May 16, 2019

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

Re: K190472
Trade/Device Name: Aptima CV/TV Assay
Regulation Number: 21 CFR 866.3975
Regulation Name: Device that detects nucleic acid sequences from microorganisms associated with vaginitis and bacterial vaginosis
Regulatory Class: Class II
Product Code: PQA, NSU
Dated: February 25, 2019
Received: February 26, 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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K190472

Device Name
Aptima CV/TV Assay

Indications for Use *(Describe)*
The Aptima CV/TV assay is an *in vitro* nucleic acid amplification test for the detection of RNA from microorganisms associated with vulvovaginal candidiasis and trichomoniasis. The assay utilizes real time transcription-mediated amplification (TMA) to detect and qualitatively report results for the following organisms:

- Candida species group (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*)
- *Candida glabrata*
- *Trichomonas vaginalis*

The assay differentiates between *Candida glabrata* and the *Candida* species group (C spp) by targeting the RNA component of RNAse P ribonucleoprotein; the assay does not differentiate among C spp. For *Trichomonas vaginalis*, the assay targets ribosomal RNA (rRNA) and differentiates the result from results for *Candida glabrata* and C spp. The assay is intended to aid in the diagnosis of vulvovaginal candidiasis and trichomoniasis on the automated Panther system using clinician-collected and patient-collected vaginal swab specimens from females with a clinical presentation consistent with vaginitis or vulvovaginitis.

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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510(k) SUMMARY
Aptima CV/TV Assay

I. SUBMITTER

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Date Prepared: February 20, 2019

II. DEVICE

Proprietary Name of Device:	Aptima CV/TV Assay
Classification Name:	Device that detects nucleic acid sequences from microorganisms associated with vaginitis and bacterial vaginosis
Regulation Number:	21 CFR 866.3975
Regulatory Class:	Class II
Product Code:	PQA, NSU

III. PREDICATE DEVICE

The predicate device is the BD MAX Vaginal Panel (DEN160001; approved 10/28/2016, BD Diagnostics).

IV. DEVICE DESCRIPTION

The Aptima CV/TV assay is an in vitro nucleic acid amplification test for the detection and quantitation of RNA from microorganisms associated with vulvovaginal candidiasis and trichomoniasis in women with a clinical presentation consistent with vaginitis or vulvovaginitis. The Aptima CV/TV assay utilizes the automated Panther system to provide qualitative results to aid in the diagnosis of vulvovaginal candidiasis and trichomoniasis.

Principles of the Procedure

The Aptima CV/TV assay involves three main steps, all of which take place in a single tube on the Panther system: target capture, target amplification by TMA, and detection of the amplification products (amplicon) by fluorescent labeled probes (torches). The assay incorporates an internal control (IC) in every test to monitor nucleic acid capture, amplification and detection.

Specimens are collected in a tube containing specimen transport media (STM) that lyses the organisms, releases the RNA, and protects it from degradation during storage. When the assay is performed, capture oligonucleotides hybridize to highly conserved regions of the target RNA, if present, in the test specimen. The hybridized target is then captured onto magnetic microparticles that are separated from the specimen in a magnetic field. Wash steps remove extraneous components from the reaction tube.

Target amplification occurs via TMA, a transcription-based nucleic acid amplification method that utilizes two enzymes, Moloney murine leukemia virus (MMLV) reverse transcriptase and T7 RNA polymerase. The reverse transcriptase is used to generate a DNA copy of the target RNA sequence, adding a promoter sequence for T7 RNA polymerase. T7 RNA polymerase produces multiple copies of RNA amplicon from the DNA copy template.

Detection is achieved using single-stranded nucleic acid torches that are present during the amplification of the target and hybridize specifically to the amplicon in real time. Each torch has a fluorophore and a quencher. The quencher suppresses the fluorescence of the fluorophore when the torch is not hybridized to the amplicon. When the torch binds to the amplicon, the fluorophore is separated from the quencher and emits a signal at a specific wavelength when excited by a light source. The Panther system detects and discriminates between four fluorescent signals corresponding to C spp, *C. glabrata*, *T. vaginalis* and IC amplification products. The Panther system software uses an Aptima CV/TV assay-specific algorithm that interprets the amplification signal emergence times to generate a Positive or Negative status for each target organism in the sample.

Assay Components

The Aptima CV/TV assay is provided as a 100-test kit. The Aptima CV/TV assay master kit contains 8 reagents, 1 calibrator, and 2 controls required for sample processing. There are 4 boxes that make up the assay master kit. Boxes 1 and 2 contain the Aptima CV/TV assay reagents packaged according to storage conditions. Box 3 contains the calibrator, and Box 4 contains the controls when provided as part of the master kit. The Aptima CV/TV Calibrator and Controls kit may also be procured separately if customers need additional calibrators or controls. A listing of the components that are required to perform the Aptima CV/TV assay are detailed in **Table 1.** In addition, there is one ancillary kit required to run the assay, and one collection kit utilized for collection of specimens (**Table 2**).

Table 1: Reagents Required to Perform the Aptima CV/TV Assay

Box	Components Description
1	Amplification Reagent
	Enzyme Reagent
	Promoter Reagent
	Internal Control
2	Amplification Reconstitution Solution
	Enzyme Reconstitution Solution
	Promoter Reconstitution Solution
	Target Capture Reagent
3	Positive Calibrator
4	Negative Control
	Positive Control

Table 2: Ancillary and Collection Kits Required to Perform the Aptima CV/TV Assay

Aptima Assay Fluids Kit
Aptima Multitest Swab Specimen Collection Kit

Instrumentation

The Aptima CV/TV 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 CV/TV 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

The Aptima CV/TV assay is an *in vitro* nucleic acid amplification test for the detection of RNA from microorganisms associated with vulvovaginal candidiasis and trichomoniasis. The assay utilizes real time transcription-mediated amplification (TMA) to detect and qualitatively report results for the following organisms:

- *Candida* species group (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*)
- *Candida glabrata*
- *Trichomonas vaginalis*

The assay differentiates between *Candida glabrata* and the *Candida* species group (C spp) by targeting the RNA component of RNAse P ribonucleoprotein; the assay does not differentiate among C spp. For *Trichomonas vaginalis*, the assay targets ribosomal RNA (rRNA) and differentiates the result from results for *Candida glabrata* and C spp. The assay is intended to aid in the diagnosis of vulvovaginal candidiasis and trichomoniasis on the automated Panther system using clinician-collected and patient-collected vaginal swab specimens from females with a clinical presentation consistent with vaginitis or vulvovaginitis.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

A comparison of the Aptima CV/TV assay to the predicate device, BD MAX Vaginal Panel, is summarized in **Table 4** (similarities) and **Table 5** (differences).

