Aptima® BV Assay

Instructions for Use
For *in vitro* diagnostic use
Rx only

General Information

Intended Use

The Aptima® BV Assay is an *in vitro* nucleic acid amplification test that utilizes real time Transcription-Mediated Amplification (TMA) technology for detection and quantitation of ribosomal RNA from bacteria associated with bacterial vaginosis (BV), including *Lactobacillus* (*L. gasseri, L. crispatus, and L. jensenii*), *Gardnerella vaginalis (G. vaginalis)*, and *Atropbium vaginae (A. vaginae)*. The assay reports a qualitative result for BV and does not report results for individual organisms. The assay is intended to aid in the diagnosis of BV on the automated Panther® System using clinician-collected and patient-collected vaginal swab specimens from females with a clinical presentation consistent with vaginitis and/or vaginosis.

Summary and Explanation of the Test

Vaginitis syndrome is characterized by a spectrum of conditions: vaginal and vulvar irritation, odor, discharge, and pruritus (1). Causes of vaginitis include mechanical and chemical factors (feminine hygiene products, contraceptive materials, etc.) as well as infectious agents (1). Up to 90% of infectious vaginitis cases are caused by BV, vulvovaginal candidiasis (candida vaginitis, CV) and trichomoniasis (*Trichomonas vaginalis*, TV) (2). BV has been diagnosed in 22–50% of symptomatic patients, CV in 17–39%, and TV in 4–35% (1, 2).

BV is responsible for the majority of infectious vaginitis cases. BV is characterized by a change in the vaginal microbiota dominated by *Lactobacillus* species to a polymicrobial anaerobe-dominated microbiota that includes *G. vaginalis*, *A. vaginae*, *Prevotella*, *Bacteroides*, *Peptostreptococcus*, *Mobiluncus*, *Sneathia* (*Leptotrichia*), *Mycoplasma*, and BV associated bacteria (3). This change in vaginal microbiota is associated with the onset of Amsel clinical signs, resulting from the biochemical and cytological changes in the vaginal mileu that are pathognomonic for BV (11). BV has been associated with pelvic inflammatory disease (4), cervicitis (5), elevated risk of acquisition of STIs, such as chlamydia, gonorrhea, HSV, HIV (6, 7, 8), spontaneous abortion, and preterm birth (9, 10).

Diagnosis of BV based on clinical criteria (vaginal pH, presence of clue cells, whiff test, and discharge) has been proposed by Amsel (11). Nugent et al. proposed a classification for BV based on microscopic description of observed types of bacteria via Gram stain in vaginal swabs (12). Recent studies suggest that molecular diagnostic tools would be beneficial to improve diagnosis of BV and that nucleic acid amplification, targeting several BV-associated bacteria, could be utilized (13).

The Aptima BV Assay is a real time TMA assay developed for use on the automated Panther System that detects and discriminates RNA markers from the *Lactobacillus* species group (*L. gasseri, L. crispatus* and *L. jensenii*), *G. vaginalis*, and *A. vaginae* in clinician-collected and patient-collected vaginal swab specimens from symptomatic females. The Aptima BV Assay uses an algorithm to report a qualitative result for BV based on detection of target organisms. The Aptima BV Assay includes an internal control (IC).

Principles of the Procedure

The Aptima BV 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 IC in every test to monitor nucleic acid capture, amplification, and detection.

Specimens are collected in a tube containing Aptima® Specimen Transport Media (STM) that lyses the cells, releases the RNA, and protects it from degradation during storage. When the Aptima BV 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 *Lactobacillus* group, *A. vaginae*, *G. vaginalis,* and IC amplification products. The Panther System software compares signal emergence times for each target organism to calibration information to determine the BV Positive or Negative status of each sample.

Summary of Safety and Performance

The SSP (Summary of Safety and Performance) is available in the European database on medical devices (Eudamed), where it is linked to the device identifiers (Basic UDI-DI). To locate the SSP for the Aptima BV Assay, refer to the Basic Unique Device Identifier (BUDI): **54200455DIAGAPTBVRB**.

Warnings and Precautions

A. For *in vitro* diagnostic use.

B. For professional use.

C. To reduce the risk of invalid results, carefully read the entire package insert and refer to the *Panther/Panther Fusion® System Operator's Manual for procedural information* prior to performing the assay on the Panther System.

D. Only personnel adequately trained in the use of the Aptima BV Assay and in handling potentially infectious materials should perform this procedure. If a spill occurs, immediately disinfect following appropriate site procedures.

E. For additional specific warnings, precautions, and procedures to control contamination for the Panther System, consult the *Panther*/*Panther Fusion System Operator's Manual.*

Laboratory Related

F. Use only supplied or specified disposable laboratory ware.

G. Use routine laboratory precautions. Do not eat, drink or smoke in designated work areas. Wear disposable, powderless gloves, protective eye wear, and laboratory coats when handling specimens and kit reagents. Wash hands thoroughly after handling specimens and kit reagents.

H. Work surfaces, pipettes, and other equipment must be regularly decontaminated with 2.5% to 3.5% (0.35 M to 0.5 M) sodium hypochlorite solution.

I. Dispose of all materials that have come in contact with specimens and reagents in accordance with applicable national, international, and regional regulations. Thoroughly clean and disinfect all work surfaces.

J. Use good standard practices for molecular laboratories including environmental monitoring. See *Procedural Notes* for suggested Lab Contamination Monitoring Protocol for the Panther System.

Specimen Related

K. Expiration dates listed on the collection kits pertain to the collection site and not the testing facility. Samples collected any time prior to the expiration date of the collection kit, and transported and stored in accordance with the package insert, are valid for testing even if the expiration date on the collection tube has passed.

L. Specimens may be infectious. Use Universal Precautions when performing this assay. Proper handling and disposal methods should be established according to local regulations. Only personnel adequately trained in the use of the Aptima BV Assay and trained in handling infectious materials should perform this diagnostic procedure.

M. Avoid cross-contamination during the specimen handling steps. Specimens can contain extremely high levels of organisms. Ensure that specimen containers from different patients do not contact one another during specimen handling in the laboratory. Change gloves if they come in contact with a specimen.

N. Avoid cross-contamination by discarding used materials without passing over any other container.

O. Maintain proper storage conditions during specimen shipping to ensure the integrity of the specimen. Specimen stability under shipping conditions other than those recommended has not been evaluated.

P. If the lab receives an Aptima® Multitest Swab Specimen Collection Kit transport tube with no swab, two swabs, a cleaning swab, or a swab not supplied by Hologic, the specimen must be rejected.

Q. Upon piercing, liquid can discharge from Aptima transfer tube caps under certain conditions. Follow instructions in the *Panther System Test Procedure* to prevent this occurrence.

Assay Related

R. Cap and store reagents at the specified temperatures. The performance of the assay may be affected by use of improperly stored reagents. See *Reagent Storage and Handling Requirements* and *Panther System Test Procedure* for more information.

S. Use Universal Precautions when handling controls.

T. Avoid microbial and ribonuclease contamination of reagents.

U. Do not use the reagent, control, or calibrator kits after their expiration dates.

V. Do not interchange, mix, or combine assay reagents from kits with different master lot numbers. Controls, the calibrator, and assay fluids may be interchanged.

W. Do not combine any assay reagents or fluids without specific instruction. Do not top off reagents or fluids. The Panther System verifies reagent levels.

X. Some reagents in this kit are labeled with hazard information.

Note: *Hazard communication information for labeling of globally marketed products reflects the US and EU Safety Data Sheets (SDS) classifications. For hazard communication information specific to your region, refer to the region specific SDS on the Safety Data Sheet Library at www.hologicsds.com. For more information on the symbols, refer to the symbol legend on www.hologic.com/package-inserts.*

EU Hazard Information	
—	**Amplification Reagent** *Magnesium Chloride 60 - 65%* — H412 - Harmful to aquatic life with long lasting effects. P273 - Avoid release to the environment. P501 - Dispose of contents/ container to an approved waste disposal plant.
—	**Enzyme Reagent** *HEPES 1 - 5%* *Triton X-100 1 - 5%* — H412 - Harmful to aquatic life with long lasting effects. P273 - Avoid release to the environment. P501 - Dispose of contents/ container to an approved waste disposal plant.
—	**Enzyme Reconstitution Reagent** *Glycerol 20 - 25%* *Triton X-100 5 - 10%* *HEPES 1 - 5%* — H412 - Harmful to aquatic life with long lasting effects. P273 - Avoid release to the environment. P501 - Dispose of contents/ container to an approved waste disposal plant.
—	**Promoter Reagent** *Magnesium Chloride 35 - 40%* — H412 - Harmful to aquatic life with long lasting effects. P273 - Avoid release to the environment. P501 - Dispose of contents/ container to an approved waste disposal plant.

