to a region of each target amplicon, are labeled with different acridinium ester molecules. The updated version of the Aptima Combo 2 assay incorporates a second CT probe, complementary to a unique region of the existing CT amplicon. This tandem probe provides detection coverage for the variant strains of *C. trachomatis* that emerged in 2019. The labeled probes combine with amplicon to form stable 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 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.

Aptima Trichomonas Vaginalis Assay

The Aptima Trichomonas vaginalis Assay (ATV) involves the technologies of target capture,

transcription-mediated amplification (TMA), and hybridization protection assay (HPA). Specimens are collected and transferred into their respective specimen transport tubes. The transport solution in these tubes releases the rRNA target and protects it from degradation during storage. When the Aptima Trichomonas vaginalis Assay is performed in the laboratory, the target rRNA is isolated from the specimens by the use of a specific capture oligomer and magnetic microparticles in a method called target capture. The capture oligomer contains a sequence complementary to a specific region of the target molecule as well as a string of deoxyadenosine residues. During the hybridization step, the sequence-specific region of the capture oligomer binds to a specific region of the target molecule. 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 molecule 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 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 Hologic TMA reaction amplifies a specific region of the small ribosomal subunit from *T. vaginalis* via DNA and RNA intermediates and generates RNA amplicon molecules. Detection of the rRNA amplification product sequences is achieved using nucleic acid hybridization (HPA). A single stranded chemiluminescent DNA probe, which is complementary to a region of the target amplicon, is labeled with an acridinium ester molecule. The labeled DNA probe combines 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).

V. DESCRIPTION OF DEVICE MODIFICATION

As a convenience for customers processing high volume of assays, Hologic previously received clearance (K200436; cleared 03/23/2020) for a Ready-Made Reagents (RMR) format which allows customers to procure a liquid form (reconstituted) of the Amplification, Enzyme, and Probe Reagents for use on both the Tigris and Panther systems. At the time of clearance, the RMR Amplification and Enzyme reagents followed a validated manufacturing process which removed the lyophilization steps; however, the RMR Probe Reagent was still manufactured as a lyophilized reagent (cake form), and then just prior to shipping to customers, Hologic manufacturing personnel manually reconstituted the lyophilized Probe Reagent with the Probe Reconstitution Solution to reach a liquid form. Providing all three reagents in a RMR format (liquid form) allows the operator to follow the same processing steps for each reagent. The clearance of this Special 510(k) application allows for a manufacturing change to the RMR Probe Reagent to remove the lyophilization process to match the liquid manufacturing format of the RMR Amplification and Enzyme reagents. The manufacturing change does not change product design, principles of procedure, intended use, primary technological characteristics, or impact assay performance. The RMR Probe Reagent is the same formulation for either Aptima Combo 2 Assay or Aptima Trichomonas Vaginalis Assay, with the exception of the detection oligos, and is independent of the instrument platform.

VI. INDICATIONS FOR USE

There are no changes to the indications for use / intended use for each assay due to the manufacturing change of the RMR Probe Reagent.

Intended Use - Aptima Combo 2 (Panther)

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, PreservCyt® Solution liquid Pap specimens, vaginal, throat, rectal, and male urethral swab specimens; 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.

Intended Use - Aptima Combo 2 (Tigris)

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 Tigris® DTS® Automated Analyzer. 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, vaginal and male urethral swab specimens; patient-collected vaginal swab specimens[1]; 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.

[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 is not for home use.

Intended Use - Aptima Trichomonas Vaginalis (Panther)

The Aptima Trichomonas vaginalis Assay is an in vitro qualitative nucleic acid amplification test (NAAT) for the detection of ribosomal RNA (rRNA) from Trichomonas vaginalis to aid in the diagnosis of trichomoniasis using the Panther System. The assay may be used to test the following specimens from symptomatic or asymptomatic women: clinician-collected endocervical swabs, clinician-collected vaginal swabs, and specimens collected in PreservCyt Solution.