Table 4: Similarities Between Predicate Device and Subject Device

Item	BD MAX Vaginal Panel (DEN160001)	Aptima CV/TV Assay (Subject Device)
Patient Population	Women with a clinical presentation of vaginitis, trichomoniasis, or vulvovaginitis	Same
Specimen Types	Vaginal swabs in patients who are symptomatic for vaginitis, trichomoniasis, or vulvovaginitis	Same
Assay Controls	Incorporates an Internal Control in every test. Uses external positive and negative controls.	Same

Table 5: Differences Between Predicate Device and Subject Device

Item	BD MAX Vaginal Panel (DEN160001)	Aptima CV/TV Assay (Subject Device)
Organisms Detected	*Lactobacillus* (*L. crispatus*, and *L. jensenii*), *Gardnerella vaginalis, Atopobium vaginae,* Bacterial Vaginosis Associated Bacteria-2 (BVAB-2), *Megasphaera-1, Candida (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata, Candida krusei, Trichomonas vaginalis*	*Candida species* (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*); *Candida glabrata*; *Trichomonas vaginalis*
Platform/Technology Principle of Operation	BD MAX System/ Real-time polymerase chain reaction (PCR)	Panther System/ Real-time Transcription Mediated Amplification (TMA)
Analyte	DNA	RNA
Assay Calibrators	None	Positive Calibrator
Intended Use	The BD MAX Vaginal Panel performed on the BD MAX	The Aptima CV/TV assay is an *in vitro* nucleic acid amplification test

Item	BD MAX Vaginal Panel (DEN160001)	Aptima CV/TV Assay (Subject Device)
	System is an automated qualitative *in vitro* diagnostic test for the direct detection of DNA targets from bacteria associated with bacterial vaginosis (qualitative results reported based on detection and quantitation of targeted organism markers), *Candida* species associated with vulvovaginal candidiasis, and *Trichomonas vaginalis* from vaginal swabs in patients who are symptomatic for vaginitis/vaginosis. The test utilizes real-time polymerase chain reaction (PCR) for the amplification of specific DNA targets and utilizes fluorogenic target-specific hybridization probes to detect and differentiate DNA from: • Bacterial vaginosis markers (Individual markers not reported) *Lactobacillus* spp. *(L. crispatus* and *L. jensenii)* *Gardnerella vaginalis* *Atopobium vaginae* Bacterial Vaginosis Associated Bacteria-2 (BVAB-2) *Megasphaera-1* • *Candida* spp. *(C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis)* • *Candida glabrata* • *Candida krusei* • *Trichomonas vaginalis* The BD MAX Vaginal Panel is intended to aid in the diagnosis of vaginal infections in women with a clinical presentation consistent with bacterial vaginosis, vulvovaginal candidiasis and trichomoniasis.	for the detection of RNA from microorganisms associated with vulvovaginal candidiasis and trichomoniasis. The assay utilizes real time transcription-mediated amplification (TMA) to detect and qualitatively report results for the following organisms: • *Candida species* group (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*) • *Candida glabrata* • *Trichomonas vaginalis* The assay differentiates between *Candida glabrata* and the *Candida* species group (C spp) by targeting the RNA component of RNAse P ribonucleoprotein; the assay does not differentiate among C spp. For *Trichomonas vaginalis*, the assay targets ribosomal RNA (rRNA) and differentiates the result from results for *Candida glabrata* and C spp. The assay is intended to aid in the diagnosis of vulvovaginal candidiasis and trichomoniasis on the automated Panther system using clinician-collected and patient-collected vaginal swab specimens from females with a clinical presentation consistent with vaginitis or vulvovaginitis.

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 (non-clinical) studies were conducted to support the clearance of the Aptima CV/TV assay on the Panther system.

Analytical Sensitivity

The analytical sensitivity/LoD of the Aptima CV/TV assay was determined by testing a series of panels consisting of target organisms diluted in pooled negative clinical specimens or simulated vaginal swab matrix (SVSM). A minimum of 20 replicates of each panel member were tested with each of the two reagent lots, for a minimum of 40 replicates per panel member. Probit analysis was performed to generate the 95% predicted detection limit for each organism. The predicted detection limits are shown in **Table 6.**

Table 6: Limit of Detection of the Aptima CV/TV Assay

Organism	Predicted Detection Limit	Concentration	Units
C. albicans	95%	4439	CFU/mL
C. glabrata	95%	41	CFU/mL
C. parapsilosis[1]	95%	9416	CFU/mL
C. tropicalis[1]	95%	811	CFU/mL
C. dubliniensis[1]	95%	1176	CFU/mL
T. vaginalis	95%	0.0024	Cells/mL

[1]Tested in simulated vaginal swab matrix

Analytical Inclusivity

Five strains of each *Candida* target organism were tested using lysate targeting 3X LoD for *C. albicans, C. parapsilosis, C. tropicalis, C. dubliniensis,* and *C. glabrata* in SVSM. Nine strains of *T. vaginalis* including a metronidazole resistant strain were tested with cell lysate targeting 3X LoD in SVSM. The Aptima CV/TV assay was positive for all *Candida* strains

tested at 3X LoD. Eight of the nine *T. vaginalis* strains, including the metronidazole resistant strain, were detected at 3X LoD. One strain of *T. vaginalis* was detected at 4X LoD.

