February 9, 2022

Cepheid
Wei Zhang
Senior Regulatory Affairs Specialist
904 Caribbean Drive
Sunnyvale, California 94089

Re: K212213
Trade/Device Name: Xpert Xpress MVP, GeneXpert Dx System, GeneXpert Infinity System
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: July 14, 2021
Received: July 15, 2021

Dear Wei Zhang:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Maria Ines Garcia
Assistant 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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

Device Name

Indications for Use *(Describe)*

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Section 5

510(k) Summary
for
Xpert Xpress MVP

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5.0 510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (425) 420-8349 Fax number: (408) 541-4192
Contact:	Wei Zhang, PhD RAC
Date of Preparation:	February 8, 2022
Device:	
Trade name:	Xpert® Xpress MVP
Common name:	Xpert Xpress MVP
Type of Test:	Qualitative real-time polymerase chain reaction (PCR) and detection test
Regulation number, Classification name, Product code Definition	21 CFR 866.3975, Vaginitis and Bacterial Vaginosis Nucleic Acid Detection System, PQA 21 CFR 866.3860, *Trichomonas vaginalis* Nucleic Acid Amplification Test System, OUY 21 CFR 862.2570, Real Time Nucleic Acid Amplification System, OOI
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes
Predicate Device Assay:	BD MAX Vaginal Panel (K191957)

5.1 Device Description

The Xpert® Xpress MVP test is an automated *in vitro* diagnostic test for qualitative detection of DNA targets from anaerobic bacteria associated with bacterial vaginosis, *Candida* species associated with vulvovaginal candidiasis, and *Trichomonas vaginalis*, the agent of trichomoniasis. The Xpert Xpress MVP test is performed on GeneXpert Instrument Systems.

The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and detection of the target sequences in simple or complex samples using real-time PCR assays. The systems consist of an instrument, computer, and preloaded software for running tests and viewing the results. The systems require the use of single-use disposable cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized.

The Xpert Xpress MVP test includes reagents for the detection of DNA from BV organisms, *Candida* species, and *Trichomonas vaginalis* from vaginal swab samples. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge utilized by the GeneXpert System instrument. The SPC is present to control for adequate processing of the sample and to monitor for the presence of potential inhibitor(s) in the PCR reaction. The SPC also ensures that the PCR reaction conditions (temperature and time) are appropriate for the amplification reaction and that the PCR reagents are functional. The PCC verifies reagent rehydration, PCR tube filling, and confirms that all reaction components are present in the cartridge including monitoring for probe integrity and dye stability.

The Xpert Xpress MVP test is designed for use with the following specimens collected from symptomatic individuals: self-collected vaginal swabs (collected in a clinical setting) and clinician-collected vaginal swabs. The swab transport reagent included in the Xpert Swab Specimen Collection Kit is designed to collect and preserve patient specimens to allow transport to the laboratory prior to analysis with the Xpert Xpress MVP test.

5.2 Device Intended Use

The Xpert Xpress MVP test, performed on the GeneXpert Instrument Systems, is an automated qualitative *in vitro* diagnostic test for the detection of DNA targets from anaerobic bacteria associated with bacterial vaginosis (BV), *Candida* species associated with vulvovaginal candidiasis, and *Trichomonas vaginalis*. The Xpert Xpress MVP test uses clinician-collected and self-collected vaginal swabs (collected in a clinical setting) from patients who are symptomatic for vaginitis/vaginosis. The Xpert Xpress MVP 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:

- Organisms associated with bacterial vaginosis (detected organisms not reported individually)
  - *Atopobium* spp. (*Atopobium vaginae, Atopobium* novel species CCUG 55226)
  - Bacterial Vaginosis-Associated Bacterium 2 (BVAB2)
  - *Megasphaera*-1
- *Candida* spp. (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*, species not differentiated)
- *Candida glabrata/Candida krusei* (species not differentiated)
- *Trichomonas vaginalis*

The Xpert Xpress MVP test is intended to aid in the diagnosis of vaginal infections in women with a clinical presentation consistent with bacterial vaginosis, vulvovaginal candidiasis, or trichomoniasis.

5.3 Substantial Equivalence

The Xpert Xpress MVP test is substantially equivalent to the BD MAX Vaginal Panel [510(k) # K191957].

The following tables compare Xpert Xpress MVP to BD MAX Vaginal Panel (K191957). Table 5-1 shows similarities between the new device and the predicate.

Table 5-1: Similarities between New Device and Predicate Device

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® Xpress MVP	**BD MAX Vaginal Panel (K191957)**
Regulation	Same	**21CFR 866.3975** Device that detects nucleic acid sequences from microorganisms associated with vaginitis and bacterial vaginosis
Product Code	Same	PQA Vaginitis and bacterial vaginosis nucleic acid detection system
Device Class	Same	II
Intended Use	The Xpert® Xpress MVP test, performed on the GeneXpert® Instrument Systems, is an automated qualitative *in vitro* diagnostic test for the detection of DNA targets from anaerobic bacteria associated with bacterial vaginosis (BV), *Candida* species associated with vulvovaginal candidiasis, and *Trichomonas vaginalis*. The Xpert Xpress MVP test uses clinician-collected and self-collected vaginal swabs (collected in a clinical setting) from patients who are symptomatic for vaginitis/ vaginosis. The Xpert Xpress MVP 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: • Organisms associated with bacterial vaginosis (detected organisms not reported individually) ○ *Atopobium* spp. (*Atopobium vaginae, Atopobium* novel species CCUG 55226) ○ Bacterial Vaginosis-Associated Bacterium 2 (BVAB2)	The BD MAX Vaginal Panel performed on the BD MAX 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*

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® Xpress MVP	**BD MAX Vaginal Panel (K191957)**
	○ *Megasphaera*-1 • *Candida* spp. (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*, species not differentiated) • *Candida glabrata*/*Candida krusei* (species not differentiated) • *Trichomonas vaginalis* The Xpert Xpress MVP test is intended to aid in the diagnosis of vaginal infections in women with a clinical presentation consistent with bacterial vaginosis, vulvovaginal candidiasis, or trichomoniasis.	○ 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.
Laboratory Users	Same	CLIA Moderate Complexity
Specimen Type	Same	Clinician and patient-collected female vaginal swabs
Assay Technology	Same	Real-Time PCR
Single Use	Same	Yes
Automated Extraction, detection and result interpretation	Same	Yes
Assay Results	Same	Qualitative

Table 5-2 shows the differences between the new device and the predicate.

Table 5-2: Differences between New Device and Predicate Device

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® Xpress MVP	**BD MAX Vaginal Panel (K191957)**
Organisms Detected	• Organisms associated with bacterial vaginosis (detected organisms not reported individually) ○ *Atopobium* spp. (*Atopobium vaginae*, *Atopobium* novel species CCUG 55226) ○ Bacterial Vaginosis-Associated Bacterium 2 (BVAB2)	• 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)

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® Xpress MVP	**BD MAX Vaginal Panel (K191957)**
	○ *Megasphaera*-1 • *Candida* spp. (*C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*, species not differentiated) • *Candida glabrata*/*Candida krusei* (species not differentiated) • *Trichomonas vaginalis*	○ *Megasphaera*-1 • *Candida* spp. (*C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*) • *Candida glabrata* • *Candida krusei* • *Trichomonas vaginalis*
Instrument Systems	Cepheid GeneXpert Instrument Systems	BD MAX System
Collection Device	Cepheid Xpert Swab Specimen Collection kit	MAX UVE Specimen Collection Kit
Time to Result	Single test Within 60 minutes	Batch test ~ 2-4 hours

The Xpert Xpress MVP test has the same general intended use as the predicate device and technological characteristics as the predicate device. The performance of the Xpert Xpress MVP test was evaluated in a multi-site clinical study. The results of the study demonstrated that the performance of the Xpert Xpress MVP test is substantially equivalent to the predicate device. The differences between the Xpert Xpress MVP test and the predicate device do not raise different questions of safety and effectiveness.