Intended Use - Aptima Trichomonas Vaginalis (Tigris)

The Aptima Trichomonas vaginalis Assay is an *in vitro* qualitative nucleic acid amplification test (NAAT) for the detection of ribosomal RNA (rRNA) from *Trichomonas vaginalis* to aid in the diagnosis of trichomoniasis using the Tigris® DTS® System. The assay may be used to test the following specimens from symptomatic or asymptomatic women: clinician-collected endocervical swabs, clinician-collected vaginal swabs, female urine specimens, and specimens collected in PreservCyt Solution.

VII. COMPARISON OF TECHNILOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICES

A comparison of the four subject devices (with new RMR Probe Reagent) to the predicate devices (with lyophilized Amplification, Enzyme, and Probe Reagents) are summarized in **Table 1** through **Table 4**. Use of the RMR Probe Reagent does not change the principles of procedure, intended use, or primary technological characteristics. The similarities and differences between the subject and predicate devices are further discussed following the last substantial equivalence table. This discussion is the same for each assay.

Table 1: Comparison Between Predicate Device and Subject Device - AC2 on Panther

Item	**AC2 Assay (Panther) (Predicate Device) K200866**	**AC2Assay (Panther) (Subject Device)**
Technology Principle of Operation	Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA)	Same
Platform	Automated Panther System	Same
Function	Detection and differentiation of rRNA from *Chlamydia trachomatis* and *Neisseria gonorrhoeae*	Same
Organisms Detected	*Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC)	Same
Patient Population	Symptomatic and asymptomatic individuals	Same
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	Same

Item	AC2 Assay (Panther) (Predicate Device) K200866	AC2Assay (Panther) (Subject Device)
	specimens from symptomatic and asymptomatic individuals: clinician-collected endocervical, PreservCyt® Solution liquid Pap specimens, vaginal, throat, rectal, and male urethral swab specimens; 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.	

Table 2: Comparison Between Predicate Device and Subject Device - AC2 on Tigris

Item	AC2 Assay (Tigris) (Predicate Device) K200866	AC2 Assay (Tigris) (Subject Device)
Technology Principle of Operation	Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA)	Same
Platform	Automated Tigris System	Same
Function	Detection and differentiation of rRNA from *Chlamydia trachomatis* and *Neisseria gonorrhoeae*	Same
Organisms Detected	*Chlamydia trachomatis* (CT) and/or *Neisseria gonorrhoeae* (GC)	Same
Patient Population	Symptomatic and asymptomatic individuals	Same
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 Tigris® DTS® Automated Analyzer. 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, vaginal and male urethral swab specimens; patient-collected vaginal swab specimens[1]; 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. [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 is not for home use.	Same

Table 3: Comparison Between Predicate Device and Subject Device - ATV on Panther

Item	ATV Assay (Panther) (Predicate Device) K122062	ATV Assay (Panther) (Subject Device)
Technology Principle of Operation	Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA)	Same
Platform	Automated Panther System	Same
Function	Detection and differentiation of rRNA from *Trichomonas vaginalis*	Same
Organisms Detected	*Trichomonas vaginalis*	Same
Patient Population	Symptomatic and asymptomatic individuals	Same
Intended Use	The Aptima Trichomonas vaginalis Assay is an *in vitro* qualitative nucleic acid amplification test (NAAT) for the detection of ribosomal RNA (rRNA) from *Trichomonas vaginalis* to aid in the diagnosis of trichomoniasis using the Panther System. The assay may be used to test the following specimens from symptomatic or asymptomatic women: clinician-collected endocervical swabs, clinician-collected vaginal swabs, and specimens collected in PreservCyt Solution.	Same

Table 4: Comparison Between Predicate Device and Subject Device – ATV on Tigris

Item	ATV Assay (Tigris) (Predicate Device) K102911	ATV Assay (Tigris) (Subject Device)
Technology Principle of Operation	Target Capture (TC), Transcription-Mediated Amplification (TMA), Hybridization Protection Assay (HPA)	Same
Platform	Automated Tigris System	Same
Function	Detection and differentiation of rRNA from *Trichomonas vaginalis*	Same
Organisms Detected	*Trichomonas vaginalis*	Same
Patient Population	Symptomatic and asymptomatic individuals	Same
Intended Use	The Aptima Trichomonas vaginalis Assay is an *in vitro* qualitative nucleic acid amplification test (NAAT) for the detection of ribosomal RNA (rRNA) from *Trichomonas vaginalis* to aid in the diagnosis of trichomoniasis using the Tigris® DTS® System. The assay may be used to test the following specimens from symptomatic or asymptomatic	Same