—	**Target Capture Reagent** *HEPES 5 - 10%* *EDTA 1 - 5%* *Lithium Hydroxide, Monohydrate 1 - 5%* — H412 - Harmful to aquatic life with long lasting effects. P273 - Avoid release to the environment. P501 - Dispose of contents/ container to an approved waste disposal plant.

Reagent Storage and Handling Requirements

A. The following table shows the storage conditions and stability for the reagents, the calibrator, and the controls.

Reagent	Unopened Storage	Open Kit (Reconstituted)	
		Storage	Stability
Amplification Reagent	2ºC to 8ºC	N/A	N/A
Amplification Reconstitution Solution	15ºC to 30ºC	2ºC to 8ºC	30 days[1]
Enzyme Reagent	2ºC to 8ºC	N/A	N/A
Enzyme Reconstitution Solution	15ºC to 30ºC	2ºC to 8ºC	30 days[1]
Promoter Reagent	2ºC to 8ºC	N/A	N/A
Promoter Reconstitution Solution	15ºC to 30ºC	2ºC to 8ºC	30 days[1]
Target Capture Reagent	15ºC to 30ºC	15ºC to 30ºC[2]	30 days[1]
Positive Calibrator	2ºC to 8ºC	N/A	Single Use Vial
Negative Control	2ºC to 8ºC	N/A	Single Use Vial
Positive Control	2ºC to 8ºC	N/A	Single Use Vial
Internal Control	2ºC to 8ºC	N/A	Single Use Vial

[1] When reagents are removed from the Panther System, they should be immediately returned to their appropriate storage temperatures.

[2] Storage condition for the working Target Capture Reagent (Target Capture Reagent with Internal Control added).

B. Discard any unused reconstituted reagents and working Target Capture Reagent (wTCR) after 30 days or after the Master Lot expiration date, whichever comes first.

C. The 100-test assay kit can be loaded onto the Panther System up to 8 times. The 250-test assay kit can be loaded onto the Panther System up to 5 times. The system logs each time the reagents are loaded.

D. The 250-test assay kit Promoter Reagent bottle is the same size as the Enzyme Reagent bottle. After loading the Promoter Reagent bottle into the reagent rack, check that the bottle is fully pushed down.

E. Reagents stored on-board the Panther System have 120 hours of on-board stability.

F. Avoid cross-contamination during reagent handling and storage. Recap all reconstituted reagents with new reagent caps each time prior to storage.

G. The Promoter Reagent and reconstituted Promoter Reagent are photosensitive. Protect these reagents from light during storage and preparation for use.

H. Do not freeze reagents.

Specimen Collection and Storage

Note: *Handle all specimens as if they contain potentially infectious agents. Use Universal Precautions.*

Note: *Take care to avoid cross-contamination during sample handling steps. For example, discard used material without passing over any other container.*

Vaginal swab specimens can be tested with the Aptima BV Assay. Assay performance has not been evaluated with specimens other than those collected with the following specimen collection kit:

- Aptima Multitest Swab Specimen Collection Kit

A. Specimen Collection

Refer to the appropriate specimen collection kit package insert for specific collection instructions.

B. Specimen Transport and Storage Before Testing

Only the following storage conditions should be used for specimens with the Aptima BV Assay.

1. Swab Specimens
   a. Option 1: After collection, swab specimens in transport tubes can be stored at 2ºC to 8ºC for up to 30 days. If longer storage is needed, specimens may be stored at –20°C or –70°C for an additional 60 days.
   b. Option 2: After collection, swab specimens in transport tubes can be stored at 15°C to 30°C for up to 30 days.

C. Specimen Storage After Testing

1. Specimens that have been assayed must be stored upright in a rack.
2. The specimen transport tubes should be covered with a new, clean plastic film or foil barrier.
3. If assayed samples need to be frozen or shipped, remove penetrable cap and place new non-penetrable caps on the specimen transport tubes. If specimens need to be shipped for testing at another facility, recommended temperatures must be maintained.
4. Prior to uncapping, specimen transport tubes must be centrifuged for 5 minutes at 420 ± 100 relative centrifugal force (RCF) to bring all of the liquid down to the bottom of the tube. **Avoid splashing and cross-contamination.**

Note: *Specimens must be shipped in accordance with applicable national, international, and regional transportation regulations.*

Panther System

Reagents for the Aptima BV Assay are listed below for the Panther System. Reagent identification symbols are also listed next to the reagent name.

Reagents and Materials Provided

Aptima BV Assay Kit

100 tests: 2 assay boxes, 1 calibrator kit, and 1 controls kit (Cat. No. PRD-05186)

250 tests: 2 assay boxes, 1 calibrator kit, and 1 controls kit (Cat. No. PRD-07662)

Aptima BV Assay Refrigerated Box (Box 1 of 2)
(store at 2ºC to 8ºC upon receipt)

Symbol	Component	Quantity	
		250-Test Kit	100-Test Kit
A	**Amplification Reagent** *Non-infectious nucleic acids dried in buffered solution.*	1 vial	1 vial
E	**Enzyme Reagent** *Reverse transcriptase and RNA polymerase dried in HEPES buffered solution.*	1 vial	1 vial
PRO	**Promoter Reagent** *Non-infectious nucleic acids dried in buffered solution.*	1 vial	1 vial
IC	**Internal Control** *Non-infectious RNA nucleic acids in buffered solution.*	1 x 0.56 mL	1 x 0.3 mL

Aptima BV Assay Room Temperature Box (Box 2 of 2)
(store at 15ºC to 30ºC upon receipt)

Symbol	Component	Quantity	
		250-Test Kit	100-Test Kit
AR	**Amplification Reconstitution Solution** *Aqueous solution containing glycerol and preservatives.*	1 x 18.5 mL	1 x 7.2 mL
ER	**Enzyme Reconstitution Solution** *HEPES buffered solution containing a surfactant and glycerol.*	1 x 11.1 mL	1 x 5.8 mL
PROR	**Promoter Reconstitution Solution** *Aqueous solution containing glycerol and preservatives.*	1 x 11.9 mL	1 x 4.5 mL
TCR	**Target Capture Reagent** *Buffered salt solution containing non-infectious nucleic acids and magnetic particles.*	1 x 54.0 mL	1 x 26.0 mL
	Reconstitution Collars	3	3
	Master Lot Barcode Sheet	1 sheet	1 sheet

Aptima BV Assay Calibrator Kit (PRD-05188)
(store at 2ºC to 8ºC upon receipt)

Symbol	Component	Quantity
PCAL	**Positive Calibrator** *Non-infectious nucleic acids in buffered solution.*	5 x 2.8 mL
	Calibrator Barcode Label	1 sheet

Aptima BV Assay Controls Kit (PRD-05187)
(store at 2ºC to 8ºC upon receipt)

Symbol	Component	Quantity
CONTROL-	**Negative Control** *Non-infectious L. crispatus cultured cells in buffered solution.*	5 x 1.7 mL
CONTROL+	**Positive Control** *Non-infectious G. vaginalis and A. vaginae cultured cells in buffered solution.*	5 x 1.7 mL
	Control Barcode Label	1 sheet

Materials Required and Available Separately

Note: *Materials available from Hologic have catalog numbers listed, unless otherwise specified.*

Material	Cat. No.
Panther® System	303095
Panther Fusion® System	PRD-04172
Panther® System Continuous Fluids and Waste (Panther Plus)	PRD-06067
Aptima® BV Assay Calibrator Kit	PRD-05188
Aptima® BV Assay Controls Kit	PRD-05187
Panther Run Kit for Real Time Assays (for real time assays only)	PRD-03455 (5000 tests)
Aptima® Assay Fluids Kit (also known as Universal Fluids Kit) *Contains Aptima® Wash Solution, Aptima® Buffer for Deactivation Fluid, and Aptima® Oil Reagent*	303014 (1000 tests)
Multi-tube units (MTUs)	104772-02
Panther® Waste Bag Kit	902731
Panther® Waste Bin Cover	504405
Or, Panther System Run Kit *When running non-real time-TMA assays in parallel with real time-TMA assays* *Contains MTUs, waste bags, waste bin covers, auto detect, and assay fluids*	303096 (5000 tests)