Cross-Reactivity and Microbial Interference

Cross-reactivity and microbial interference with the Aptima CV/TV assay was evaluated in the presence of closely related and non-targeted organisms. A panel consisting of 64 organisms and human cell lines (**Table 7**) was tested in SVSM in the absence or presence of 3X LoD *C. albicans, C. glabrata* or *T. vaginalis*. No cross-reactivity or microbial interference was observed for any of the 64 organisms and human cell lines tested in the Aptima CV/TV assay at the following concentrations.

Table 7: Cross-Reactivity and Microbial Interference Panel

Microorganism	Concentration	Microorganism	Concentration
Acinetobacter lwoffii	$1x10^6$ CFU/mL	Herpes simplex virus I	$1x10^4$ TCID 50/mL
Actinomyces israelii	$1x10^6$ CFU/mL	Herpes simplex virus II	$1x10^4$ TCID 50/mL
Alcaligenes faecalis	$1x10^6$ CFU/mL	*Klebsiella pneumoniae*	$1x10^6$ CFU/mL
Atopobium vaginae	$1x10^6$ CFU/mL	*Lactobacillus acidophilus*	$1x10^6$ CFU/mL
Bacteroides fragilis	$1x10^6$ CFU/mL	*Lactobacillus crispatus*	$1x10^6$ CFU/mL
Bifidobacterium adolescentis	$1x10^6$ CFU/mL	*Lactobacillus gasseri*	$1x10^6$ CFU/mL
BVAB-1[1]	$1x10^6$ copies/mL	*Lactobacillus iners*	$1x10^6$ CFU/mL
BVAB-2[1]	$1x10^6$ copies/mL	*Lactobacillus jensenii*	$1x10^6$ CFU/mL
Campylobacter jejuni	$1x10^6$ CFU/mL	*Lactobacillus mucosae*	$1x10^6$ CFU/mL
Candida catenulata	$1x10^6$ CFU/mL	*Leptotrichia buccalis*	$1x10^6$ CFU/mL
Candida famata[2]	$5x10^5$ CFU/mL	*Listeria monocytogenes*	$1x10^6$ CFU/mL
Candida guilliermondii	$1x10^6$ CFU/mL	*Megasphaera Type 1*[1]	$1x10^6$ copies/mL
Candida haemulonii	$1x10^6$ CFU/mL	*Mobiluncus curtisii*	$1x10^6$ CFU/mL
Candida inconspicua	$1x10^6$ CFU/mL	*Mycoplasma genitalium*	$1x10^6$ CFU/mL
Candida kefyr	$1x10^6$ CFU/mL	*Mycoplasma hominis*	$1x10^6$ CFU/mL
Candida krusei	$1x10^6$ CFU/mL	*Neisseria gonorrhoeae*	$1x10^6$ CFU/mL
Candida lusitaniae	$1x10^6$ CFU/mL	*Peptostreptococcus magnus*	$1x10^6$ CFU/mL
Candida norvegica	$1x10^6$ CFU/mL	*Pentatrichomonas hominis*	$1x10^5$ cells/mL
Candida orthopsilosis	$1x10^6$ CFU/mL	*Pichia fermentans*	$1x10^6$ CFU/mL
Chlamydia trachomatis	$1x10^6$ IFU/mL	*Prevotella bivia*	$1x10^6$ CFU/mL
Clostridium difficile	$1x10^6$ CFU/mL	*Propionibacterium acnes*	$1x10^6$ CFU/mL
Corynebacterium genitalium	$1x10^6$ CFU/mL	*Proteus vulgaris*	$1x10^6$ CFU/mL
Cryptococcus neoformans	$1x10^6$ CFU/mL	SiHa cells	$1x10^4$ cells/mL
Eggerthella lenta	$1x10^6$ CFU/mL	*Sneathia amnii*	$1x10^6$ CFU/mL
Enterobacter cloacae	$1x10^6$ CFU/mL	*Staphylococcus aureus*	$1x10^6$ CFU/mL
Enterococcus faecalis	$1x10^6$ CFU/mL	*Staphylococcus epidermidis*	$1x10^6$ CFU/mL
Escherichia coli	$1x10^6$ CFU/mL	*Streptococcus agalactiae*	$1x10^6$ CFU/mL
Fusobacterium nucleatum	$1x10^6$ CFU/mL	*Streptococcus pyogenes*	$1x10^6$ CFU/mL
Gardnerella vaginalis	$1x10^6$ CFU/mL	*Treponema pallidum*[2]	$1x10^6$ copies/mL
Haemophilus ducreyi	$1x10^6$ CFU/mL	*Trichomonas tenax*	$1x10^5$ cells/mL
HeLa cells	$1x10^4$ Cells/mL	*Ureaplasma parvum*	$1x10^6$ CFU/mL
HIV	$1x10^5$ copies/mL	*Ureaplasma urealyticum*	$1x10^6$ CFU/mL

CFU = Colony Forming Units; IFU = Inclusion Forming Units; TCID50 = Median Tissue Culture Infectious Dose

[1] *In Vitro* Transcript tested.

[2] Cross-reactivity with *Candida famata* was seen at concentrations higher than $5x10^5$ CFU/mL.

Interference

Potentially interfering substances were tested in the Aptima CV/TV assay. Panels were built in SVSM and evaluated for potential effects on assay sensitivity and specificity. Sensitivity performance was evaluated separately for *C. albicans, C. glabrata,* and *T. vaginalis* by spiking lysate at 3X LoD. Negative panels containing each substance were also evaluated for specificity.

No interference was observed in the presence of the following exogenous and endogenous substances tested at the concentrations listed in **Table 8**.

Table 8: Interfering Substances Panel

Substance	Final Concentration[1]
Whole Blood	5% V/V
Leukocytes	$1x10^6$ cells/mL
Mucus	5% V/V
Seminal Fluid	5% V/V
Contraceptive Foam	5% W/V
Contraceptive Film	5% W/V
Tioconazole[2]	2% W/V
Douche	5% W/V
Progesterone	5% W/V
Estradiol	5% W/V
Acyclovir	5% W/V
Metronidazole	5% W/V
Hemorrhoidal Cream	5% W/V
Vaginal Moisturizing Gel[3]	0.5% W/V
Lubricant	5% V/V
Spermicide	5% W/V
Anti-fungal	5% W/V
Deodorant/Spray	5% W/V
Glacial Acetic Acid[4]	4% V/V
Vagisil Cream	5% W/V

W/V = weight by volume; V/V = volume by volume

[1] Final Concentration represents final concentration in the sample when tested on the Panther instrument.