Item	ATV Assay (Tigris) (Predicate Device) K102911	ATV Assay (Tigris) (Subject Device)
	women: clinician-collected endocervical swabs, clinician-collected vaginal swabs, female urine specimens, and specimens collected in PreservCyt Solution.	

Similarities

Each of the subject devices utilize the same technology and principles of operation, mechanisms of action, conditions of use, results interpretation, have identical intended uses, and run on the same automated instrument system as compared to their predicate device. There are no differences in the performance of the assay or customer interface as a result of the RMR Probe manufacturing change.

Differences

During bulk manufacturing of the new RMR Probe Reagent, the lyophilization step is removed to match the liquid manufacturing format of the RMR Amplification and Enzyme reagents. Due to this manufacturing change, the part number for the RMR Probe reagent was updated along with a new catalog number to differentiate the RMR Probe product configuration from the current RMR format (using RMR Probe reconstituted in-house). The updated catalog number appears on the box label and in the assay package insert. There are no other labeling changes.

VIII. Design Control Activities

Hologic's overall product development activities are conducted per procedure, 'Product Development Procedure' which is in conformance with the design control requirements as specified in 21 CFR 820.30. Verification testing was performed to confirm clinical comparability between the predicate AC2 and ATV assays to the AC2 RMR and ATV RMR assays containing the new Probe Reagent. The completed verification studies demonstrate that the new RMR Probe Reagent does not impact assay performance, assay safety and effectiveness, and confirms that the modified assay meets the design input requirements.

Hologic risk analysis activities are conducted per Product Safety Risk Management Procedure which is in conformance with ISO 14971:2007. Based on the results of the risk analysis and

verification activities, and in accordance with ISO 14971:2007, all risks are reduced as far as possible and meet the pre-defined acceptability criteria. There were no hazards that fell within the "Undesirable" or "Unacceptable" residual risk regions. The device modifications do not introduce any new hazards or increase the overall residual risk as compared to the currently marketed products.

IX. ASSAY PERFORMANCE

The following performance data are provided in support of the clearance of the AC2 and ATV RMR assays containing the new RMR Probe Reagent on the Panther system and Tigris system.

Intended Use Study

Aptima Combo 2 Assay (Panther)

A comparison of Intended Use results between the predicate AC2 assay and AC2 RMR assay (containing the new RMR Probe Reagent; termed 'RMR assay' throughout this document) on the Panther system showed comparability when negative and positive panels were tested. AC2 panels consisting of a Negative panel, CT positive, GC positive, FI-nvCT positive, and CT/GC dual positive panels were run on two Panther instruments. The predicate AC2 assay was used as the baseline result. The results showed 100% agreement to the expected positivity results for each CT panel, FI-nvCT panel, GC panel, and with dual positive panel for both the predicate AC2 and AC2 RMR assays on Panther.

Aptima Combo 2 Assay (Tigris)

A comparison of Intended Use results between the predicate AC2 assay and AC2 RMR assay on the Tigris system showed comparability when negative and positive panels were tested. AC2 panels consisting of a Negative panel, CT positive, GC positive, FI-nvCT positive, and CT/GC dual positive panels were run on one Tigris instrument. The predicate AC2 assay was used as the baseline result. The results showed 100% agreement to the expected positivity results for each CT panel, FI-nvCT panel, GC Panel and with dual positive panel for both the predicate AC2 assay and AC2 RMR assay on the Tigris system.

Aptima Trichomonas vaginalis Assay (Panther)

A comparison of Intended Use results between the predicate ATV assay and ATV RMR assay on the Panther system showed comparability when negative and positive panels were tested. ATV panels consisting of a Negative panel, TV positive, and TV low positive were run on two Panther instruments. The current ATV assay was used as the baseline result. The results showed 100% agreement to the expected positivity results for each TV panel, for both the predicate ATV and ATV RMR assays on the Panther system.