5.4 Non-Clinical Study

Analytical Sensitivity

The analytical sensitivity (Limit of Detection, LoD) of the Xpert Xpress MVP test was determined by preparing dilutions for each of the target organisms detected by the test. The LoD is defined as the lowest concentration of organism sample that can be reproducibly distinguished from negative samples with 95% confidence. The near cut-off concentrations for the BV organisms were also determined. The near cut-off concentration for the BV organisms is defined as the lowest concentrations of *Atopobium vaginae* and *Megasphaera*-1, or *A. vaginae* and BVAB2, or *A. vaginae* and *Megasphaera*-1 and BVAB2, or *A. vaginae* in the absence of *Megasphaera*-1 and BVAB2 that result in BV POSITIVE test results and can be reproducibly distinguished from negative samples with a 95% confidence level. Positive samples were prepared by inoculating simulated vaginal swab matrix with each representative strain or quantified stock of plasmid DNA containing the cloned genomic target of BVAB2 or *Megasphaera*-1. Replicates of 20 were evaluated at a minimum of five concentrations for each of the target organisms. The LoD and/or near cut-off concentrations for the target organisms were estimated by probit analysis or by the classical approach using a 95% hit rate. The LoD for each *Candida* spp. and *Trichomonas vaginalis* strain was verified in natural clinical vaginal swab matrix and simulated vaginal swab matrix. The LoD and near cut-off concentrations for each BV organism were verified in simulated vaginal swab matrix. The verified LoD and near cut-off concentrations for Xpert Xpress MVP targets are presented in Table 5-3.

Table 5-3: Verified LoD and Near Cut-off concentrations for Xpert Xpress MVP

Organism	Verified LoD
Atopobium vaginae	32 CFU/mL
BVAB2 (plasmid DNA)	50 copies/mL
Megasphaera-1 (plasmid DNA)	338 copies/mL
Candida albicans	30 CFU/mL
Candida tropicalis	750 CFU/mL
Candida parapsilosis	1,339 CFU/mL
Candida dubliniensis	1,316 CFU/mL
Candida glabrata	20 CFU/mL
Candida krusei	656 CFU/mL
Trichomonas vaginalis	5 cells/mL
BV Organism	**Verified Near Cut-off Concentration**
Atopobium vaginae (in the **absence** of *Megasphaera*-1 and BVAB2)	320,000 CFU/mL
Atopobium vaginae (in the **presence** of *Megasphaera*-1 and/or BVAB2)	2,750 CFU/mL
BVAB2 plasmid DNA	50 copies/mL
Megasphaera-1 plasmid DNA	390 copies/mL

Analytical Reactivity (Inclusivity)

The analytical reactivity of the Xpert Xpress MVP test was determined with 5 strains of *Candida albicans*, 5 strains of *Candida dubliniensis*, 5 strains of *Candida tropicalis*, 5 strains of *Candida parapsilosis*, 5 strains of *Candida glabrata*, 5 strains of *Candida krusei*, 11 strains of *Atopobium* spp. (*Atopobium vaginae* and/or *Atopobium* novel species CCUG 55226), and 10 strains of *Trichomonas vaginalis* that were diluted in simulated vaginal swab matrix at 3× LoD. Each *Atopobium* spp. strain was also evaluated at 3× near cut-off concentrations diluted in simulated vaginal swab matrix in the absence or presence of BVAB2 and/or *Megasphaera*-1 DNA to confirm the correct BV POSITIVE test results were reported.

The Xpert Xpress MVP test correctly identified 46 of 51 strains upon initial testing at 3× LoD. Two strains of *Atopobium vaginae* tested at 3× LoD and three strains of *Candida albicans* tested at 3× LoD were not detected and were tested at higher concentrations to determine the minimum concentration sufficient for detection. One *Atopobium vaginae* strain was detected at ~4× LoD and the other strain was detected at ~12× LoD. One *Candida albicans* strain was detected at ~4× LoD and the other two *Candida albicans* strains were detected at ~20× LoD.

For near cut-off concentration of *Atopobium* spp. in the absence of *Megasphaera*-1 and BVAB2, the Xpert Xpress MVP test correctly reported BV POSITIVE test result for 7 of the 11 strains upon initial testing at 3× near cut-off concentration. Four strains did not meet acceptance criteria and were further tested to determine the minimum concentration sufficient for reporting BV POSITIVE test result. One *Atopobium* spp. strain reported BV POSITIVE at ~4×, two strains at ~6×, and one strain at ~12× near cut-off concentration.

For the near cut-off concentration of *Atopobium* spp. in the presence of *Megasphaera*-1 and/or BVAB2, the Xpert Xpress MVP test correctly reported BV POSITIVE test result for 7 of the 11 strains upon initial testing at 3× near cut-off concentration. Four strains did not meet acceptance criteria and were further tested to determine the minimum concentration sufficient for reporting BV POSITIVE test result. Two *Atopobium* spp. strains reported BV POSITIVE at ~4×, one strain at ~6×, and one strain at ~7× near cut-off concentration. The analytical reactivity result summary is presented in Table 5-4.

Table 5-4: Analytical Reactivity of the Xpert Xpress MVP Test

Organism	Strain	Concentration	Result			
			BV	Candida group	Candida glab-krus	TV
Negative Control			Negative	Not Detected	Not Detected	Not Detected
Atopobium spp. LoD (Below the near cut-off concentrations and not generating BV POSITIVE result) [a]	CCUG 39382	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 42099	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 43049	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 44061	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 44116	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 44125	120 CFU/mL [b]	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 44156	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected

	CCUG 44258	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 48515	400 CFU/mL [c]	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 55227	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
	CCUG 55226	96 CFU/mL	pos [a]	Not Detected	Not Detected	Not Detected
Atopobium spp. In the **absence** of *Megasphaera*-1 and BVAB2	CCUG 39382	9.6×10^5 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 42099	9.6×10^5 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 43049	9.6×10^5 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44061	9.6×10^5 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44116	9.6×10^5 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44125	1.2×10^6 CFU/mL [d]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44156	2.0×10^6 CFU/mL [e]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44258	9.6×10^5 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 48515	4.0×10^6 CFU/mL [f]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55227	9.6×10^5 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55226	2.0×10^6 CFU/mL [g]	Positive	Not Detected	Not Detected	Not Detected
Atopobium spp. In the **presence** of BVAB2	CCUG 39382	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 42099	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 43049	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44061	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44116	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44125	10,000 CFU/mL [h]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44156	17,000 CFU/mL [i]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44258	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 48515	17,000 CFU/mL [j]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55227	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55226	10,000 CFU/mL [k]	Positive	Not Detected	Not Detected	Not Detected
Atopobium spp. In the **presence** of *Megasphaera*-1	CCUG 39382	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 42099	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 43049	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44061	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44116	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44125	10,000 CFU/mL [h]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44156	17,000 CFU/mL [i]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44258	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 48515	20,000 CFU/mL [j]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55227	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55226	10,000 CFU/mL [k]	Positive	Not Detected	Not Detected	Not Detected
Atopobium spp.	CCUG 39382	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 42099	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected

In the **presence** of *Megasphaera*-1 and BVAB2	CCUG 43049	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44061	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44116	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44125	10,000 CFU/mL [h]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44156	17,000 CFU/mL [i]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 44258	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 48515	17,000 CFU/mL [j]	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55227	8,250 CFU/mL	Positive	Not Detected	Not Detected	Not Detected
	CCUG 55226	10,000 CFU/mL [k]	Positive	Not Detected	Not Detected	Not Detected
Candida albicans	ATCC 38289	120 CFU/mL [l]	Negative	Detected	Not Detected	Not Detected
	ATCC 62376	600 CFU/mL [m]	Negative	Detected	Not Detected	Not Detected
	ATCC 96113	90 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 60193	90 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 753	600 CFU/mL [n]	Negative	Detected	Not Detected	Not Detected
Candida dubliniensis	ATCC MYA-179	3,948 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC MYA-577	3,948 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC MYA-646	3,948 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC MYA-580	3,948 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC MYA-581	3,948 CFU/mL	Negative	Detected	Not Detected	Not Detected
Candida tropicalis	ATCC 34139	2,250 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 90874	2,250 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 204318	2,250 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC MYA-2733	2,250 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC MYA-277	2,250 CFU/mL	Negative	Detected	Not Detected	Not Detected
Candida parapsilosis	ATCC 7330	4,017 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 60548	4,017 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 90875	4,017 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 96139	4,017 CFU/mL	Negative	Detected	Not Detected	Not Detected
	ATCC 96140	4,017 CFU/mL	Negative	Detected	Not Detected	Not Detected
Candida glabrata	ATCC 32312	60 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC 32554	60 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC 15126	60 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC 2001	60 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC MYA-276	60 CFU/mL	Negative	Not Detected	Detected	Not Detected
Candida krusei	ATCC 28870	1,968 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC 32672	1,968 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC 90878	1,968 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC 200917	1,968 CFU/mL	Negative	Not Detected	Detected	Not Detected
	ATCC 201748	1,968 CFU/mL	Negative	Not Detected	Detected	Not Detected

Trichomonas vaginalis	ATCC 30184	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 30187	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 30238*	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 30240	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 30245	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 50139	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 50141	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 50167	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC 50183	15 cells/mL	Negative	Not Detected	Not Detected	Detected
	ATCC PRA-95	15 cells/mL	Negative	Not Detected	Not Detected	Detected

[a] The LoD for *Atopobium vaginae* is for information only. All *Atopobium* spp. strains tested at ~3× LoD level reported BV NEGATIVE result calls as expected, as the concentration of *Atopobium* spp. strains tested was below the near cut-off concentration either in the presence or absence of Mega1-BVAB2 target. Replicates reporting Atop gp Ct values of ≤ 40.0 was treated as positive (pos) when *Atopobium* spp. strains were tested at ~ 3× LoD.
[b] *Atopobium vaginae* CCUG 44125 was tested at ~ 4× LoD (120 CFU/mL) to obtain 3 of 3 Atop gp Ct values of ≤ 40.0 results.
[c] *Atopobium vaginae* CCUG 48515 was tested at ~ 12× LoD (400 CFU/mL) to obtain 3 of 3 Atop gp Ct values of ≤ 40.0 results.
[d] *Atopobium vaginae* CCUG 44125 was tested at ~ 4× near cut-off concentration (1.2×10^6 CFU/mL) in the absence of BVAB2 and *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[e] *Atopobium vaginae* CCUG 44156 was tested at ~ 6× near cut-off concentration (2.0×10^6 CFU/mL) in the absence of BVAB2 and *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[f] *Atopobium vaginae* CCUG 48515 was tested at ~ 12× near cut-off concentration (4.0×10^6 CFU/mL) in the absence of BVAB2 and *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[g] *Atopobium* novel species CCUG 55226 was tested at ~ 6× near cut-off concentration (2.0×10^6 CFU/mL) in the absence of BVAB2 and *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[h] *Atopobium vaginae* CCUG 44125 was tested at ~ 4× near cut-off concentration (10,000 CFU/mL) in the presence of BVAB2 and/or *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[l] *Atopobium vaginae* CCUG 44156 was tested at ~ 6× near cut-off concentration (17,000 CFU/mL) in the presence of BVAB2 and/or *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[j] *Atopobium vaginae* CCUG 48515 was tested at ~ 6× (17,000 CFU/mL) to ~ 7× (20,000 CFU/mL) near cut-off concentration in the presence of BVAB2 and/or *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[k] *Atopobium* novel species CCUG 55226 was tested at ~ 4× near cut-off concentration (10,000 CFU/mL) in the presence of BVAB2 and/or *Megasphaera*-1 to obtain 3 of 3 BV POSITIVE result calls.
[l] *Candida albicans* ATCC 38289 was tested at ~ 4× LoD (120 CFU/mL) to obtain 3 of 3 Candida group DETECTED result calls.
[m] *Candida albicans* ATCC 62376 was tested at ~ 20× LoD (600 CFU/mL) to obtain 3 of 3 Candida group DETECTED result calls.
[n] *Candida albicans* ATCC 753 was tested at ~ 20× LoD (600 CFU/mL) to obtain 3 of 3 Candida group DETECTED result calls.
[*] metronidazole-resistant strain

Analytical Specificity (Exclusivity)

The analytical specificity of the Xpert Xpress MVP test was evaluated by testing a panel of 115 potentially cross-reactive microorganisms that are likely to be found in the vaginal flora/female genital tract. All strains were tested in triplicates in simulated vaginal swab matrix at a concentration of at least 10^6 CFU/mL, 10^5 cells/mL, 10^5 $TCID_{50}$/mL, or 10^4 International Unit (IU)/mL. Three replicates were tested for each strain. No cross-reactivity

was observed for all microorganisms tested with the Xpert Xpress MVP test at the concentrations listed in Table 5-5.