Material	Cat. No.
Aptima Assay Fluids Kit *Contains Aptima Wash Solution, Aptima Buffer for Deactivation Fluid, and Aptima Oil Reagent*	303014 (1000 tests)
Multi-tube units (MTUs)	104772-02
Tips, 1000 µL filtered, conductive, liquid sensing, and disposable. *Not all products are available in all regions. Contact your representative for region-specific information*	901121 (10612513 Tecan) 903031 (10612513 Tecan) MME-04134 (30180117 Tecan) MME-04128
Aptima® Multitest Swab Specimen Collection Kit	PRD-03546
Bleach, 5.0% to 8.25% (0.7 M to 1.16 M) sodium hypochlorite solution	—
Disposable, powderless gloves	—
Aptima® penetrable caps	105668
Replacement non-penetrable caps	103036A
Reagent Replacement Caps for the 100-test kits *Amplification, Enzyme, and Promoter reagent reconstitution bottles* *TCR bottle*	 CL0041 (100 caps) 501604 (100 caps)
Reagent Replacement Caps for the 250-test kits *Amplification reagent reconstitution bottle* *Enzyme and Promoter reagent reconstitution bottles* *TCR bottle*	 CL0041 (100 caps) 501616 (100 caps) CL0040 (100 caps)
Plastic-backed laboratory bench covers	—
Lint-free wipes	—
Pipettor	—
Tips	—

Optional Materials

Material	Cat. No.
Hologic® Bleach Enhancer for Cleaning *For routine cleaning of surfaces and equipment*	302101
Tube Rocker	—

Panther System Test Procedure

Note: *See the Panther/Panther Fusion System Operator's Manual for additional Panther System procedural information.*

A. Work Area Preparation

1. Clean work surfaces where reagents will be prepared. Wipe down work surfaces with 2.5% to 3.5% (0.35 M to 0.5 M) sodium hypochlorite solution. Allow the sodium hypochlorite solution to contact surfaces for at least 1 minute and then follow with a deionized (DI) water rinse. Do not allow the sodium hypochlorite solution to dry. Cover the bench surface on which the reagents and samples will be prepared with clean, plastic-backed absorbent laboratory bench covers.
2. Clean a separate work surface where samples will be prepared. Use the procedure described above (Step A.1).
3. Clean any pipettors. Use the cleaning procedure described above (Step A.1).

B. Reagent Reconstitution/Preparation of a New Kit

Note: *Reagent reconstitution should be performed prior to beginning any work on the Panther System.*

1. Prior to testing, Amplification, Enzyme, and Promoter Reagents must be reconstituted by combining contents of the bottles of lyophilized reagent with the appropriate reconstitution solution.
   a. Allow the lyophilized reagents to reach room temperature (15°C to 30°C) before use.
   b. Pair each reconstitution solution with its lyophilized reagent. Before attaching the reconstitution collar, ensure that the reconstitution solution and reagent have matching label symbols.
   c. Check the lot numbers on the Master Lot Barcode Sheet to ensure that the appropriate reagents are paired. Label caps of reconstitution solution bottles.
   d. Open the lyophilized reagent glass vial and firmly insert the notched end of the reconstitution collar into the glass vial opening (Figure 1, Step 1).
   e. Open the matching reconstitution solution bottle, and set the cap on a clean, covered work surface.
   f. While holding the reconstitution solution bottle on the bench, firmly insert the other end of the reconstitution collar into the bottle opening (Figure 1, Step 2).
   g. Slowly invert the assembled bottles. Allow the solution to drain from the bottle into the glass vial (Figure 1, Step 3).
   h. Pick up the assembled bottles and swirl the assembled bottles for at least 10 seconds. Avoid creating foam while swirling the bottle (Figure 1, Step 4).
   i. Wait at least 15 minutes to ensure the lyophilized reagent goes completely into solution. Swirl the bottles again for at least 10 seconds and then slightly rock the solution within the glass vial back and forth to mix thoroughly.
   j. Visually check to see if reagent is completely in solution with no powder, clumps, or wavy lines.
   k. Slowly tilt the assembled bottles again to allow all of the solution to drain back into the reconstitution solution bottle (Figure 1, Step 5).
   l. Remove the reconstitution collar and glass vial (Figure 1, Step 6).

m. Recap the plastic bottle with either the saved, labeled cap that corresponds to the reagent or a new cap. Do not mismatch caps. Record operator initials and reconstitution date on the label (Figure 1, Step 7).

n. Discard the reconstitution collar and glass vial (Figure 1, Step 8).

o. Thoroughly mix each reagent by gently inverting prior to loading onto the Panther System.

Option: Additional mixing of the Amplification, Enzyme, and Promoter reagents is allowed by placing the recapped plastic bottles on a tube rocker set at a moderate speed and tilt for a minimum of 5 minutes. Ensure reagents are thoroughly mixed.

Warning: *Avoid creating foam when reconstituting reagents. Foam compromises the level-sensing in the Panther System.*

Warning: *Adequate mixing of the reagents is necessary to achieve expected assay results.*

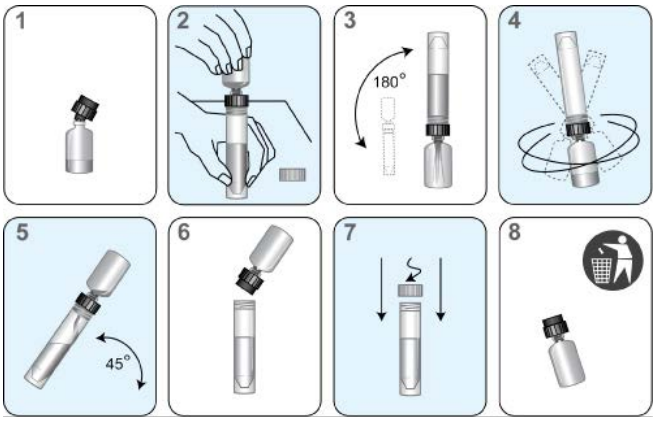

Figure 1. Reagent Reconstitution Process

2. Prepare Working Target Capture Reagent (wTCR)

a. Pair the appropriate bottles of TCR and IC.

b. Check the reagent lot numbers on the Master Lot Barcode Sheet to make sure that the appropriate reagents in the kit are paired.

c. Open the bottle of TCR, and set the cap on a clean, covered work surface.

d. Open the bottle of IC and pour the entire contents into the bottle of TCR. Expect a small amount of liquid to remain in the IC bottle.

e. Cap the bottle and gently swirl the solution to mix the contents. Avoid creating foam during this step.

f. Record operator initials and the current date on the label.

g. Discard the IC bottle and cap.

C. Reagent Preparation for Previously Prepared Reagents

1. Previously prepared Amplification, Enzyme, and Promoter reagents must reach room temperature (15°C to 30°C) prior to the start of the assay.

Option: The reconstituted Amplification, Enzyme, and Promoter reagents capped plastic bottles may be placed on a tube rocker set at a moderate speed and tilt for a

minimum of 25 minutes to ensure reagents reach room temperature and are thoroughly mixed.

2. If wTCR contains precipitate, warm wTCR at 42°C to 60°C for up to 90 minutes. Allow the wTCR to equilibrate to room temperature prior to use. Do not use if precipitate persists.
3. Verify that the reagents have not exceeded their storage stability times, including on-board stability.
4. Thoroughly mix each reagent by gently inverting prior to loading on the system. Avoid creating foam when inverting reagents.
5. Do not top off reagent bottles. The Panther System will recognize and reject bottles that have been topped off.

Warning: *Adequate mixing of the reagents is necessary to achieve expected assay results.*

D. Calibrator and Control Preparation

1. Remove the calibrator and controls from storage (2°C to 8°C) and allow the calibrator and controls to reach room temperature (15°C to 30°C) prior to processing.

E. Specimen Handling

1. Visually confirm that each specimen tube meets the following criteria:
   a. The presence of a single pink Aptima collection swab in a swab specimen transport tube.
2. Allow the specimens to reach room temperature (15°C to 30°C) prior to processing.

   Note: *Prior to testing and/or to resolve suspected specimen related invalid results, specimen may be vortexed at high speed for a minimum of 3 minutes, followed by low speed vortexing for 1 minute (to draw the fluid down into the tube).*
3. Inspect specimen tubes before loading into rack:
   a. If a specimen tube contains bubbles in the space between the liquid and the cap, centrifuge the tube for 5 minutes at 420 RCF to eliminate the bubbles.
   b. If a specimen tube has a lower volume than typically observed when collection instructions have been followed, centrifuge the tube for 5 minutes at 420 RCF to ensure that no liquid is in the cap.

   Note: *Failure to follow Steps 3a–3b may result in liquid discharge from the specimen tube cap.*

   Note: *Up to 4 separate aliquots can be tested from each specimen tube. Attempts to pipette more than 4 aliquots from the specimen tube can lead to processing errors.*

F. System Preparation

1. Set up the system according to the instructions in the *Panther*/*Panther Fusion System Operator's Manual* and *Procedural Notes*. Make sure that the appropriately sized reagent racks and TCR adapters are used.
2. Load samples.