[2] Tioconazole 6.5% Ointment: Interference was observed at ≥ 3% W/V for all analytes. No interference was observed at 2% W/V for all analytes.

[3] Vaginal Moisturizing Gel: Interference was observed at ≥ 1% W/V for *C. albicans*, 5% W/V for *C. glabrata*, and ≥ 3% W/V for *T. vaginalis*. No interference was observed at 0.5% W/V for *C. albicans*, 4% W/V for *C. glabrata*, and 2% W/V for *T. vaginalis.*

[4] Glacial Acetic Acid: Interference was observed at 5% V/V for *C. albicans.* No interference was observed at 4% V/V for *C. albicans*, 5% V/V for *C. glabrata*, and 5% V/V for *T. vaginalis.*

Within Laboratory Precision

Within Lab Precision was evaluated on three Panther systems at one site. Three operators performed testing across 22 days and three reagent lots. Each operator performed two runs per day using a 7-member panel. Each run consisted of three replicates of each panel member. The panel members were made with *C. albicans*, *C. glabrata* or *T. vaginalis* in SVSM. The six positive panel members targeted *C. albicans* at Low and Moderate Positive, *C. glabrata* at Low and Moderate Positive, and *T. vaginalis* at Low and Moderate Positive. One Negative panel member contained matrix with no added target analytes.

The CV/TV percent positive results are presented in **Table 9**. Signal variability (TTime) of the Aptima CV/TV assay was also calculated for analyte positive panel members. Variability calculated between instruments, between operators, between lots, between days, between runs, within runs, and overall, is shown in **Table 10**.

Table 9: Precision - Agreement of Aptima CV/TV Assay with Expected Results

Panel (analyte composition)	Positive / Total n	Expected Positivity	Percent Positivity (95% CI)
Negative (SVSM)	0/162	0%	0 (0.0-2.3)
Low Positive (*C. albicans*)	162/162	≥95%	100 (97.7-100.0)
Low Positive (*C. glabrata*)	162/162	≥95%	100 (97.7-100.0)
Low Positive (*T. vaginalis*)	162/162	≥95%	100 (97.7-100.0)
Moderate Positive (*C. albicans*)	162/162	≥95%	100 (97.7-100.0)
Moderate Positive (*C. glabrata*)	162/162	≥95%	100 (97.7-100.0)
Moderate Positive (*T. vaginalis*)	162/162	≥95%	100 (97.7-100.0)

Table 10: Signal Variability of the Aptima CV/TV Assay by Analyte Positive Panel Member

			Between Days		Between Instruments		Between Operators		Between Lots		Between Runs		Within Run		Total	
Panel Description	**N**	**Mean TTime**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**
C. albicans Low Positive	162	14.96	0.12	0.82	0.00	0.00	0.24	1.59	0.54	3.58	0.23	1.52	0.28	1.84	0.70	4.66
C. glabrata Low Positive	162	21.07	0.00	0.00	0.15	0.69	0.25	1.18	0.14	0.65	0.19	0.89	0.40	1.91	0.55	2.59
T. vaginalis Low Positive	162	24.09	0.00	0.00	0.33	1.38	0.22	0.93	0.01	0.05	0.21	0.87	0.59	2.46	0.75	3.09
C. albicans Moderate Positive	162	14.62	0.11	0.72	0.00	0.00	0.22	1.47	0.43	2.95	0.26	1.77	0.24	1.62	0.60	4.14
C. glabrata Moderate Positive	162	20.63	0.00	0.00	0.00	0.00	0.26	1.27	0.31	1.50	0.26	1.25	0.52	2.51	0.71	3.42
T. vaginalis Moderate Positive	162	22.73	0.00	0.00	0.12	0.54	0.24	1.08	0.18	0.80	0.28	1.23	0.41	1.79	0.59	2.61

CV = Coefficient of variation

Note: Variability from some factors may be numerically negative. This can occur if the variability due to those factors is very small. In these cases, SD and CV are shown as 0.00.

Co-Infection

A co-infection study evaluated the ability of the Aptima CV/TV assay to detect *Candida* species, *C. glabrata*, and *T. vaginalis* when more than one organism is present in the same specimen. Low concentration of one target lysate and high concentration of another target lysate in SVSM were tested in combination. Panel composition and concentrations are listed in **Table 11**. All testing resulted in 100% detection for both targets present except for the combinations of low *C. glabrata* (3X LoD) and high *T. vaginalis* ($1x10^4$ cells/mL or $1x10^5$ cells/mL). Further testing was conducted and resulted in 100% detection for the combination of low *C. glabrata* (3X LoD) and high *T. vaginalis* ($1x10^3$ cells/mL).

Table 11: Co-Infection Panel

Panel Member	*C. albicans* Concentration	*C. glabrata* Concentration	*T. vaginalis* Concentration
C. albicans Low; *C. glabrata* High	13317 CFU/mL[1]	$1x10^6$ CFU/mL	N/A
C. albicans Low; *T. vaginalis* High	13317 CFU/mL[1]	N/A	$1x10^5$ cells/mL
C. glabrata Low; *T. vaginalis High*	N/A	123 CFU/mL[2]	$1x10^3$ cells/mL
C. albicans High; *C. glabrata* Low	$1x10^6$ CFU/mL	123 CFU/mL[2]	N/A
C. albicans High; *T. vaginalis* Low	$1x10^6$ CFU/mL	N/A	0.0072 cells/mL[3]
C. glabrata High; *T. vaginalis* Low	N/A	$1x10^6$ CFU/mL	0.0072 cells/mL[3]

CFU = Colony Forming Units
[1]3X LoD *C. albicans.*
[2] 3X LoD *C. glabrata.*
[3] 3X LoD *T. vaginalis.*

Brief Description of Clinical Studies

Clinical testing of the Aptima CV/TV assay on the Panther system included performance and reproducibility testing. Substantial equivalence is based in part on the performance study.