Table 5-5: Organisms Tested for Analytical Specificity

Organism	Concentration	Organism	Concentration
Bacteria		**Bacteria**	
Acinetobacter baumannii	1×10^6 CFU/mL	*Neisseria gonorrhoeae*	1×10^6 CFU/mL
Acinetobacter calcoaceticus	1×10^6 CFU/mL	*Olsenella uli*	1×10^6 CFU/mL
Actinomyces israelii	1×10^6 CFU/mL	*Pantoea agglomerans*	1×10^6 CFU/mL
Actinomyces pyogenes	1×10^6 CFU/mL	*Peptoniphilus asaccharolyticus*	1×10^6 CFU/mL
Aerococcus viridans	1×10^6 CFU/mL	*Peptoniphilus anaerobius*	1×10^6 CFU/mL
Alcaligenes faecalis	1×10^6 CFU/mL	*Peptostreptococcus anaerobius*	1×10^6 CFU/mL
Anaerococcus tetradius	1×10^6 CFU/mL	*Plesiomonas shigelloides*	1×10^6 CFU/mL
Atopobium minutum	1×10^6 CFU/mL	*Porphyromonas asaccharolytica*	1×10^6 CFU/mL
Atopobium parvulum	1×10^6 CFU/mL	*Prevotella bivia*	1×10^6 CFU/mL
Atopobium rimae	1×10^6 CFU/mL	*Prevotella melaninogenica*	1×10^6 CFU/mL
Bacillus subtilis	1×10^6 CFU/mL	*Prevotella oralis*	1×10^6 CFU/mL
Bacteroides caccae	1×10^6 CFU/mL	*Propionibacterium acnes*	1×10^6 CFU/mL
Bacteroides fragilis	1×10^6 CFU/mL	*Proteus mirabilis*	1×10^6 CFU/mL
Bacteroides stercoris	1×10^6 CFU/mL	*Providencia stuartii*	1×10^6 CFU/mL
Bacteroides ureolyticus	1×10^6 CFU/mL	*Pseudomonas aeruginosa*	1×10^6 CFU/mL
Bifidobacterium adolescentis	1×10^6 CFU/mL	*Salmonella typhimurium*	1×10^6 CFU/mL
Bifidobacterium breve	1×10^6 CFU/mL	*Serratia marcescens*	1×10^6 CFU/mL
Bifidobacterium longum	1×10^6 CFU/mL	*Shigella flexneri*	1×10^6 CFU/mL
Brevibacterium linens	1×10^6 CFU/mL	*Sneathia amnii*	1×10^6 CFU/mL
Burkholderia cepacian	1×10^6 CFU/mL	*Sneathia sanguinegens*	1×10^6 CFU/mL
BVAB1	1×10^6 copies/mL	*Staphylococcus aureus*	1×10^6 CFU/mL
Campylobacter jejuni	1×10^6 CFU/mL	*Staphylococcus epidermidis*	1×10^6 CFU/mL
Chlamydia trachomatis	1×10^6 CFU/mL	*Streptococcus agalactiae*	1×10^6 CFU/mL
Citrobacter freundii	1×10^6 CFU/mL	*Streptococcus mitis*	1×10^6 CFU/mL
Clostridium perfringens	1×10^6 CFU/mL	*Streptococcus mutans*	1×10^6 CFU/mL
Corynebacterium genitalium	1×10^6 CFU/mL	*Streptococcus salivarius*	1×10^6 CFU/mL
Dialister micraerophilus	1×10^6 CFU/mL	*Treponema pallidum*	1×10^6 copies/mL
Eikenella corrodens	1×10^6 CFU/mL	*Veillonella atypica*	1×10^6 CFU/mL
Enterobacter aerogenes	1×10^6 CFU/mL	*Veillonella parvula*	1×10^6 CFU/mL
Enterococcus faecalis	1×10^6 CFU/mL	*Vibrio parahaemolyticus*	1×10^6 CFU/mL
Enterococcus faecium	1×10^6 CFU/mL	*Yersinia enterocolitica*	1×10^6 CFU/mL
Erysipelothrix rhusiopathiae	1×10^6 CFU/mL	**Protozoans**	
Escherichia coli	1×10^6 CFU/mL	*Pentatrichomonas hominis*	5×10^4 cells/mL

Finegoldia magna	1×10^6 CFU/mL	*Trichomonas tenax*	10 cells/mL
Fusobacterium nucleatum	1×10^6 CFU/mL	**Yeasts**	
Gardnerella vaginalis	1×10^6 CFU/mL	*Candida catenulate*	1×10^6 CFU/mL
Gemella haemolysans	1×10^6 CFU/mL	*Candida famata*	1×10^6 CFU/mL
Kingella denitrificans	1×10^6 CFU/mL	*Candida haemulonii*	1×10^6 CFU/mL
Klebsiella pneumoniae	1×10^6 CFU/mL	*Candida inconspicua*	1×10^6 CFU/mL
Kocuria rhizophila	1×10^6 CFU/mL	*Candida intermedia*	1×10^6 CFU/mL
Lactobacillus acidophilus	1×10^6 CFU/mL	*Candida kefyr*	1×10^6 CFU/mL
Lactobacillus crispatus	1×10^6 CFU/mL	*Candida lusitaniae*	1×10^6 CFU/mL
Lactobacillus gasseri	1×10^6 CFU/mL	*Candida norvegica*	1×10^6 CFU/mL
Lactobacillus helveticus	1×10^6 CFU/mL	*Candida orthopsilosis*	1×10^2 CFU/mL
Lactobacillus iners	1×10^6 CFU/mL	*Candida rugosa*	1×10^6 CFU/mL
Lactobacillus jensenii	1×10^6 CFU/mL	*Candida utilis*	1×10^6 CFU/mL
Lactobacillus johnsonii	1×10^6 CFU/mL	*Kodamaea ohmeri*[b]	1×10^6 CFU/mL
Lactobacillus vaginalis	1×10^6 CFU/mL	*Pichia fermentans*	1×10^6 CFU/mL
Legionella pneumophila	1×10^6 CFU/mL	*Pichia norvegensis*[c]	1×10^6 CFU/mL
Mageeibacillus indolicus[a]	1×10^6 CFU/mL	*Pichia occidentalis*[d]	1×10^6 CFU/mL
Megasphaera-2	1×10^6 copies/mL	*Saccharomyces cerevisiae*	1×10^6 CFU/mL
Megasphaera elsdenii	1×10^6 CFU/mL	**Viruses**	
Mobiluncus curtisii	1×10^6 CFU/mL	Hepatitis B virus	1×10^5 IU/mL
Mobiluncus mulieris	1×10^6 CFU/mL	Hepatitis C virus	1×10^5 IU/mL
Moraxella catarrhalis	1×10^6 CFU/mL	Herpes simplex virus I	1×10^5 $TCID_{50}$/mL
Morganella morganii	1×10^6 CFU/mL	HIV-1	3×10^4 IU/mL[e]
Mycobacterium smegmatis	1×10^6 CFU/mL	Human herpesvirus 2	1×10^5 $TCID_{50}$/mL
Mycoplasma genitalium	1×10^6 CFU/mL	Human papilloma virus	4.3×10^5 cells/mL
Mycoplasma hominis	1×10^6 CFU/mL	Varicella-zoster virus	1×10^5 copies/mL

[a]*Mageeibacillus indolicus* is formerly named BVAB3.
[b]*Kodamaea ohmeri* is also reported as *Pichia ohmeri* and *Candida guilliermondii.*
[c]*Pichia norvegensis* is also reported as *Candida norvegensis.*
[d]*Pichia occidentalis* is also reported as *Issatchenkia occidentalis* and *Candida sorbose*
[e]Evaluated at highest concentration available

Microbial Interference

An interfering microorganism study was performed to assess the inhibitory effects of microorganisms that may be encountered in vaginal specimens on the performance of Xpert Xpress MVP. Thirteen microorganisms were tested for potential interference at $\geq10^6$ CFU/mL for bacteria and at $\geq10^4$ International Unit/mL or cells/mL for viruses (Table 5-6). Each of the microorganisms was tested in simulated vaginal swab matrix in the presence of a mixture of *Atopobium vaginae* at 3× near cut-off concentrations, *Megasphaera*-1 and BVAB2 targets each at ~1.5× near cut-off concentrations, and *Candida albicans*, *Candida glabrata* and *Trichomonas vaginalis* targets each at 3× LoD, in the absence of any Xpert

Xpress MVP test targets. The results showed that the presence of the tested microorganisms did not interfere with the performance of the Xpert Xpress MVP test.