Procedural Notes

A. Calibrator and Controls

1. The positive calibrator, positive control and negative control tubes can be loaded in any rack position or in any Sample Bay Lane on the Panther System. Specimen pipetting will begin when one of the following 2 conditions has been met:
   a. The calibrator and controls are currently being processed by the system.
   b. Valid results for the calibrator and controls are registered on the system.
2. Once the calibrator and control tubes have been pipetted and are processing for a specific reagent kit, patient specimens can be tested with the associated kit up to 24 hours **unless:**
   a. The calibrator result or control results are invalid.
   b. The associated assay reagent kit is removed from the system.
   c. The associated assay reagent kit has exceeded stability limits.
3. Each calibrator or each control tube can be used once. Attempts to use more than once can lead to processing errors.

B. Glove Powder

As in any reagent system, excess powder on some gloves may cause contamination of opened tubes. Powderless gloves are recommended.

C. Lab Contamination Monitoring Protocol for the Panther System

There are many laboratory-specific factors that may contribute to contamination, including testing volume, workflow, disease prevalence, and various other laboratory activities. These factors should be taken into consideration when contamination monitoring frequency is being established. Intervals for contamination monitoring should be established based on each laboratory's practices and procedures.

To monitor for laboratory contamination, the following procedure may be performed using the Aptima Multitest Swab Specimen Collection Kit:

1. Label swab transport tubes with numbers corresponding to the areas to be tested.
2. Remove the specimen collection swab from its packaging, wet the swab in the swab transport medium, and swab the designated area using a circular motion.
3. Immediately insert the swab into transport tube.
4. Carefully break the swab shaft at the score line; use care to avoid splashing of the contents.
5. Recap the swab transport tube tightly.
6. Repeat Steps 2 to 5 for each area to be swabbed.
7. Test samples with the Aptima BV Assay on the Panther System.
8. Further investigation should be performed if any samples yield a positive result.

For test interpretation, see *Test Interpretation*. For additional Panther System-specific contamination monitoring information, contact Hologic Technical Support.

Quality Control

An operator may invalidate an individual specimen or an entire run if it was observed and documented that a procedural, technical, or instrument-related error occurred while performing the assay.

Assay Calibration

To generate valid results, an assay calibration must be completed. The calibrator is run in triplicate each time a reagent kit is loaded on the Panther System. Once established, the calibration is valid for up to 24 hours. Software on the Panther System alerts the operator when a calibration is required. The operator scans the calibration coefficients found on the Master Lot Barcode Sheet provided with each reagent kit.

During processing, criteria for acceptance of the calibrator is automatically verified by the software on the Panther System. If less than two of the calibrator replicates are valid, the software automatically invalidates the run. Samples in an invalidated run must be retested using a freshly prepared calibrator and freshly prepared controls.

Negative and Positive Controls

To generate valid results, a set of assay controls must be tested. One replicate each of the negative control and the positive control must be tested each time a reagent kit is loaded on the Panther System. Once established, the controls are valid for up to 24 hours. Software on the Panther System alerts the operator when controls are required.

During processing, criteria for acceptance of controls are automatically verified by software on the Panther System. If any one of the controls has an invalid result, the software automatically invalidates the run. Samples in an invalidated run must be retested using a freshly prepared calibrator and freshly prepared controls.

Internal Control

An IC is added to each sample with the wTCR. During processing, IC acceptance criteria are automatically verified by the Panther System software. Detection of the internal control is not required for samples that are BV positive.

The IC must be detected in all samples that are negative for BV; samples that fail to meet that criteria will be reported as invalid. Each sample with an invalid result must be retested.

The Panther System software is designed to accurately verify processes when procedures are performed following the instructions provided in this package insert and the *Panther*/*Panther Fusion System Operator's Manual*.

Test Interpretation

Test results are automatically determined by the assay software. The table below shows the possible results reported in a valid run and result interpretations. The first valid result is the result that should be reported. Samples with invalid test results should be retested. If the result is invalid upon retest, a new specimen should be collected.

Table 1: Result Interpretation

BV Result	Result[1]	Interpretation
Positive	Valid	Positive for BV
Negative	Valid	Negative for BV
Invalid	Invalid	Invalid test

[1]The valid or invalid status of the reaction is shown in the Result column. The Result column considers the internal control and positive or negative status of analytes.

Limitations

A. Use of this assay is limited to personnel who have been trained in the procedure. Failure to follow the instructions given in this package insert may result in erroneous results.

B. The effects of tampon use, douching, and specimen collection variables have not been evaluated for their impact on assay performance.

C. Performance with specimen types other than vaginal swab specimens has not been evaluated.

D. Reliable results are dependent on adequate specimen collection, transport, storage, and processing. Failure to observe proper procedures in any one of these steps can lead to incorrect results. Because the transport system used for this assay does not permit microscopic assessment of specimen adequacy, training of clinicians in proper specimen collection techniques is necessary. See *Specimen Collection and Storage* for instructions. Refer to the package insert of the appropriate Hologic specimen collection kit.

E. Therapeutic failure or success cannot be determined with the Aptima BV Assay since nucleic acid may persist following appropriate antimicrobial therapy.

F. Bacterial species targeted by the Aptima BV Assay may comprise part of the normal microbiome for a significant number of women; a BV positive result should be interpreted in conjunction with other clinical data available to the clinician.

G. A negative result does not preclude a possible infection because results are dependent on adequate specimen collection. Test results may be affected by improper specimen collection, technical error, specimen mix-up, or target levels below the assay limit of detection (LoD).

H. The Aptima BV Assay provides qualitative results. Therefore, a correlation cannot be drawn between the magnitude of a positive assay signal and the number of organisms in a specimen.

I. The performance of the Aptima BV Assay has not been evaluated in individuals less than 14 years of age.

J. Customers must independently validate an LIS transfer process.

K. The Aptima BV Assay has not been evaluated for use with specimens collected by patients at home.

L. Collection and testing of patient-collected vaginal swab specimens with the Aptima BV Assay is not intended to replace clinical examination.

M. Public health recommendations should be consulted regarding testing for additional sexually transmitted infections (STI) for patients with a positive result with the Aptima BV Assay.

N. Additional microorganisms not detected by the Aptima BV Assay such as *Prevotella* species and *Mobiluncus* species, *Ureaplasma*, *Mycoplasma*, and numerous fastidious or uncultivated anaerobes have also been found in women with BV, but are less associated with BV due to their relatively low prevalence, sensitivity, and/or specificity (14).

O. Interference with the Aptima BV Assay was observed in the presence of the following substances: mucus (1.5% V/V), vaginal moisturizing gel (0.5% W/V) and tioconazole (5% W/V).

P. Cross-reactivity was observed with the Aptima BV Assay in the presence of *Lactobacillus acidophilus* ($1x10^4$ CFU/mL).

Q. A positive test result does not necessarily indicate the presence of viable organisms. A positive result is indicative of the presence of target RNA.

Panther System Expected Values

The prevalence of BV in patient populations depends on age, ethnicity, risk factors, the type of clinic, and the sensitivity of the test used to detect infections. A summary of the BV positivity in symptomatic subjects, as determined by the Aptima BV Assay on the Panther System, is shown in Table 2 for the multicenter study, by clinical site and overall.

Table 2: Positivity as Determined by the Aptima BV Assay in Symptomatic Women by Specimen Type and Clinical Site

	% Positivity (# positive/# tested with valid results)	
Site	**Clinician-collected Vaginal Swabs**	**Patient-collected Vaginal Swabs**
1	40.0 (6/15)	46.7 (7/15)
2	20.0 (1/5)	0.0 (0/5)
3	63.6 (14/22)	63.6 (14/22)
4	51.9 (108/208)	60.5 (124/205)
5	48.5 (64/132)	50.8 (66/130)
6	46.5 (33/71)	50.7 (36/71)
7	68.1 (130/191)	69.3 (131/189)
8	100.0 (1/1)	100.0 (1/1)
9	48.0 (49/102)	54.9 (56/102)
10	70.6 (12/17)	70.6 (12/17)
11	50.7 (34/67)	50.7 (34/67)
12	32.8 (41/125)	34.1 (42/123)
13	63.2 (43/68)	62.3 (43/69)
14	55.6 (5/9)	55.6 (5/9)
15	50.0 (2/4)	50.0 (2/4)
16	58.6 (17/29)	65.5 (19/29)
17	49.4 (39/79)	51.3 (41/80)
18	64.4 (56/87)	64.4 (56/87)
19	45.6 (31/68)	50.0 (34/68)
20	11.1 (4/36)	19.4 (7/36)
21	58.4 (45/77)	57.9 (44/76)
All	**52.0 (735/1413)**	**55.1 (774/1405)**

Panther System Assay Performance

Reproducibility

Aptima BV Assay reproducibility was evaluated on the Panther System at three US sites using seven panel members. Two operators performed testing at each site. Each operator performed one run per day over six days using one reagent lot over the course of testing. Each run had three replicates of each panel member.