Aptima Trichomonas vaginalis Assay (Tigris)

A comparison of Intended Use results between the predicate ATV assay and ATV RMR assay on the Tigris system showed comparability when negative and positive panels were tested. ATV panels consisting of a Negative panel, TV positive, and TV low positive were run on one Tigris instrument. The predicate ATV assay was used as the baseline result. The results showed 100% agreement to the expected positivity results for each TV panel, for both the predicate ATV and ATV RMR assays on the Tigris system.

Limit of Detection

Aptima Combo 2 Assay (Panther)

The Limit of Detection (LoD) for *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (GC), and Finnish new variant CT (FI-nvCT) for AC2 RMR assay was determined to be within ½ log of the LoD for the predicate AC2 assay on the Panther system. The limit of detection was estimated for the predicate AC2 and AC2 RMR assays by using stocks of CT and GC organisms as well as FI-nvCT in vitro transcript in negative clinical liquid pap specimens collected in PreservCyt solution (ThinPrep). These panels were tested on two Panther systems using two lots for each reagent format. The equivalency was shown as the results of the lowest concentration ≥ 95% positivity for CT target on the predicate AC2 assay (0.1 IFU/mL) and for AC2 RMR assay (0.03 IFU/mL) on the Panther were within ½ log. The equivalency for the GC target was equivalent as shown by the lowest concentration ≥ 95% positivity for the predicate AC2 assay (0.3 CFU/mL) and for the AC2 RMR assay (1 CFU/mL) on the Panther were within ½ log. The equivalency for the FI-nvCT target was equivalent as shown by the lowest concentration ≥ 95%

positivity for the predicate AC2 assay and for the AC2 RMR assay of 40 copies/mL on the Panther.

Aptima Combo 2 Assay (Tigris)

The Limit of Detection (LoD) for *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (GC), and Finnish new variant CT (FI-nvCT) for AC2 RMR assay was determined to be within ½ log of the LoD for the predicate AC2 assay on the Tigris system. The limit of detection was estimated for the predicate AC2 and AC2 RMR assays by using stocks of CT and GC organisms as well as FI-nvCT in vitro transcript in negative clinical liquid pap specimens collected in PreservCyt solution (ThinPrep). These panels were tested on two Tigris systems using two reagent lots for each format. The equivalency was shown as the results of the lowest concentration ≥ 95% positivity for CT target on the predicateAC2 assay and for AC2 RMR assay on Tigris was 0.003 IFU/mL. The equivalency for the GC target was equivalent as shown by the lowest concentration ≥ 95% positivity for the predicate AC2 assay and for the AC2 RMR assay on Tigris was 0.3 CFU/mL. The equivalency for the FI-nvCT target was equivalent as shown by the lowest concentration ≥ 95% positivity for the predicate AC2 assay and for the AC2 RMR assay on Tigris was 20 copies/mL.

Aptima Trichomonas vaginalis Assay (Panther)

The Limit of Detection (LoD) for *Trichomonas vaginalis* for ATV RMR assay was determined to be within ½ log of the LoD for the predicate ATV assay on the Panther System. The limit of detection was estimated for the predicate ATV and ATV RMR assays by using stocks of TV organisms in negative clinical liquid pap specimens collected in PreservCyt solution (ThinPrep). These panels were tested on two Panther systems using two lots for each reagent format. The equivalency was shown as the results of the lowest concentration ≥ 95% positivity for TV target on the predicate ATV assay and for the ATV RMR assay on Panther was 0.003 cells/mL.

Aptima Trichomonas vaginalis Assay (Tigris)

The Limit of Detection (LoD) for *Trichomonas vaginalis* for ATV RMR assay was determined to be within ½ log of the LoD for the predicate ATV assay on the Tigris System. The limit of detection was estimated for the predicate ATV and ATV RMR assays by using stocks of TV

organisms in negative clinical liquid pap specimens collected in PreservCyt solution (ThinPrep). These panels were tested on one Tigris system using two reagent lots for each format. The equivalency was shown as the results of the lowest concentration ≥ 95% positivity for TV target on the predicate ATV assay and for the ATV RMR assay on Tigris was 0.01 cells/mL.