Table 5-6: Potentially Interfering Microorganisms Tested

Microorganism
Dialister micraerophilus
Gardnerella vaginalis
Lactobacillus crispatus
Lactobacillus jensenii
Lactobacillus iners
Mageeibacillus indolicus
Mobiluncus curtisii
Porphyromonas asaccharolytica
Prevotella bivia
Sneathia amnii
Streptococcus agalactiae
HIV-1*
Human papilloma virus**

*Evaluated at highest concentration available (3×10^4 IU/mL)
**Evaluated at 1×10^4 cells/mL

Competitive Interference

Competitive interference between targets (BV, Candida group, Candida glab-krus and TV) of the Xpert Xpress MVP test caused by co-infections was evaluated by testing each target at low positive concentration in the presence of another target at high concentration in simulated vaginal swab matrix. Competitive inhibitory effects between the BV analytes (Atop gp and Mega1-BVAB2) were also evaluated in simulated vaginal swab matrix. The conditions simulating co-infections were presented in Table 5-7. Under the conditions of this study, competitive inhibitory effects were not observed between MVP targets or between BV analytes with the Xpert Xpress MVP test.

Table 5-7: Competitive Interference Testing Conditions

	Testing Panel	Testing Target/Organisms (Low Positive)	Competitive Target/Organisms (High Positive)
Competitive Interference Evaluation between MVP Targets	1	*Atopobium vaginae* (< 3× near cut-off concentration) and BVAB2 (< 3× near cut-off concentration)	*Candida albicans* (1×10^6 CFU/mL)
	2		*Candida glabrata* (1×10^6 CFU/mL)
	3		*Trichomonas vaginalis* (1×10^5 cells/mL)

	Testing Panel	Testing Target/Organisms (Low Positive)	Competitive Target/Organisms (High Positive)
	4	*Atopobium vaginae* (< 3× near cut-off concentration) and *Megasphaera*-1 (< 3× near cut-off concentration)	*Candida albicans* (1×10^6 CFU/mL)
	5		*Candida glabrata* (1×10^6 CFU/mL)
	6		*Trichomonas vaginalis* (1×10^5 cells/mL)
	7	*Atopobium vaginae* (< 3× near cut-off concentration), BVAB2 (< 1.5× near cut-off concentration) and *Megasphaera*-1 (< 1.5× near cut-off concentration)	*Candida albicans* (1×10^6 CFU/mL)
	8		*Candida glabrata* (1×10^6 CFU/mL)
	9		*Trichomonas vaginalis* (1×10^5 cells/mL)
	10	*Atopobium vaginae* (< 3× near cut-off concentration) in the absence of BVAB2 and *Megasphaera*-1	*Candida albicans* (1×10^6 CFU/mL)
	11		*Candida glabrata* (1×10^6 CFU/mL)
	12		*Trichomonas vaginalis* (1×10^5 cells/mL)
	13	*Candida albicans* (< 3× LoD)	*Atopobium vaginae* (1×10^7 CFU/mL), BVAB2 (1×10^7 copies/mL) and *Megasphaera*-1 (1×10^7 copies/mL)
	14		*Atopobium vaginae* (1×10^7 CFU/mL) in the absence of BVAB2 and *Megasphaera*-1
	15		*Candida glabrata* (1×10^6 CFU/mL)
	16		*Trichomonas vaginalis* (1×10^5 cells/mL)
	17	*Candida glabrata* (< 3× LoD)	*Atopobium vaginae* (1×10^7 CFU/mL), BVAB2 (1×10^7 copies/mL) and *Megasphaera*-1 (1×10^7 copies/mL)
	18		*Atopobium vaginae* (1×10^7 CFU/mL) in the absence of BVAB2 and *Megasphaera*-1
	19		*Candida albicans* (1×10^6 CFU/mL)
	20		*Trichomonas vaginalis* (1×10^5 cells/mL)
	21	*Trichomonas vaginalis* (< 3× LoD)	*Atopobium vaginae* (1×10^7 CFU/mL), BVAB2 (1×10^7 copies/mL) and *Megasphaera*-1

	Testing Panel	Testing Target/Organisms (Low Positive)	Competitive Target/Organisms (High Positive)
			(1×10^7 copies/mL)
	22		*Atopobium vaginae* (1×10^7 CFU/mL) in the absence of BVAB2 and *Megasphaera*-1
	23		*Candida albicans* (1×10^6 CFU/mL)
	24		*Candida glabrata* (1×10^6 CFU/mL)
Competitive Interference Evaluation between BV Organisms	25	*Atopobium vaginae* (< 3× near cut-off concentration)	BVAB2 (1×10^7 copies/mL) and *Megasphaera*-1 (1×10^7 copies/mL)
	26	BVAB2 (< 3× near cut-off concentration)	*Atopobium vaginae* (1×10^6 CFU/mL)
	27	*Megasphaera*-1 (< 3× near cut-off concentration)	*Atopobium vaginae* (1×10^6 CFU/mL)
	28	BVAB2 (< 1.5× near cut-off concentration) and *Megasphaera*-1 (< 1.5× near cut-off concentration)	*Atopobium vaginae* (1×10^6 CFU/mL)

Interfering Substances

Twenty substances that may be present in the vaginal swab specimens with the potential to interfere with the performance of Xpert Xpress MVP test were evaluated. The potentially interfering substances included prescription and over-the-counter drugs, creams and/or gels, blood, hormones, semen and mucus. The substances, active ingredients, and concentrations tested are listed in Table 5-8. Potential interferents were tested in simulated vaginal swab matrix in the presence and absence of Xpert Xpress MVP targets at 3× LoD/3× near cut-off concentrations. With the exception of the 5.5% concentration of mucin (from porcine stomach), no clinically significant inhibitory effects from substances that may be encountered in vaginal specimens were observed on the performance of the Xpert Xpress MVP test. When mucin was tested at a concentration of 4.0%, no clinically significant inhibitory effect was observed on the performance of the Xpert Xpress MVP test.

Table 5-8: Potential Interfering Substances Tested

Substance/Class	Active Ingredient	Concentration Tested
Blood	Blood	5.0% v/v
Seminal Fluid	Semen	5.0% v/v
Mucus	Mucin (porcine stomach)	**5.5% v/v (Interference Observed)**
		4.0% v/v (Interference not Observed)
Leukocytes	Leukocytes	10^5 cells/mL

Substance/Class	Active Ingredient	Concentration Tested
Intravaginal Hormones	Estradiol; Progesterone	7mg/mL Progesterone + 0.07mg/mL Beta Estradiol
Over the counter (OTC) Vaginal Products; Contraceptives; Vaginal treatments	Benzocaine 5%; Resorcinol 2%	0.25% w/v
	Clotrimazole 2%	0.25% w/v
	Miconazole Nitrate 4%	0.25% w/v
	Tioconazole 6.5%	0.25% w/v
	5% w/w acyclovir	0.25% w/v
	Glycerin, Propylene glycol	0.25% w/v
	Glycerin; carbomer	0.25% w/v
	Glycerin; sodium hydroxide; carbomer	0.25% w/v
	Glycerin, Hydroxyethyl cellulose	0.25% w/v
	Berberis Vulgaris 6X HPUS (Barberry), Borax 3X HPUS (Sodium Borate), Collinsonia Canadensis 3X HPUS (Stone Root), Hamamelis Virginiana 6X HPUS (Witch Hazel), *Bacillus coagulans* (Lactospore®)	0.25% w/v
	Povidone-iodine 10% (topical)	0.25% v/v
	Povidone-iodine 0.3% (douche)	0.25% v/v
	Nonoxynol-9 12.5%	0.25% w/v
	Metronidazole 0.75%	0.25% w/v
Hemorrhoidal Cream	Glycerin 14%; Pramoxine HCl 1%	0.25% w/v