The panel members were made using a simulated vaginal swab matrix (SVSM), which contains STM spiked with simulated vaginal fluid negative for *Lactobacillus* species, *G. vaginalis*, and *A. vaginae*. Six panel members contained cell lysates of at least 1 of the following organisms: *L. crispatus*, *L. jensenii*, *G. vaginalis*, or *A. vaginae*; different bacterial combinations were prepared to represent the variety of targeted BV organism combinations present in vaginal specimens. One negative panel member contained only the matrix with no added target analytes.

The agreement with expected results was 100% for all panel members.

Signal variability of the Aptima BV Assay was calculated for each target in analyte positive panel members. Only samples with valid results were included in the analyses. Variability, calculated between sites, between operators, between days, between runs, within run, and overall, is shown in Table 3 to Table 5 for *Lactobacillus*, *G. vaginalis*, and *A. vaginae* positive panel members, respectively.

Table 3: Signal Variability for Lactobacillus Positive Panel Members

Panel Description	N	Mean TTime[1]	Between Sites		Between Operators		Between Days		Between Runs		Within Run		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
L. crispatus BV Negative[2]	108	19.73	0.30	1.53	0.61	3.07	0.13	0.64	0.63	3.17	0.12	0.62	0.94	4.76
L. jensenii BV Low Positive[2]	108	24.31	0.00	0.00	0.77	3.16	0.00	0.00	0.80	3.28	0.15	0.62	1.12	4.60

CV = coefficient of variation; **SD** = standard deviation; **TTime** = threshold time.

[1] TTime is shown for *Lactobacillus* only.

[2] Panel member contains 2 different organisms; results are shown for only the *Lactobacillus* component.

Note: *In the event that variability from some factors is numerically negative, SD and CV are shown as 0.00.*

Table 4: Signal Variability for G. vaginalis Positive Panel Members

Panel Description	N	Mean TTime[1]	Between Sites		Between Operators		Between Days		Between Runs		Within Run		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
G. vaginalis Low Positive	108	15.69	0.35	2.26	0.40	2.52	0.00	0.00	0.38	2.43	0.15	0.96	0.67	4.28
G. vaginalis Moderate Positive	108	14.33	0.30	2.07	0.37	2.58	0.00	0.00	0.35	2.41	0.14	0.98	0.60	4.21

CV = coefficient of variation; **SD** = standard deviation; **TTime** = threshold time.

[1] TTime is shown for *G. vaginalis* only.

Note: *In the event that variability from some factors is numerically negative, SD and CV are shown as 0.00.*

Table 5: Signal Variability for A. vaginae Positive Panel Members

Panel Description	N	Mean TTime[1]	Between Sites		Between Operators		Between Days		Between Runs		Within Run		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
A. vaginae BV Negative[2]	108	18.01	0.39	2.15	0.44	2.46	0.08	0.45	0.47	2.59	0.18	0.97	0.78	4.30
A. vaginae Low Positive	108	14.95	0.38	2.52	0.41	2.75	0.00	0.00	0.39	2.61	0.14	0.93	0.69	4.64
A. vaginae BV Low Positive[2]	108	14.94	0.41	2.76	0.37	2.51	0.00	0.00	0.37	2.45	0.17	1.13	0.69	4.60
A. vaginae Moderate Positive	108	13.99	0.29	2.08	0.36	2.60	0.03	0.18	0.39	2.82	0.14	1.00	0.63	4.48

CV = coefficient of variation; **SD** = standard deviation; **TTime** = threshold time.

[1] TTime is shown for *A. vaginae* only.

[2] Panel member contains 2 different organisms; results are shown for only the *A. vaginae* component.

Note: *In the event that variability from some factors is numerically negative, SD and CV are shown as 0.00.*

Panther System Clinical Performance

A prospective, multicenter clinical study was conducted to establish the clinical performance characteristics of the Aptima BV Assay on the Panther System. Female subjects presenting with symptoms of vaginitis were enrolled at 21 geographically and ethnically diverse US clinical sites, including private and academic family practice, obstetric-gynecologic, family planning, public health, sexually transmitted infections (STI), medical group clinics, and clinical research centers.

Three (3) vaginal swab samples were collected from each subject: one clinician-collected swab sample and one patient-collected swab sample were collected using the Aptima Multitest Swab Specimen Collection Kit for Aptima BV Assay testing, and one clinician-collected swab sample was collected for reference method testing. Aptima samples were tested with the Aptima BV Assay on the Panther System at three sites. BV infection status was determined using a combination of Nugent interpretations and Amsel criteria from the final vaginal swab sample.

- Samples with normal flora as per the Nugent interpretation were considered negative; samples positive for BV flora were considered positive.
- Samples with intermediate Nugent interpretations were classified as positive or negative for BV using modified Amsel criteria. Samples positive for ≥20% clue cells and at least 1 of the 2 following criteria were considered Amsel positive: vaginal pH >4.5 and positive whiff test.
- Samples that were unable to be assessed for the Nugent criteria, and samples with indeterminate Nugent interpretation for which a modified Amsel result was not available, were considered to have unknown BV infection status.

Performance characteristics for each sample, with corresponding 2-sided 95% Score confidence intervals (CIs), were estimated relative to the BV infection status.

Of the 1519 symptomatic subjects enrolled, 102 were not evaluable due to withdrawal (n = 17) or unknown BV infection status (n = 85). The remaining 1417 subjects were evaluable for at least one of the sample types. Table 6 shows the demographics of evaluable subjects.

Table 6: Demographics of Evaluable Subjects

Characteristics		Total
Total, N	N	1417
Age (years)	Mean ± SD	34.7 ± 11.11
	Median	33.0
	Range	14–75
Age category (years), n (%)	14–17	4 (0.3)
	18–29	537 (37.9)
	30–39	469 (33.1)
	40–49	235 (16.6)
	>50	172 (12.1)
Ethnicity, n (%)	Asian	67 (4.7)
	Black or African American	731 (51.6)
	White (Hispanic or Latino)	248 (17.5)
	White (Not Hispanic or Latino)	307 (21.7)
	Other[1]	64 (4.5)

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

For the 1417 evaluable subjects, 1413 clinician-collected vaginal swab samples and 1405 patient-collected vaginal swab samples were included in the analyses. The sensitivity and specificity of the Aptima BV Assay for the detection of BV are shown for both sample types overall and by site in Table 7. Assay performance is shown stratified by ethnicity in Table 8, and by clinical condition in Table 9.

Table 7: Performance Characteristics by Collection Site in Symptomatic Women

	Clinician-collected Vaginal Swabs				Patient-collected Vaginal Swabs			
Site	**N**	**Prev (%)**	**Sensitivity % (95% CI)[1]**	**Specificity % (95% CI)[1]**	**N**	**Prev (%)**	**Sensitivity % (95% CI)[1]**	**Specificity % (95% CI)[1]**
All	**1413**	**49.2**	**95.0 (93.1–96.4) 660/695[2]**	**89.6 (87.1–91.6) 643/718[3]**	**1405**	**49.3**	**97.3 (95.8–98.2) 673/692[4]**	**85.8 (83.1–88.2) 612/713[5]**
1	15	40.0	100 (61.0–100) 6/6	100 (70.1–100) 9/9	15	40.0	100 (61.0–100) 6/6	88.9 (56.5–98.0) 8/9
2	5	20.0	100 (20.7–100) 1/1	100 (51.0–100) 4/4	5	20.0	0.0 (0.0–79.3) 0/1	100 (51.0–100) 4/4
3	22	59.1	100 (77.2–100) 13/13	88.9 (56.5–98.0) 8/9	22	59.1	100 (77.2–100) 13/13	88.9 (56.5–98.0) 8/9
4	208	53.4	89.2 (82.0–93.7) 99/111	90.7 (83.3–95.0) 88/97	205	53.7	96.4 (91.0–98.6) 106/110	81.1 (72.0–87.7) 77/95
5	132	39.4	96.2 (87.0–98.9) 50/52	82.5 (72.7–89.3) 66/80	130	40.0	98.1 (89.9–99.7) 51/52	80.8 (70.7–88.0) 63/78
6	71	45.1	90.6 (75.8–96.8) 29/32	89.7 (76.4–95.9) 35/39	71	45.1	100 (89.3–100) 32/32	89.7 (76.4–95.9) 35/39
7	191	66.0	97.6 (93.2–99.2) 123/126	89.2 (79.4–94.7) 58/65	189	65.6	98.4 (94.3–99.6) 122/124	86.2 (75.7–92.5) 56/65
8	1	100.0	100 (20.7–100) 1/1	NC	1	100.0	100 (20.7–100) 1/1	NC
9	102	48.0	87.8 (75.8–94.3) 43/49	88.7 (77.4–94.7) 47/53	102	48.0	95.9 (86.3–98.9) 47/49	83.0 (70.8–90.8) 44/53
10	17	76.5	92.3 (66.7–98.6) 12/13	100 (51.0–100) 4/4	17	76.5	92.3 (66.7–98.6) 12/13	100 (51.0–100) 4/4
11	67	46.3	96.8 (83.8–99.4) 30/31	88.9 (74.7–95.6) 32/36	67	46.3	96.8 (83.8–99.4) 30/31	88.9 (74.7–95.6) 32/36
12	125	28.0	94.3 (81.4–98.4) 33/35	91.1 (83.4–95.4) 82/90	123	29.3	91.7 (78.2–97.1) 33/36	89.7 (81.5–94.5) 78/87
13	68	55.9	100 (90.8–100) 38/38	83.3 (66.4–92.7) 25/30	69	55.1	97.4 (86.5–99.5) 37/38	80.6 (63.7–90.8) 25/31
14	9	44.4	100 (51.0–100) 4/4	80.0 (37.6–96.4) 4/5	9	44.4	100 (51.0–100) 4/4	80.0 (37.6–96.4) 4/5