Clinical Performance Study

A study was performed to demonstrate clinical performance characteristics for the Aptima CV/TV assay. A multicenter study was conducted using prospectively-collected patient- and clinician-collected vaginal swab samples from women ≥14 years who exhibited signs and/or symptoms of vaginitis. Twenty-one participating geographically diverse US clinical sites, including private and academic family practice, obstetric-gynecologic, family planning, public health, sexually transmitted infections (STI), and medical group clinics, and clinical research centers, obtained vaginal swab samples from 1519 symptomatic women.

For each symptomatic subject, two (2) vaginal swab samples (one patient-collected, one clinician-collected) were tested with the investigational Aptima CV/TV assay. Three vaginal swab samples were used for *Candida* and *T. vaginalis* culture and/or NAAT testing to determine *Candida* and *T. vaginalis* infection status. *Candida* species group and *C. glabrata* reference results were established based on a combination of *Candida* growth in culture, as well as PCR/bi-directional sequencing of both Aptima swab samples leftover after testing, for subjects with positive *Candida* culture results. For *T. vaginalis*, a patient infected status (PIS) was

determined for each subject based on results from testing with an FDA-cleared molecular TV assay and an FDA-cleared culture- based TV test.

Contrived *C. glabrata* samples were also tested with the Aptima CV/TV assay to supplement clinical performance results in symptomatic subjects.

The clinical performance of the Aptima CV/TV assay was estimated relative to the *Candida* species group and *C. glabrata* reference results and *T. vaginalis* PIS; sensitivity, specificity, PPV, and NPV were calculated for each analyte and Aptima sample type, along with corresponding 2-sided 95% CIs. Agreement with known positive or known negative status was calculated for contrived *C. glabrata* samples.

Of the 1519 subjects enrolled, 23 were not evaluable due to withdrawal (n = 17) or unknown or missing swabs or testing results (n = 6). The remaining 1496 subjects were evaluable for at least one analyte in at least one sample type. **Table 12** shows the demographic and baseline clinical characteristics of evaluable subjects.

Table 12: Demographics of Evaluable Subjects in the Aptima CV/TV Assay Evaluation

	Symptomatic
Total, N	1496
Age, years	
Mean ± SD	35.3 ± 11.76
Median	33.0
Range	14-79
Age category (years), n (%)	
14-17	5 (0.3)
18-29	554 (37.0)
30-39	480 (32.1)
40-49	247 (16.5)
>50	210 (14.0)
Race/Ethnicity, n (%)	
Asian	73 (4.9)
Black or African American	752 (50.3)
White (Hispanic or Latino)	268 (17.9)
White (Not Hispanic or Latino)	339 (22.7)
Other[1]	64 (4.3)

[1]Includes patient-reported other, mixed, and unknown races

From the 1496 evaluable symptomatic subjects, results from 1477 patient-collected Aptima vaginal swab samples (98.7%, 1477/1496) and 1485 clinician-collected vaginal swab samples (99.3%, 1485/1496) were included in the analyses for *Candida* species group, 1475 patient-collected Aptima vaginal swab samples (98.6%, 1475/1496) and 1483 clinician-collected vaginal swab samples (99.1%, 1483/1496) were included in the analyses for *C. glabrata*, and 1433 patient-collected Aptima vaginal swab samples (95.8%, 1433/1496) and 1438 clinician-collected vaginal swab samples (96.1%, 1438/1496) were included in the analyses for *T. vaginalis*. Performance characteristics for detection of *Candida* species group, *C. glabrata*, and *T. vaginalis* infection for patient-collected and clinician-collected vaginal swab samples were calculated overall (see **Tables 13** through **15**) and by race/ethnicity (see **Tables 16** through **18**).

Anticipated low prevalence of *C. glabrata* triggered the supplemental assessment of the assay using contrived *C. glabrata* samples. For contrived *C. glabrata* samples, the agreement with known status was 100% for all samples (see **Table 19**), regardless of the organism load. This confirmed that the performance of the investigational assay for the detection of *C. glabrata* was acceptable.

Table 13: Aptima CV/TV Assay Performance for *Candida* species Group Relative to *Candida* Infection Status in Symptomatic Subjects

Specimen Type	N	TP	FP	TN	FN	Prevalence[1]	Sensitivity (95% CI)[2]	Specificity (95% CI)[2]	PPV (95% CI)[3]	NPV (95% CI)[3]
Patient-collected	1477	392	95	960	30	28.6	92.9 (90.0-95.0)	91.0 (89.1-92.6)	80.5 (77.4-83.4)	97.0 (95.8-97.9)
Clinician-collected	1485	389	54	1007	35	28.6	91.7 (88.7-94.0)	94.9 (93.4-96.1)	87.8 (84.8-90.4)	96.6 (95.5-97.6)

FN = false negative, FP = false positive, NPV = negative predictive value, PPV = positive predictive value, TP = true positive, TN = true negative

[1]Study prevalence reported. [2]Score CI. [3]PPV 95% CI computed from the exact 95% CI for positive likelihood ratio; NPV 95% CI computed from the 95% for the negative likelihood ratio

Table 14: Aptima CV/TV Assay Performance for *C. glabrata* Relative to *Candida* Infection Status in Symptomatic Subjects

Specimen Type	N	TP	FP	TN	FN	Prevalence[1]	Sensitivity (95% CI)[2]	Specificity (95% CI)[2]	PPV (95% CI)[3]	NPV (95% CI)[3]
Patient-collected	1475	50	18[4]	1399	8[5]	3.9	86.2 (75.1-92.8)	98.7 (98.0-99.2)	73.5 (63.7-82.2)	99.4 (99.0-99.7)
Clinician-collected	1483	50	13[6]	1411	9[7]	4.0	84.7 (73.5-91.8)	99.1 (98.4-99.5)	79.4 (69.4-87.5)	99.4 (98.9-99.7)

FN = false negative, FP = false positive, NPV = negative predictive value, PPV = positive predictive value, TP = true positive, TN = true negative

[1]Study prevalence reported. [2]Score CI. [3]PPV 95% CI computed from the exact 95% CI for positive likelihood ratio; NPV 95% CI computed from the 95% for the negative likelihood ratio

[4] Of the 18 samples with false positive results, 2 showed high (4+) growth, 2 showed low (≤2+) growth, and 14 showed no growth of *C. glabrata* on chromogenic agar.