Clinical Performance Study

Aptima Combo 2 Assay (Panther)

The clinical comparability was determined between the predicate AC2 assay and the AC2 RMR assay on the Panther system when evaluating clinical positive and negative specimens. Hologic demonstrated comparability using the AC2 assay as representative of both the ATV and AC2 assays.

Two hundred nineteen (219) remnant clinical swab specimens were evaluated with the predicate AC2 assay and the AC2 RMR assay using two reagent lots of each assay format and across two Panther systems. The predicate AC2 assay was used as the reference result. The positive, negative and overall agreement between the predicate AC2 and AC2 RMR assays were calculated for both CT and GC target interpretations.

Table 5: CT Target Agreement Results

CT Results		AC2 Lyo Result		
		Positive	Negative	Total
Panther AC2 RMR Result	Positive	39	0	39
	Negative	0	180	180
	Total	39	180	219

Positive agreement (95% CI) = 100.0% (91.0% - 100.0%)
Negative agreement (95% CI) = 100.0% (97.9 - 100.0%)
Overall agreement (95% CI) = 100.0% (98.3% - 100.0%)

Table 6: GC Target Agreement Results

GC Results		AC2 Lyo Result		
		Positive	Negative	Total
Panther AC2 RMR Result	Positive	48	0	48
	Negative	0	171	171
	Total	48	171	219

Positive agreement (95% CI) = 100.0% (92.6% - 100.0%)
Negative agreement (95% CI) = 100.0% (97.8% - 100.0%)
Overall agreement (95% CI) = 100.0% (98.3% - 100.0%)

This study demonstrates that the performance of the predicate AC2 assay and AC2 RMR assay is comparable when testing clinical specimens on the Panther system.

Aptima Combo 2 Assay (Tigris)

The clinical comparability was determined between the predicate AC2 assay on the Panther system and the AC2 RMR assay on the Tigris system when evaluating clinical positive and negative specimens. Hologic demonstrated comparability using the AC2 assay as representative of both the ATV and AC2 assays.

Two hundred (200) remnant clinical swab specimens were evaluated with the predicate AC2 assay on Panther and the AC2 RMR assay on Tigris using two reagent lots of each assay format and across two instrument systems. The predicate AC2 assay was used as the reference result. The positive, negative and overall agreement between the predicate AC2 and AC2 RMR assays were calculated for both CT and GC target interpretations.

Table 7: CT Target Agreement Results

CT Results		AC2 Lyo Result		
		Positive	Negative	Total
TIGRIS AC2 RMR Result	Positive	34	0	34
	Negative	0	166	166
	Total	34	166	200

Positive agreement (95% CI) = 100.0% (89.8% - 100.0%)
Negative agreement (95% CI) = 100.0% (97.7% - 100.0%)
Overall agreement (95% CI) = 100.0% (98.1% - 100.0%)

Table 8: GC Target Agreement Results

GC Results		AC2 Lyo Result		
		Positive	Negative	Total
TIGRIS AC2 RMR Result	Positive	47	0	47
	Negative	0	153	153
	Total	47	153	200

Positive agreement (95% CI) = 100.0% (92.4% - 100.0%)
Negative agreement (95% CI) = 100.0% (97.6% - 100.0%)
Overall agreement (95% CI) = 100.0% (98.1% - 100.0%)

This study demonstrates that the performance of the predicate AC2 assay and AC2 RMR assay is comparable when testing clinical specimens on the Tigris system.

X. CONCLUSIONS

A comparison of the intended use, technological characteristics, and results from the analytical performance studies demonstrate that the AC2 RMR assay and ATV RMR assay on the Panther and Tigris systems performs comparably to their predicate devices. The results of this evaluation demonstrated that the existing assay performance and claims of the AC2 and ATV assays were not impacted due to the new RMR Probe Reagent.