Table 7: Performance Characteristics by Collection Site in Symptomatic Women (continued)

	Clinician-collected Vaginal Swabs				Patient-collected Vaginal Swabs			
Site	N	Prev (%)	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]	N	Prev (%)	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]
15	4	25.0	100 (20.7–100) 1/1	66.7 (20.8–93.9) 2/3	4	25.0	100 (20.7–100) 1/1	66.7 (20.8–93.9) 2/3
16	29	55.2	93.8 (71.7–98.9) 15/16	84.6 (57.8–95.7) 11/13	29	55.2	100 (80.6–100) 16/16	76.9 (49.7–91.8) 10/13
17	79	45.6	97.2 (85.8–99.5) 35/36	90.7 (78.4–96.3) 39/43	80	45.0	100 (90.4–100) 36/36	88.6 (76.0–95.0) 39/44
18	87	60.9	98.1 (90.1–99.7) 52/53	88.2 (73.4–95.3) 30/34	87	60.9	100 (93.2–100) 53/53	91.2 (77.0–97.0) 31/34
19	68	42.6	100 (88.3–100) 29/29	94.9 (83.1–98.6) 37/39	68	42.6	100 (88.3–100) 29/29	87.2 (73.3–94.4) 34/39
20	36	16.7	66.7 (30.0–90.3) 4/6	100 (88.6–100) 30/30	36	16.7	66.7 (30.0–90.3) 4/6	90.0 (74.4–96.5) 27/30
21	77	54.5	100 (91.6–100) 42/42	91.4 (77.6–97.0) 32/35	76	53.9	97.6 (87.4–99.6) 40/41	88.6 (74.0–95.5) 31/35

CI = confidence interval; **NC** = not calculable; **Prev** = prevalence.

[1] Score CI.

[2] Of the 35 false negatives results, 10 subjects were Nugent intermediates and had BV infection status determined by Amsel criteria, and 15 were negative by Amsel.

[3] Of the 75 false positive results, 46 subjects were Nugent intermediates and had BV infection status determined by Amsel criteria, and 6 were positive by Amsel.

[4] Of the 19 false negative results, 6 subjects were Nugent intermediates and had BV infection status determined by Amsel criteria, and 7 were negative by Amsel.

[5] Of the 101 false positive results, 55 subjects were Nugent intermediates and had BV infection status determined by Amsel criteria, and 9 were positive by Amsel.

Table 8: Performance Characteristics by Ethnicity in Symptomatic Women

Specimen Type	Ethnicity	N	Prev (%)	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]
Clinician-collected Vaginal Swabs	**All**	**1413**	**49.2**	**95.0 (93.1–96.4) 660/695**	**89.6 (87.1–91.6) 643/718**
	Asian	67	31.3	95.2 (77.3–99.2) 20/21	91.3 (79.7–96.6) 42/46
	Black/African-American	729	61.0	95.5 (93.2–97.1) 425/445	89.1 (84.9–92.2) 253/284
	White (Hispanic/Latino)	247	46.2	96.5 (91.3–98.6) 110/114	86.5 (79.6–91.3) 115/133
	White (Not Hispanic/Latino)	306	28.8	88.6 (80.3–93.7) 78/88	91.7 (87.3–94.7) 200/218
	Other[2]	64	42.2	100 (87.5–100) 27/27	89.2 (75.3–95.7) 33/37

Table 8: Performance Characteristics by Ethnicity in Symptomatic Women (continued)

Specimen Type	Ethnicity	N	Prev (%)	Sensitivity % (95% CI)[1]	Specificity % (95% CI)[1]
Patient-collected Vaginal Swabs	**All**	**1405**	**49.3**	**97.3 (95.8–98.2) 673/692**	**85.8 (83.1–88.2) 612/713**
	Asian	65	30.8	95.0 (76.4–99.1) 19/20	86.7 (73.8–93.7) 39/45
	Black/African-American	727	61.2	97.5 (95.6–98.6) 434/445	84.8 (80.1–88.5) 239/282
	White (Hispanic/Latino)	246	45.9	99.1 (95.2–99.8) 112/113	83.5 (76.2–88.8) 111/133
	White (Not Hispanic/Latino)	303	28.7	93.1 (85.8–96.8) 81/87	87.5 (82.4–91.3) 189/216
	Other[2]	64	42.2	100 (87.5–100) 27/27	91.9 (78.7–97.2) 34/37

CI = confidence interval; **Prev** = prevalence.
[1] Score CI.
[2] Includes patient-reported other, mixed, and unknown ethnicities.

Table 9: Performance Characteristics by Clinical Condition in Symptomatic Women

Collection Type	Clinical Condition	N[1]	Prev (%)	Sensitivity % (95% CI)[2]	Specificity % (95% CI)[2]
Clinician-collected Vaginal Swabs	**All**	**1413**	**49.2**	**95.0 (93.1–96.4) 660/695**	**89.6 (87.1–91.6) 643/718**
	Use of antibiotics	3	33.3	100 (20.7–100) 1/1	100 (34.2–100) 2/2
	Use of antifungals	8	25.0	100 (34.2–100) 2/2	100 (61.0–100) 6/6
	Use of estrogen therapy	2	0.0	NC	100 (34.2–100) 2/2
	Recurrent symptoms of vaginitis in the last 12 months	832	49.8	95.2 (92.7–96.9) 394/414	88.8 (85.4–91.4) 371/418
	Unprotected intercourse in the last 24 hours	94	57.4	92.6 (82.4–97.1) 50/54	85.0 (70.9–92.9) 34/40
	Pregnant	20	45.0	100 (70.1–100) 9/9	100 (74.1–100) 11/11
	With Menses	111	46.8	96.2 (87.0–98.9) 50/52	86.4 (75.5–93.0) 51/59
	Without Menses	1177	50.6	95.6 (93.7–97.0) 569/595	89.3 (86.6–91.6) 520/586
	Post-menopausal	125	38.4	85.4 (72.8–92.8) 41/48	93.5 (85.7–97.2) 72/77

Table 9: Performance Characteristics by Clinical Condition in Symptomatic Women (continued)

Collection Type	Clinical Condition	N[1]	Prev (%)	Sensitivity % (95% CI)[2]	Specificity % (95% CI)[2]
Patient-collected Vaginal Swabs	**All**	**1405**	**49.3**	**97.3 (95.8–98.2) 673/692**	**85.8 (83.1–88.2) 612/713**
	Use of antibiotics	3	33.3	100 (20.7–100) 1/1	100 (34.2–100) 2/2
	Use of antifungals	8	25.0	100 (34.2–100) 2/2	100 (61.0–100) 6/6
	Use of estrogen therapy	2	0.0	NC	100 (34.2–100) 2/2
	Recurrent symptoms of vaginitis in the last 12 months	828	49.9	98.1 (96.2–99.0) 405/413	85.1 (81.3–88.2) 353/415
	Unprotected intercourse in the last 24 hours	94	57.4	98.1 (90.2–99.7) 53/54	75.0 (59.8–85.8) 30/40
	Pregnant	20	45.0	100 (70.1–100) 9/9	90.9 (62.3–98.4) 10/11
	With Menses	109	47.7	100 (93.1–100) 52/52	84.2 (72.6–91.5) 48/57
	Without Menses	1175	50.6	97.5 (95.9–98.5) 579/594	85.4 (82.3–88.0) 496/581
	Post-menopausal	121	38.0	91.3 (79.7–96.6) 41/46	90.7 (82.0–95.4) 68/75

CI = confidence interval; **NC** = not calculable; **Prev** = prevalence.