[5] Of the 8 samples with false negative results, 7 showed no growth and 1 showed high (4+) growth of *C. glabrata* on chromogenic agar.

[6] Of the 13 samples with false positive results, 2 showed high (4+) growth, 2 showed low (≤2+) growth, and 9 showed no growth of *C. glabrata* on chromogenic agar.

[7] All 9 samples with false negative results showed no growth of *C. glabrata* on chromogenic agar.

Table 15: Aptima CV/TV Assay Performance for *T. vaginalis* Relative to the Patient Infected Status in Symptomatic Subjects

Specimen Type	N	TP	FP	TN	FN	Prevalence[1]	Sensitivity (95% CI)[2]	Specificity (95% CI)[2]	PPV (95% CI)[3]	NPV (95% CI)[3]
Patient-collected	1433	136	14[4]	1279	4[5]	9.8	97.1 (92.9-98.9)	98.9 (98.2-99.4)	90.7 (85.5-94.5)	99.7 (99.2-99.9)
Clinician-collected	1438	137	63[6]	1233	5[7]	9.9	96.5 (92.0-98.5)	95.1 (93.8-96.2)	68.5 (63.2-73.8)	99.6 (99.1-99.9)

FN = false negative, FP = false positive, NPV = negative predictive value, PPV = positive predictive value, TP = true positive, TN = true negative

[1]Study prevalence reported. [2]Score CI. [3]PPV 95% CI computed from the exact 95% CI for positive likelihood ratio; NPV 95% CI computed from the 95% for the negative likelihood ratio

[4] Of the 14 samples with false positive results, 8 were positive with a second FDA-cleared TV NAAT.

[5] Of the 4 samples with false negative results, 3 were negative with a second FDA-cleared TV NAAT.

[6] Of the 63 samples with false positive results, 56 were positive with a second FDA-cleared TV NAAT.

[7] Of the 5 samples with false negative results, 3 were negative with a second FDA-cleared TV NAAT.

Table 16: Aptima CV/TV Assay Performance for *Candida* species Group Relative to *Candida* Infection Status in Symptomatic Subjects, by Race/Ethnicity

Race/Ethnicity	N	TP	FP	TN	FN	Prev[1] (%)	Sensitivity (95% CI)[2]	Specificity (95% CI)[2]	PPV (95% CI)[3]	NPV (95% CI)[3]
Patient-collected										
Asian	71	18	5	48	0	25.4	100 (82.4-100)	90.6 (79.7-95.9)	78.3 (62.2-91.6)	100 (93.9- 100)
Black / African American	745	207	55	462	21	30.6	90.8 (86.3-93.9)	89.4 (86.4-91.7)	79.0 (74.7-83.1)	95.7 (93.7-97.2)
White (Hispanic/Latino)	265	71	19	170	5	28.7	93.4 (85.5-97.2)	89.9 (84.8-93.5)	78.9 (71.3-85.9)	97.1 (94.0-99.0)
White (Not Hispanic/Latino)	332	75	12	242	3	23.5	96.2 (89.3-98.7)	95.3 (91.9-97.3)	86.2 (78.8-92.1)	98.8 (96.7-99.7)
Other[4]	64	21	4	38	1	34.4	95.5 (78.2-99.2)	90.5 (77.9-96.2)	84.0 (69.4-94.6)	97.4 (88.9-99.9)
Clinician-collected										
Asian	73	19	3	51	0	26.0	100 (83.2-100)	94.4 (84.9-98.1)	86.4 (69.6-96.8)	100 (94.1- 100)
Black / African American	747	206	31	489	21	30.4	90.7 (86.3-93.9)	94.0 (91.7-95.8)	86.9 (82.7-90.5)	95.9 (94.1-97.3)
White (Hispanic/Latino)	265	71	12	177	5	28.7	93.4 (85.5-97.2)	93.7 (89.2-96.3)	85.5 (77.9-91.6)	97.3 (94.2-99.0)
White (Not Hispanic/Latino)	336	73	6	250	7	23.8	91.3 (83.0-95.7)	97.7 (95.0-98.9)	92.4 (85.4-96.9)	97.3 (94.9-98.8)
Other[4]	64	20	2	40	2	34.4	90.9 (72.2-97.5)	95.2 (84.2-98.7)	90.9 (75.6-98.6)	95.2 (86.6-99.3)

FN = false negative, FP = false positive, NPV = negative predictive value, PPV = positive predictive value, Prev = prevalence TP = true positive, TN = true negative

[1]Study prevalence reported. [2]Score CI. [3]PPV 95% CI computed from the exact 95% CI for positive likelihood ratio; NPV 95% CI computed from the 95% for the negative likelihood ratio. [4]Includes patient-reported other, mixed, and unknown races.