Carry-Over Contamination

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent specimen and amplicon carry-over contamination from very high titer positive samples into successively run negative samples when processed in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately after processing a very high BV positive sample (an *A. vaginae* strain at 2.8×10^7 CFU/mL and BVAB2 plasmid DNA at 5.0×10^8 copies/mL), a very high Candida group positive sample (a *C. albicans* strain at 3.0×10^6 CFU/mL), or a very high TV positive sample (a *T. vaginalis* strain at 5.0×10^6 cells/mL) in simulated vaginal swab matrix. The testing scheme was repeated 20 times in a single GeneXpert module for a total of 41 runs (20 high positive samples and 21 negative samples per module) across 3 GeneXpert modules. There was no evidence of any carry-over contamination. All 63 negative samples were correctly reported as negative/not detected. All 60 positive samples were correctly reported as positive/detected.

Time to Result

The time to result is defined as the time from the initiation of cartridge processing on the GeneXpert system to the time a result is displayed on the test screen. The time to result for the Xpert Xpress MVP test was determined by evaluating the test time of 50 random tests

that were conducted as part of the clinical study. The Xpert Xpress MVP test has a turnaround time of within 60 minutes, and the data from this study is representative for the GeneXpert Instrument Systems.

Reproducibility and Precision

Reproducibility and precision of the Xpert Xpress MVP test was established through a multicenter (3 sites), blinded study utilizing a multi-factor nested design consisting of contrived panel members spanning the relevant limit of detection (LoD) spectrum (or, in the case of BV, the near cut-off concentration) for the 4 intended target types.

A panel of ten panel members with varying concentrations of the intended target types were tested by two operators in duplicate on six different days at three sites using three lots of Xpert Xpress MVP test cartridges. The total number of tests for each panel member was 144 (3 sites × 3 lots × 2 days × 2 operators × 2 runs × 2 replicates). The three concentrations for each intended target type included two positive levels (moderate positives at ~3× LoD/near cut-off concentration, low positives at ~1× LoD/near cut-off concentration) and one negative. For the BV target, a high negative level (<1× near the cut-off concentration) was also included.

Percent agreement for each panel member was analyzed across each of the 6 operators and across each of the 3 sites. Overall percent agreement for each panel member was calculated, as well as the Wilson Score 95% confidence interval for each proportion of concordance (Table 5-9).

Table 5-9: Summary of Reproducibility and Precision Results

Panel member	Site 01			Site 02			Site 03			Overall Agreement and 95% CI
	Op 1	Op 2	Subtotal	Op 1	Op 2	Subtotal	Op 1	Op 2	Subtotal	
Negative	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144) 97.4% - 100%
BV, High Neg	66.7% (16/24)	83.3% (20/24)	75.0% (36/48)	41.7% (10/24)	62.5% (15/24)	52.1% (25/48)	54.2% (13/24)	45.8% (11/24)	50.0% (24/48)	59.0% (85/144) 50.9% - 66.7%
BV, Low Pos	91.7% (22/24)	100% (24/24)	95.8% (46/48)	95.8% (23/24)	95.8% (23/24)	95.8% (46/48)	100% (24/24)	100% (24/24)	100% (48/48)	97.2% (140/144) 93.1% - 98.9%
BV, Mod Pos	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144) 97.4% - 100%
C. albicans, Low Pos	95.8% (23/24)	100% (24/24)	97.9% (47/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	99.3% (143/144) 96.2% - 99.9%
C. albicans, Mod Pos	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144) 97.4% - 100%

Panel member	Site 01			Site 02			Site 03			Overall Agreement and 95% CI
	Op 1	Op 2	Subtotal	Op 1	Op 2	Subtotal	Op 1	Op 2	Subtotal	
C. glabrata, Low Pos	100% (24/24)	100% (24/24)	100% (48/48)	95.8% (23/24)	100% (24/24)	97.9% (47/48)	100% (24/24)	100% (24/24)	100% (48/48)	99.3% (143/144) 96.2% - 99.9%
C. glabrata, Mod Pos	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144) 97.4% - 100%
TV, Low Pos	95.8% (23/24)	95.8% (23/24)	95.8% (46/48)	91.7% (22/24)	95.8% (23/24)	93.8% (45/48)	87.5% (21/24)	100% (24/24)	93.8% (45/48)	94.4% (136/144) 89.4% - 97.2%
TV, Mod Pos	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (24/24)	100% (24/24)	100% (48/48)	100% (144/144) 97.4% - 100%

Abbreviations: Mod, moderate; Neg, negative; Op, operator; Pos, positive

The reproducibility of the Xpert Xpress MVP test was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-lots, between-days, between-operators, between-runs and within-run for each panel member are presented in Table 5-10.

Table 5-10. Results of Reproducibility for the Xpert Xpress MVP Test

Panel Member	Analyte	N[a]	Mean Ct	Site		Lot		Day		Operator		Between-Run		Within-run		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Negative	SPC	144	32.66	0.06	0.2	0.17	0.5	0	0	0.24	0.7	0	0	0.37	1.1	0.48	1.5
BV, High Neg	Atop gp	144	32.45	0.07	0.2	0.17	0.5	0	0	0.12	0.4	0.05	0.2	0.28	0.9	0.36	1.1
BV, Low Pos		144	31.95	0.03	0.1	0.19	0.6	0	0	0	0	0.27	0.8	0.51	1.6	0.61	1.9
BV, Mod Pos		144	30.56	0	0	0.2	0.7	0.13	0.4	0.1	0.3	0.14	0.4	0.3	1.0	0.42	1.4
BV, High Neg	Mega1-BVAB2	111	41.08	0.26	0.6	0.27	0.7	0	0	0.35	0.9	0	0	1.28	3.1	1.38	3.4
BV, Low Pos		144	36.31	0	0	0.31	0.9	0	0	0	0	0.23	0.6	0.58	1.6	0.7	1.9
BV, Mod Pos		144	35.25	0.16	0.5	0.19	0.5	0.19	0.5	0	0	0	0	0.59	1.7	0.67	1.9
C. albicans, Low Pos	Cgroup	144	36.67	0	0	0.22	0.6	0	0	0.19	0.5	0.56	1.5	0.78	2.1	1.01	2.7

Panel Member	Analyte	N[a]	Mean Ct	Site		Lot		Day		Operator		Between-Run		Within-run		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
C. albicans, Mod Pos		144	35.00	0.27	0.8	0	0	0	0	0.6	1.7	0.45	1.3	0.55	1.6	0.96	2.8
C. glabrata, Low Pos	Cglab-krus	143	31.79	0	0	0.35	1.1	0	0	0	0	0.37	1.2	1.35	4.2	1.44	4.5
C. glabrata, Mod Pos		144	29.75	0.54	1.8	0.22	0.8	0.34	1.1	0.47	1.6	0.07	0.2	0.9	3.0	1.22	4.1
TV, Low Pos	TV	136	38.41	0.21	0.6	0.22	0.6	0	0	0.33	0.9	0	0	1.23	3.2	1.3	3.4
TV, Mod Pos		144	35.97	0.15	0.4	0.09	0.3	0	0	0.07	0.2	0.23	0.6	0.5	1.4	0.58	1.6

Abbreviations: Atop gp, Atopobium group; Cglab-krus, *C. glabrata/C. krusei*; Cgroup, *Candida* spp.; CV, coefficient of variance; Mega1; *Megasphaera*-1; Mod, moderate; Neg, negative; Pos, positive; SD, standard deviation; SPC; sample processing control

[a]Number of samples with Ct values out of 144.