[1] Subjects may report multiple clinical conditions; sum of subject numbers in all subgroups does not equal the total number of subjects.

[2] Score CI.

The detection of an imbalance in the vaginal microbiome is relevant for treatment decisions. Although the Aptima BV Assay is not intended for use in testing samples from asymptomatic women, organisms associated with BV infection and detected by the Aptima BV Assay also may be present in asymptomatic women. Presence of the Aptima BV Assay bacterial targets was assessed in clinician-collected vaginal swab samples from 172 asymptomatic women. A summary of the BV detection rates, as determined by the Aptima BV Assay, is shown in Table 10 for the multicenter study overall and by ethnicity.

Table 10: Positivity as Determined by the Aptima BV Assay in Asymptomatic Women

Ethnicity	% Positivity (# positive/# tested with valid results)
All	**40.7% (70/172)**
Asian	40.0% (2/5)
Black/African American	52.0% (39/75)
White (Hispanic/Latino)	43.9% (18/41)
White (Not Hispanic/Latino)	15.9% (7/44)
Other[1]	57.1% (4/7)

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

A total of 3175 clinician- and patient-collected samples from symptomatic and asymptomatic subjects were processed in valid Aptima BV Assay runs to establish clinical performance. Of

these, 0.7% had initial invalid results. Upon retest, 0.1% remained invalid and were excluded from all analyses.

Panther System Analytical Performance

Analytical Sensitivity

The analytical sensitivity (Limit of Detection or LoD) and BV positivity limits of the Aptima BV Assay were determined by testing a series of panels consisting of *L. crispatus, L. gasseri, L. jensenii, G. vaginalis,* or *A. vaginae* cell lysates diluted into SVSM. A minimum of 20 replicates of each panel member were tested with each of two reagent lots for a minimum of 40 replicates per panel member. The predicted detection limits for each organism calculated using Probit analysis are shown in Table 11.

Table 11: Limit of Detection of the Aptima BV Assay

Organism	Predicted Detection Limit	CFU/mL
A. vaginae	95%	290[1]
G. vaginalis	95%	55[1]
L. crispatus	95%	143
L. gasseri	95%	2,207
L. jensenii	95%	10

CFU = colony-forming units.

[1] Predicted BV positivity limits (C_{95}) for *A. vaginae* and *G. vaginalis* in the Aptima BV Assay are approximately 5.10 log CFU/mL and 4.86 log CFU/mL, respectively.

Analytical Inclusivity

Five strains of each target organism were tested using lysate targeting 3X C_{95} for *G. vaginalis* and *A. vaginae*, and 3X LoD for Lactobacillus species (*L. crispatus*, *L. gasseri,* and *L. jensenii*) in SVSM. The Aptima BV Assay was BV positive for all five strains of *G. vaginalis* and *A. vaginae* at 3X C_{95}. All five strains of *L. crispatus* and *L. gasseri* were detected at 3X LoD. Three of the five strains of *L. jensenii* were detected at 3X LoD, and the remaining two strains at 10X LoD.

Cross-Reactivity and Microbial Interference

Cross-reactivity and microbial interference with the Aptima BV Assay were evaluated in the presence of non-targeted organisms. A panel consisting of 62 organisms (Table 12) was tested in SVSM in the absence or in the presence of *L. crispatus* at 3X LoD, *G. vaginalis* at 3X C_{95}, or *A. vaginae* at 3X C_{95}. No cross-reactivity or microbial interference was observed for any of the 62 organisms tested in the Aptima BV Assay at the concentrations listed in Table 12.

Table 12: Cross-Reactivity and Microbial Interference Panel

Microorganism	Concentration	Microorganism	Concentration
Acinetobacter lwoffii	$1x10^6$ CFU/mL	Herpes simplex virus I	$1x10^4$ TCID50/mL
Actinomyces israelii	$1x10^6$ CFU/mL	Herpes simplex virus II	$1x10^4$ TCID50/mL
Alcaligenes faecalis	$1x10^6$ CFU/mL	HIV	$1x10^5$ copies/mL
Atopobium minutum	$1x10^6$ CFU/mL	*Klebsiella pneumoniae*	$1x10^6$ CFU/mL
Atopobium parvulum	$1x10^6$ CFU/mL	*Lactobacillus acidophilus*	$1x10^3$ CFU/mL[2]
Atopobium rimae	$1x10^6$ CFU/mL	*Lactobacillus iners*	$1x10^6$ CFU/mL

Table 12: Cross-Reactivity and Microbial Interference Panel (continued)

Microorganism	Concentration	Microorganism	Concentration
Bacteroides fragilis	$1x10^6$ CFU/mL	*Lactobacillus mucosae*	$1x10^6$ CFU/mL
Bifidobacterium adolescentis	$1x10^6$ CFU/mL	*Leptotrichia buccalis*	$1x10^6$ CFU/mL
Bifidobacterium breve	$1x10^6$ CFU/mL	*Listeria monocytogenes*	$1x10^6$ CFU/mL
BVAB-1[1]	$1x10^6$ copies/mL	*Megasphaera Type 1*[1]	$1x10^6$ copies/mL
BVAB-2[1]	$1x10^6$ copies/mL	*Mobiluncus curtisii*	$1x10^6$ CFU/mL
Campylobacter jejuni	$1x10^6$ CFU/mL	*Mycoplasma genitalium*	$1x10^6$ CFU/mL
Candida albicans	$1x10^6$ CFU/mL	*Mycoplasma hominis*	$1x10^6$ CFU/mL
Candida dubliniensis	$1x10^6$ CFU/mL	*Neisseria gonorrhoeae*	$1x10^6$ CFU/mL
Candida glabrata	$1x10^6$ CFU/mL	*Pentatrichomonas hominis*	$1x10^5$ cells/mL
Candida krusei	$1x10^6$ CFU/mL	*Peptostreptococcus magnus*	$1x10^6$ CFU/mL
Candida lusitaniae	$1x10^6$ CFU/mL	*Pichia fermentans*	$1x10^6$ CFU/mL
Candida orthopsilosis	$1x10^6$ CFU/mL	*Prevotella bivia*	$1x10^6$ CFU/mL
Candida parapsilosis	$1x10^6$ CFU/mL	*Propionibacterium acnes*	$1x10^6$ CFU/mL
Candida tropicalis	$1x10^6$ CFU/mL	*Proteus vulgaris*	$1x10^6$ CFU/mL
Chlamydia trachomatis	$1x10^6$ IFU/mL	SiHa cells	$1x10^4$ cells/mL
Clostridium difficile	$1x10^6$ CFU/mL	*Sneathia amnii*	$1x10^6$ CFU/mL
Corynebacterium genitalium	$1x10^6$ CFU/mL	*Staphylococcus aureus*	$1x10^6$ CFU/mL
Cryptococcus neoformans	$1x10^6$ CFU/mL	*Staphylococcus epidermidis*	$1x10^6$ CFU/mL
Eggerthella lenta	$1x10^6$ CFU/mL	*Streptococcus agalactiae*	$1x10^6$ CFU/mL
Enterobacter cloacae	$1x10^6$ CFU/mL	*Streptococcus pyogenes*	$1x10^6$ CFU/mL
Enterococcus faecalis	$1x10^6$ CFU/mL	*Treponema pallidum*[1]	$1x10^6$ copies/mL
Escherichia coli	$1x10^6$ CFU/mL	*Trichomonas tenax*	$1x10^5$ cells/mL
Fusobacterium nucleatum	$1x10^6$ CFU/mL	*Trichomonas vaginalis*	$1x10^5$ cells/mL
Haemophilus ducreyi	$1x10^6$ CFU/mL	*Ureaplasma parvum*	$1x10^6$ CFU/mL
HeLa cells	$1x10^4$ cells/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] *Lactobacillus acidophilus* affects BV positivity at $1x10^4$ CFU/mL or higher.

Interference

Potentially interfering substances were tested in the Aptima BV Assay. Panels were built in SVSM and evaluated for potential effects on assay sensitivity and specificity. Sensitivity performance was evaluated separately for *L. crispatus* by spiking lysate at 3X LoD, and for *G. vaginalis* and *A. vaginae* by spiking lysate at 3X C_{95}. 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 13.

Table 13: Interfering Substances Panel

Substance	Final Concentration[1]
Whole Blood	5% V/V
Leukocytes	$1x10^6$ cells/mL
Mucus[2]	1.5% V/V

Table 13: Interfering Substances Panel (continued)

Substance	Final Concentration[1]
Seminal Fluid	5% V/V
Contraceptive Foam	5% W/V
Contraceptive Film	5% W/V
Tioconazole[3]	1% 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[4]	0.4% W/V
Lubricant	5% V/V
Spermicide	5% W/V
Anti-fungal	5% W/V
Deodorant/Spray	5% W/V
Glacial Acetic Acid	5% 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] Interference was observed with mucus at ≥2% V/V and not observed at 1.5% V/V.