Table 17: Aptima CV/TV Assay Performance for *C. glabrata* Relative to *Candida* Infection Status in Symptomatic Subjects, by Race/Ethnicity

Race/Ethnicity	N	TP	FP	TN	FN	Prev[1] (%)	Sensitivity (95% CI)[2]	Specificity (95% CI)[2]	PPV (95% CI)[3]	NPV (95% CI)[3]
Patient-collected										
Asian	71	3	1	67	0	4.2	100 (43.9-100)	98.5 (92.1-99.7)	75.0 (27.6-99.2)	100 (97.0- 100)
Black / African American	744	24	9	704	7	4.2	77.4 (60.2-88.6)	98.7 (97.6-99.3)	72.7 (58.0-85.0)	99.0 (98.2-99.6)
White (Hispanic/Latino)	264	7	2	254	1	3.0	87.5 (52.9-97.8)	99.2 (97.2-99.8)	77.8 (49.1-97.0)	99.6 (98.4- 100)
White (Not Hispanic/Latino)	332	13	5	314	0	3.9	100 (77.2-100)	98.4 (96.4-99.3)	72.2 (53.0-88.9)	100 (99.0- 100)
Other[4]	64	3	1	60	0	4.7	100 (43.9-100)	98.4 (91.3-99.7)	75.0 (27.9-99.2)	100 (96.6- 100)
Clinician-collected										
Asian	72	3	0	69	0	4.2	100 (43.9-100)	100 (94.7-100)	100 (44.8- 100)	100 (97.0- 100)
Black / African American	747	23	9	707	8	4.1	74.2 (56.8-86.3)	98.7 (97.6-99.3)	71.9 (57.1-84.7)	98.9 (98.1-99.5)
White (Hispanic/Latino)	264	7	1	255	1	3.0	87.5 (52.9-97.8)	99.6 (97.8-99.9)	87.5 (56.5-99.5)	99.6 (98.4- 100)
White (Not Hispanic/Latino)	336	14	3	319	0	4.2	100 (78.5-100)	99.1 (97.3-99.7)	82.4 (61.7-95.8)	100 (99.0- 100)
Other[4]	64	3	0	61	0	4.7	100 (43.9-100)	100 (94.1-100)	100 (44.9- 100)	100 (96.6- 100)

FN = false negative, FP = false positive, NPV = negative predictive value, PPV = positive predictive value, Prev = prevalence TP = true positive, TN = true negative

[1]Study prevalence reported. [2]Score CI. [3]PPV 95% CI computed from the exact 95% CI for positive likelihood ratio; NPV 95% CI computed from the 95% for the negative likelihood ratio. [4]Includes patient-reported other, mixed, and unknown races.

Table 18: Aptima CV/TV Assay Performance for *T. vaginalis* Relative to Patient Infected Status in Symptomatic Subjects, by Race/Ethnicity

Race/Ethnicity	N	TP	FP	TN	FN	Prev[1] (%)	Sensitivity (95% CI)[2]	Specificity (95% CI)[2]	PPV (95% CI)[3]	NPV (95% CI)[3]
Patient-collected										
Asian	66	4	0	62	0	6.1	100 (51.0-100)	100 (94.2-100)	100 (52.8- 100)	100 (96.3- 100)
Black / African American	724	99	8	615	2	14.0	98.0 (93.1-99.5)	98.7 (97.5-99.3)	92.5 (86.5-96.5)	99.7 (98.9- 100)
White (Hispanic/Latino)	258	16	5	236	1	6.6	94.1 (73.0-99.0)	97.9 (95.2-99.1)	76.2 (58.6-90.1)	99.6 (98.0- 100)
White (Not Hispanic/Latino)	324	12	1	310	1	4.0	92.3 (66.7-98.6)	99.7 (98.2-99.9)	92.3 (69.6-99.7)	99.7 (98.5- 100)
Other[4]	61	5	0	56	0	8.2	100 (56.6-100)	100 (93.6-100)	100 (58.3- 100)	100 (95.5- 100)
Clinician-collected										
Asian	67	4	1	62	0	6.0	100 (51.0-100)	98.4 (91.5-99.7)	80.0 (40.3-99.4)	100 (96.3- 100)
Black / African American	727	101	42	582	2	14.2	98.1 (93.2-99.5)	93.3 (91.0-95.0)	70.6 (64.3-76.6)	99.7 (98.8- 100)
White (Hispanic/Latino)	257	16	12	228	1	6.6	94.1 (73.0-99.0)	95.0 (91.5-97.1)	57.1 (43.0-71.3)	99.6 (98.0- 100)
White (Not Hispanic/Latino)	326	11	8	305	2	4.0	84.6 (57.8-95.7)	97.4 (95.0-98.7)	57.9 (39.9-75.8)	99.3 (98.1-99.9)
Other[4]	61	5	0	56	0	8.2	100 (56.6-100)	100 (93.6-100)	100 (58.3- 100)	100 (95.5- 100)

FN = false negative, FP = false positive, NPV = negative predictive value, PPV = positive predictive value, Prev = prevalence TP = true positive, TN = true negative

[1]Study prevalence reported. [2]Score CI. [3]PPV 95% CI computed from the exact 95% CI for positive likelihood ratio; NPV 95% CI computed from the 95% for the negative likelihood ratio. [4]Includes patient-reported other, mixed, and unknown races.

Table 19: Performance of the Aptima CV/TV Assay with *C. glabrata* Contrived Specimens

	N	Aptima *C. glabrata* Positive	Aptima *C. glabrata* Negative	PPA (95% CI)[1]	NPA (95% CI)[1]
Low Positive (3× LOD)	30	30	0	100 (88.6-100)	NC
Moderate Positive (10× LOD)	15	15	0	100 (79.6-100)	NC
High Positive (20× LOD)	15	15	0	100 (79.6-100)	NC
True Negative	60	0	60	NC	100 (94.0-100)

NC = Not Calculated, NPA = negative percent agreement, PPA = positive percent agreement
[1]Score CI

Evaluation of the Aptima CV/TV Assay in Asymptomatic Women

Although the Aptima CV/TV assay is not intended for testing specimens from asymptomatic women, presence of *Candida* species and *C. glabrata* as colonizing normal flora has been reported in this population. The Aptima CV/TV assay was evaluated for detection of *Candida* species group (C spp) and *C. glabrata* with clinician-collected vaginal specimens collected from 171 asymptomatic women ≥ 14 years. Aptima CV/TV assay C spp and *C. glabrata* targets were detected with rates varying from 8.8% for *C. glabrata* to 21.1% for C spp. Results from the evaluation are presented in **Table 20** below which also includes results for the most prevalent ethnic groups enrolled. C spp and *C. glabrata* were detected in all ethnic categories, except for Asian.