Note: The variance estimate from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

Precision of the BV Target

Due to the diversity of organisms associated with the detection of BV, a separate single-site study was conducted to establish precision of the BV target. To establish the assay precision for the BV target in the Xpert Xpress MVP test, a single-center, blinded precision study was conducted utilizing samples with unique combinations of contrived BV organisms.

A panel of nine panel members were tested by two operators in duplicate on ten different days using one lot of Xpert Xpress MVP test cartridges. The total number of tests for each panel member was 80 (1 site × 1 lot × 10 days × 2 operators × 2 runs × 2 replicates). The panel included 1 negative panel member, a high negative level (<1× the near cut-off concentration), and two positive levels (low positives at ~1× the near cut-off concentration, and moderate positives at ~3× the near cut-off concentration) utilizing unique combinations of the BV organisms (*Atopobium vaginae*, *Megasphaera*-1, and BVAB2). Table 5-11 presented agreement for each panel member, as well as the Wilson Score 95% confidence interval for each proportion of concordance.

Table 5-11: Summary of Precision Results for the BV Target

Sample Type	Overall Agreement	95% CI
Negative	100% (80/80)	95.4% - 100%
A. vaginae, Low positive	97.5% (78/80)	91.3% - 99.3%
A. vaginae and BVAB2, High negative	66.3% (53/80)	55.4% - 75.7%
A. vaginae and BVAB2, Low positive	97.5% (78/80)	91.3% - 99.3%
A. vaginae and *Megasphaera*-1, High negative	23.8% (19/80)	15.8% - 34.1%
A. vaginae and *Megasphaera*-1, Low positive	95.0% (76/80)	87.8% - 98.0%
A. vaginae, BVAB2, and *Megasphaera*-1, High negative	53.8% (43/80)	42.9% - 64.3%
A. vaginae, BVAB2, and *Megasphaera*-1, Low positive	96.3% (77/80)	89.5% - 98.7%
A. vaginae, BVAB2, and *Megasphaera*-1, Moderate positive	100% (80/80)	95.4% - 100%

Abbreviations: *A. vaginae; Atopobium vaginae*

Precision for BV targets was evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-days, between-operators, between-runs and within-run for each panel member are presented in Table 5-12.

Table 5-12. Results of Precision for the BV Target

Panel member	Analyte	N[a]	Mean Ct	Day		Operator		Between-Run		Within-run		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Negative	SPC	80	32.84	0.00	0.0	0.49	1.5	0.22	0.7	0.90	2.7	1.05	3.2
A. vaginae, Low Pos	Atop gp	80	24.98	0.00	0.0	0.00	0.0	0.03	0.1	0.32	1.3	0.32	1.3
A. vaginae and BVAB2, High Neg	SPC	80	32.64	0.17	0.5	0.17	0.5	0.12	0.4	0.37	1.1	0.46	1.4
	Atop gp	80	32.35	0.00	0.0	0.16	0.5	0.00	0.0	0.20	0.6	0.26	0.8
	Mega1-BVAB2[b]	75	41.30	0.37	0.9	0.00	0.0	0.26	0.6	1.15	2.8	1.24	3.0
A. vaginae and BVAB2, Low Pos	Atop gp	80	32.20	0.00	0.0	0.04	0.1	0.08	0.3	0.22	0.7	0.24	0.7
	Mega1-BVAB2[b]	80	40.03	0.00	0.0	0.00	0.0	0.30	0.7	0.90	2.2	0.94	2.4
A. vaginae and Mega-1, High Neg	SPC	80	32.63	0.11	0.3	0.17	0.5	0.00	0.0	0.39	1.2	0.44	1.3
	Atop gp	80	32.62	0.00	0.0	0.04	0.1	0.00	0.0	0.33	1.0	0.34	1.0
	Mega1-BVAB2[b]	28	38.98	0.00	0.0	1.01	2.6	0.21	0.6	0.84	2.2	1.33	3.4
A. vaginae and Mega-1, Low Pos	Atop gp	79	32.07	0.00	0.0	0.15	0.5	0.18	0.6	0.41	1.3	0.47	1.5
	Mega1-BVAB2[b]	80	35.48	0.00	0.0	0.29	0.8	0.00	0.0	0.71	2.0	0.77	2.2

Panel member	Analyte	N[a]	Mean Ct	Day		Operator		Between-Run		Within-run		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
A. vaginae, BVAB2, and Mega-1, High Neg	SPC	80	32.74	0.15	0.5	0.12	0.4	0.17	0.5	0.33	1.0	0.41	1.3
	Atop gp	80	32.53	0.00	0.0	0.15	0.5	0.00	0.0	0.22	0.7	0.27	0.8
	Mega1-BVAB2[b]	63	41.57	0.30	0.7	0.00	0.0	0.39	0.9	1.02	2.5	1.13	2.7
A. vaginae, BVAB2, and Mega-1, Low Pos	Atop gp	79	31.81	0.00	0.0	0.22	0.7	0.28	0.9	1.16	3.6	1.21	3.8
	Mega1-BVAB2[b]	80	36.25	0.15	0.4	0.00	0.0	0.10	0.3	0.69	1.9	0.71	2.0
A. vaginae, BVAB2, and Mega-1, Mod Pos	Atop gp	80	30.67	0.13	0.4	0.09	0.3	0.00	0.0	0.33	1.1	0.37	1.2
	Mega1-BVAB2[b]	80	35.64	0.00	0.0	0.26	0.7	0.00	0.0	0.48	1.3	0.54	1.5

Abbreviations: Atop gp, Atopobium group; CV, coefficient of variance; Mega1, *Megasphaera*-1; Mod; moderate; Neg, negative; Pos, positive; SD, standard deviation; SPC, sample processing control

[a] Number of samples with non-zero Ct values out of 80.

[b] Samples with Mega1-BVAB2 that did not generate a Ct value were excluded from analysis.

Note: The variance estimate from some factors may be numerically negative, which can occur if the variability due to those factors is very small. When this occurs, the variability as measured with SD and CV is set to 0.

5.5 Clinical Studies

The clinical evaluation of the Xpert Xpress MVP test was a multi-site, prospective observational, method comparison clinical study that included twelve (12) sites from geographically diverse locations in the United States. Of the 12 sites, 10 participated in specimen collection and Xpert testing, 1 performed reference/comparator testing and specimen collection, and 1 site participated in specimen collection only.

All sites prospectively collected one (1) self-collected (collected in a clinical setting, SVS) and five (5) clinician-collected vaginal swab (CVS) specimens from symptomatic patients, defined as female patients ≥ 14 years of age who presented with signs and/or symptoms of vaginitis/vaginosis (including abnormal vaginal discharge; dysuria; vulvar/vaginal itching, burning, irritation, pain or vulvar edema; coital pain; or vaginal odor). The SVS specimen was always collected first. The study population comprised of 1,478 female patients 14 to ≥ 50 years of age. A total of 2,947 vaginal swabs were tested and were eligible for inclusion in the Xpert Xpress MVP study.