[3] Interference was observed with tioconazole 6.5% ointment at 5% W/V and not observed at 1% W/V.

[4] Interference was observed with vaginal moisturizing gel at ≥0.5% W/V and not observed at 0.4% W/V.

Within Laboratory Precision

Within Lab Precision was evaluated on three Panther Systems at one site. Three operators performed testing across 21 days and three reagent lots. Each operator performed two runs per day using an 11 member panel. Each run consisted of three replicates of each panel member.

The panel members were made using SVSM negative for *Lactobacillus* species, *G. vaginalis*, and *A. vaginae*. Ten panel members contained cell lysates of at least 1 of the following organisms: *L. crispatus*, *L. jensenii*, *G. vaginalis*, or *A. vaginae*; different bacterial combinations were prepared to represent the variety of targeted BV organism combinations present in vaginal specimens. Ten panel members targeted BV Negative (<5% BV Positive), BV High Negative (20–80% BV positive), BV Low Positive (≥95% BV positive) and BV Moderate Positive (100% BV positive) results. One negative panel member contained matrix with no added target analytes.

BV percent positive results for each panel are presented in Table 14. Signal variability (TTime) of the Aptima BV Assay was calculated for each target in analyte positive panel

members. Variability calculated between operators, between instruments, between days, between lots, between runs, within run, and overall, is shown in Table 15 through Table 17.

Table 14: BV Positivity of Precision Panels

Panel Description	BV Positive/ Total n	Expected BV Positivity	BV Positivity (95% CI)
SVSM	0/168	0%	0 (0.0–1.6)
L. crispatus, A. vaginae BV Negative	0 /168	<5%	0 (0.0–1.6)
L. crispatus, G. vaginalis BV High Negative	76 /168	20–80%	45.2 (37.9–52.8)
L. crispatus, G. vaginalis, A. vaginae BV High Negative	131/165[1]	20–80%	79.4 (72.6–84.9)
G. vaginalis BV Low Positive	168/168	≥95%	100 (98.4–100.0)
A. vaginae BV Low Positive	168/168	≥95%	100 (98.4–100.0)
L. jensenii, A. vaginae BV Low Positive	168/168	≥95%	100 (98.4–100.0)
G. vaginalis, A. vaginae BV Low Positive	168/168	≥95%	100 (98.4–100.0)
L. crispatus, G. vaginalis, A. vaginae BV Low Positive	168/168	≥95%	100 (98.4–100.0)
G. vaginalis BV Mod Positive	168/168	100%	100 (98.4–100.0)
A. vaginae BV Mod Positive	168/168	100%	100 (98.4–100.0)

[1] Three invalid results were excluded from the analysis.

Table 15: Signal Variability of Lactobacillus Panel Members

Panel Description	N	Mean TTime[1]	Between Operators		Between Instruments		Between Days		Between Lots		Between Runs		Within Run		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
L. crispatus BV Negative[2]	168	19.87	0.10	0.49	0.16	0.80	0.14	0.71	1.03	5.18	0.17	0.09	0.18	0.93	1.08	5.46
L. crispatus BV High Negative[2]	168	23.95	0.11	0.47	0.12	0.52	0.19	0.79	1.22	5.11	0.18	0.77	0.28	1.15	1.29	5.40
L. crispatus BV High Negative[3]	165[4]	22.40	0.09	0.40	0.17	0.74	0.20	0.87	1.22	5.47	0.09	0.39	0.27	1.21	1.29	5.74
L. jensenii BV Low Positive[2]	168	24.80	0.10	0.38	0.14	0.57	0.14	0.57	1.33	5.35	0.17	0.69	0.25	1.01	1.38	5.56
L. crispatus BV Low Positive[3]	168	23.51	0.15	0.63	0.09	0.40	0.17	0.73	1.36	5.77	0.10	0.44	0.31	1.31	1.42	6.02

CV = coefficient of variation; **SD** = standard deviation; **TTime** = threshold time.

[1] TTime is shown for *Lactobacillus* only.

[2] Panel member contains 2 different organisms: results are shown for only the *Lactobacillus* component.

[3] Panel member contains 3 different organisms: results are shown for only the *Lactobacillus* component.

[4] Three invalid results were excluded from the analysis.

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.*

Table 16: Signal Variability of G. vaginalis Panel Members

Panel Description	N	Mean TTime[1]	Between Operators		Between Instruments		Between Days		Between Lots		Between Runs		Within Run		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
G. vaginalis BV High Negative[2]	168	17.11	0.00	0.00	0.18	1.08	0.17	0.99	0.47	2.75	0.17	0.96	0.16	0.94	0.58	3.39
G. vaginalis BV High Negative[3]	165[4]	15.71	0.00	0.00	0.19	1.19	0.18	1.12	0.48	3.05	0.11	0.72	0.12	0.79	0.57	3.62
G. vaginalis BV Low Positive	168	15.80	0.00	0.00	0.16	1.00	0.14	0.89	0.43	2.70	0.15	0.97	0.15	0.92	0.52	3.30
G. vaginalis BV Mod Positive	168	14.46	0.00	0.00	0.17	1.18	0.05	0.35	0.38	2.63	0.16	1.09	0.18	1.25	0.48	3.35
G. vaginalis BV Low Positive[2]	168	15.01	0.00	0.00	0.14	0.93	0.14	0.91	0.40	2.67	0.16	1.08	0.13	0.86	0.49	3.28
G. vaginalis BV Low Positive[3]	168	14.06	0.00	0.00	0.16	1.11	0.15	1.09	0.39	2.75	0.14	0.99	0.16	1.16	0.49	3.51

CV = coefficient of variation; **Mod** = moderate; **SD** = standard deviation; **TTime** = threshold time.

[1] TTime is shown for *G. vaginalis* only.

[2] Panel member contains 2 different organisms: results are shown for only the *G. vaginalis* component.

[3] Panel member contains 3 different organisms: results are shown for only the *G. vaginalis* component.

[4] Three invalid results were excluded from the analysis.

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.*

Table 17: Signal Variability of A. vaginae Panel Members

Panel Description	N	Mean TTime[1]	Between Operators		Between Instruments		Between Days		Between Lots		Between Runs		Within Run		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
A. vaginae BV Negative[2]	168	18.20	0.02	0.11	0.25	1.36	0.15	0.84	0.58	3.17	0.19	1.02	0.19	1.05	0.70	3.84
A. vaginae BV High Negative[3]	165[4]	16.56	0.00	0.00	0.25	1.53	0.18	1.11	0.56	3.38	0.13	0.79	0.12	0.70	0.67	4.02
A. vaginae BV Low Positive	168	15.11	0.00	0.00	0.19	1.25	0.15	0.97	0.51	3.40	0.12	0.82	0.12	0.78	0.59	3.92
A. vaginae BV Low Positive[2]	168	15.13	0.00	0.00	0.20	1.30	0.12	0.80	0.51	3.34	0.14	0.89	0.16	1.07	0.59	3.92
A. vaginae BV Mod Positive	168	14.13	0.08	0.54	0.21	1.50	0.17	1.21	0.51	3.63	0.08	0.57	0.20	1.40	0.62	4.41
A. vaginae BV Low Positive[2]	168	15.78	0.03	0.16	0.17	1.09	0.10	0.65	0.50	3.17	0.16	1.00	0.12	0.75	0.57	3.64
A. vaginae BV Low Positive[3]	168	15.61	0.00	0.00	0.23	1.47	0.15	0.94	0.51	3.29	0.10	0.66	0.18	1.15	0.62	3.95

CV = coefficient of variation; **Mod** = moderate; **SD** = standard deviation; **TTime** = threshold time.

[1] TTime is shown for *A. vaginae* only.

[2] Panel member contains 2 different organisms: results are shown for only the *A. vaginae* component.

[3] Panel member contains 3 different organisms: results are shown for only the *A. vaginae* component.

[4] Three invalid results were excluded from the analysis.

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.*

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Serious incidents occurring in relation to the device in the European Union should be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

AW-31481-001 Rev. 002

2025-05

Revision History	Date	Description
AW-31481 Rev. 002	May 2025	• Removed certain subsection titles in the Panther System Clinical Performance section for clarity of text. • Implemented routine administrative updates.
AW-31481 Rev. 001	December 2024	• Created a global, IVDR-compliant Aptima BV Assay IFU AW-31481 Rev. 001 based on AW-31481-REG Rev. 002 to provide commercialization support for a 250-test kit (Cat. No. PRD-07662). • Implemented routine administrative updates.