Table 20: Positivity of CV/TV Infection as Determined by the Aptima CV/TV Assay in Asymptomatic Subjects

	% Positivity (# positive/# tested with valid results)	
	Candida species group	*Candida glabrata*
All	21.1% (36/171)	8.8% (15/171)
Asian	0.0% (0/5)	0.0% (0/5)
Black / African American	28.0% (21/75)	12.0% (9/75)
White (Hispanic/Latino)	17.1% (7/41)	4.9% (2/41)
White (Not Hispanic/Latino)	11.6% (5/43)	7.0% (3/43)
Other[1]	42.9% (3/7)	14.3% (1/7)

Reproducibility

Aptima CV/TV assay reproducibility was evaluated at three US sites using seven panel members. Testing was performed using one lot of assay reagents and six operators (two at each site). At each site, testing was performed for at least six days. Each run had three replicates of each panel member.

The panel members were made using a simulated vaginal swab matrix ('SVSM', which contains specimen transport media (STM) spiked with simulated vaginal fluid) negative for *Candida* species (including *C. glabrata*) and *T. vaginalis*. Six panel members contained cell lysates of

one of the following organisms: *C. albicans* (used as a representative of the *Candida* species group), *C. glabrata, or T. vaginalis*. Low positive and moderate positive concentrations of each analyte were tested. One negative panel member contained only the matrix with no added target analytes.

The agreement with expected results was 100% for all panel members containing *C. albicans, C. glabrata, or T. vaginalis*, as shown in **Table 21**.

Table 21: Agreement of Aptima CV/TV Assay Results with Expected Results

Target	Concentration	Agreed/n	Agreement, % (95% CI)
C. albicans	Negative[1]	536/536	100 (99.3-100)
	Low Positive[2]	108/108	100 (96.6-100)
	Mod Positive[3]	107/107	100 (96.5-100)
C. glabrata	Negative[1]	538/538	100 (99.3-100)
	Low Positive[2]	106/106	100 (96.5-100)
	Mod Positive[3]	107/107	100 (96.5-100)
T. vaginalis	Negative[1]	536/536	100 (99.3-100)
	Low Positive[2]	108/108	100 (96.6-100)
	Mod Positive[3]	107/107	100 (96.5-100)

CI = Score confidence interval, Mod=moderate, Neg = negative, Pos = positive

[1] Includes all panel members without the target present.

[2] Target concentration for low positive panel members is: approximately 2× C_{95} for *C. albicans* and 2× LOD for *C. glabrata* and *T. vaginalis*.

[3] Target concentration for moderate positive panel members is:3× C_{95} for *C. albicans* and3× LOD for *C. glabrata* and *T. vaginalis*.

Across organisms/panel members, the total %CV values ranged from 5.64% to 6.77%; total SD values were ≤1.59. For most panel members, the "between sites", "between runs", and "within runs" factors were the largest contributors to total variability; for all other sources of variation, SD values were ≤0.30 (%CV values were ≤1.46%), as shown in **Table 22**.

Table 22: Signal Variability of the Aptima CV/TV Assay by Analyte-positive Panel Member

			Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
Panel Description	N	Mean TTime[1]	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Calb Low Pos	108	14.68	0.66	4.47	0.00	0.00	0.00	0.00	0.00	0.00	0.30	2.02	0.83	5.64
Calb Mod Pos	107	14.37	0.66	4.58	0.14	0.99	0.00	0.00	0.00	0.00	0.28	1.98	0.81	5.64
Cglab Low Pos	106	21.36	0.84	3.94	0.18	0.84	0.00	0.00	0.00	0.00	0.62	2.89	1.26	5.88
Cglab Mod Pos	107	20.54	0.99	4.83	0.30	1.46	0.00	0.00	0.00	0.00	0.48	2.34	1.37	6.68
Tvag Low Pos	108	24.32	1.16	4.77	0.00	0.00	0.00	0.00	0.00	0.00	0.60	2.48	1.59	6.54
Tvag Mod Pos	107	23.09	1.18	5.13	0.00	0.00	0.00	0.00	0.00	0.00	0.56	2.41	1.56	6.77

Calb = *C. albicans*, Cglab = *C. glabrata*, CV = coefficient of variation, Mod = moderate, Pos = positive, SD = standard deviation, TTime = emergence time of a signal (above a specific threshold), Tvag = *T. vaginalis*

Note: If variability from a factor was numerically negative, SD and CV are shown as 0.00.

[1] The assay reports TTime for each assay analyte separately; the mean and signal variability reported are for the TTime corresponding to the analyte(s) present in each panel member.

For Aptima CV/TV assay controls and positive calibrators, the total %CV values ranged from 4.2.9% to 6.89%; total SD values were ≤1.36 (see **Tables 23** and **24**, respectively).

Table 23: Signal Variability of the Aptima CV/TV Assay Positive Controls

			Between Sites		Between Operators		Between Days		Within Runs		Total	
Control	N	Mean TTime	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Candida species group–	36	13.73	0.38	2.79	0.20	1.46	0.00	0.00	0.40	2.92	0.59	4.29
C. glabrata–	36	19.78	0.09	0.47	0.68	3.44	0.00	0.00	1.18	5.94	1.36	6.89
T. vaginalis	36	17.44	0.43	2.44	0.34	1.93	0.00	0.00	0.79	4.56	0.96	5.52

CV = coefficient of variation, SD = standard deviation, TTime = emergence time of a signal (above a specific threshold)

Note: If variability from a factor was numerically negative, SD and CV are shown as 0.00.

Table 24: Signal Variability of the Aptima CV/TV Assay Positive Calibrator

			Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
Analyte	N	Mean TTime	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Candida species group	101	14.76	0.68	4.64	0.21	1.42	0.00	0.00	0.40	2.72	0.20	1.38	0.85	5.73

CV = coefficient of variation, SD = standard deviation, TTime = emergence time of a signal (above a specific threshold)

Note: If variability from a factor was numerically negative, SD and CV are shown as 0.00.

VIII. CONCLUSIONS

The analytical and clinical study results demonstrate that the Aptima CV/TV assay on the Panther system performs comparably to the predicate device that is currently marketed for the same intended use. Hardware and software verification and validation demonstrate that the Aptima CV/TV assay on the Panther system will perform as intended.