Performance of the Xpert Xpress MVP test in vaginal swab specimens was determined relative to comparator methods. Specifically, positive percent agreement (PPA)/negative percent agreement (NPA) for BV was assessed relative to an FDA-cleared nucleic acid amplification test (NAAT). Sensitivity and specificity for Candida group and Candida glab-krus targets were assessed relative to yeast culture followed by mass spectrometry for species identification. PPA and NPA for TV were assessed relative to a patient infected status (PIS) algorithm that included results from an FDA-cleared NAAT and TV culture. When applicable, investigation of discrepant results was performed by testing specimens with another FDA-cleared NAAT.

Performance of the Xpert Xpress MVP test is presented in Table 5-13. The Xpert Xpress MVP test demonstrated PPA and NPA of 93.8% and 93.8% for BV detection in CVS specimens, respectively, and 94.0% and 92.9% in SVS specimens, respectively. For Candida group detection, the Xpert Xpress MVP test demonstrated sensitivity and specificity of 98.0% and 94.6% in CVS specimens, respectively, and 97.5% and 92.1% in SVS specimens, respectively. The Xpert Xpress MVP test demonstrated sensitivity and specificity of 93.6% and 99.6% for Candida glab-krus detection in CVS specimens, respectively, and 97.8% and 99.4% in SVS specimens, respectively. For TV detection, the Xpert Xpress MVP test demonstrated PPA and NPA of 97.3% and 99.6% in CVS specimens, respectively, and 97.3% and 99.8% in SVS specimens, respectively.

Table 5-13: Overall Performance of the Xpert Xpress MVP Test

	Clinician-collected (CVS)		Self-collected (SVS)	
	Sensitivity/PPA (95% CI)	**Specificity/NPA (95% CI)**	**Sensitivity/PPA (95% CI)**	**Specificity/NPA (95% CI)**
BV	93.8% 531/566 [a] (91.5% - 95.5%)	93.8% 808/861 [b] (92.0% - 95.3%)	94.0% 533/567 [c] (91.7% - 95.7%)	92.9% 794/855 [d] (90.9% - 94.4%)
Candida group*	98.0% 396/404 [e] (96.1% - 99.0%)	94.6% 984/1040 [f] (93.1% - 95.8%)	97.5% 393/403 [g] (95.5% - 98.7%)	92.1% 954/1036 [h] (90.3% - 93.6%)
Candida glab-krus Fresh Prospective	93.6% 44/47 [i] (82.8% - 97.8%)	99.6% 1392/1397 [j] (99.2% - 99.9%)	97.8% 45/46 [k] (88.7% - 99.6%)	99.4% 1384/1393 [l] (98.8% - 99.7%)
Candida glab-krus Contrived**	99.0% 98/99 (94.5% - 99.8%)	96.4% 27/28 (82.3% - 99.4%)	N/A	N/A
TV	97.3% 73/75 [m] (90.8% - 99.3%)	99.6% 1332/1337 [n] (99.1% - 99.8%)	97.3% 72/74 [o] (90.7% - 99.3%)	99.8% 1330/1333 [p] (99.3% - 99.9%)

*Target includes *C. albicans, C. tropicalis, C. parapsilosis,* and *C. dubliniensis*
**Contrived specimens were prepared using individual negative clinical CVS and SVS specimens.
[a] Testing results with a second FDA-cleared NAAT: 14 were also negative and 21 were positive.
[b] Testing results with a second FDA-cleared NAAT: 25 were also positive and 28 were negative.
[c] Testing results with a second FDA-cleared NAAT: 12 were also negative and 22 were positive.
[d] Testing results with a second FDA-cleared NAAT: 23 were also positive and 38 were negative.
[e] Testing results with an FDA-cleared NAAT: 5 were also negative and 3 were positive.
[f] Testing results with an FDA-cleared NAAT: 31 were also positive and 24 were negative and 1 had no result.
[g] Testing results with an FDA-cleared NAAT: 5 were also negative and 5 were positive.
[h] Testing results with an FDA-cleared NAAT: 38 were also positive and 43 were negative and 1 had no result.
[i] Testing results with an FDA-cleared NAAT: 2 were also negative and 1 was positive.
[j] Testing results with an FDA-cleared NAAT: 5 were negative.
[k] Testing results with an FDA-cleared NAAT: 1 was also negative.
[l] Testing results with an FDA-cleared NAAT: 9 were negative.
[m] Testing results a second FDA-cleared NAAT: 1 was also negative and 1 was positive.
[n] Testing results a second FDA-cleared NAAT: 4 were also positive and 1 had no result.
[o] Testing results a second FDA-cleared NAAT: 1 was also negative and 1 was positive.
[p] Testing results a second FDA-cleared NAAT: 3 were also positive.

Asymptomatic Population

Although the Xpert Xpress MVP test is not intended for use in an asymptomatic patient population, positivity rates were calculated from CVS and SVS specimens collected from asymptomatic patients to assess how often patients who, despite being asymptomatic, harbored microbial flora associated with vaginosis and candidiasis that could be detected by the Xpert Xpress MVP test. Positivity rates are presented by target and by race/ethnicity in Table 5-14.

Table 5-14: Positivity Rates in Asymptomatic Patients According to the Xpert Xpress MVP Test

	Target	Overall	Black /African American^	White		Others*
				Hispanic/Latino	Not Hispanic/Latino	
CVS	BV	32.9% (52/158)	51.0% (26/51)	25.5% (14/55)	19.5% (8/41)	36.4% (4/11)
	Candida group	17.1% (27/158)	25.5% (13/51)	16.4% (9/55)	7.3% (3/41)	18.2% (2/11)
	Candida glab-krus	4.4% (7/158)	2.0% (1/51)	5.5% (3/55)	4.9% (2/41)	9.1% (1/11)
SVS	BV	31.5% (51/162)	49.1% (26/53)	24.1% (13/54)	16.3% (7/43)	41.7% (5/12)
	Candida group	19.1% (31/162)	28.3% (15/53)	18.5% (10/54)	7.0% (3/43)	25.0% (3/12)
	Candida glab-krus	4.9% (8/162)	1.9% (1/53)	7.4% (4/54)	4.7% (2/43)	8.3% (1/12)

*Including: American Indian or Alaska Native, Asian, Mixed/Unknown

^Includes one Black/African American who was of Hispanic or Latino descent for CVS specimens; includes two Black/African American who was of Hispanic or Latino descent for SVS specimens.

Non-Determinate Rate

Of the 2,947 Xpert Xpress MVP runs performed in the clinical study, 130 resulted in non-determinate ("Error", "Invalid" or "No Results") results on first attempt. Upon retest of these 130 specimens, 22 remained non-determinate. The initial non-determinate rate was 4.4% (130/2947) and the overall non-determinate rate was 0.7% (22/2947).

The initial non-determinate rate for CVS specimens was 3.9% (58/1473) and the overall non-determinate rate was 0.5% (8/1473). The initial non-determinate rate for SVS specimens was 4.9% (72/1474) and the overall non-determinate rate was 0.9% (14/1474).

5.6 Conclusions

The results of the non-clinical analytical and clinical performance studies summarized above demonstrated that the Xpert Xpress MVP test is substantially equivalent to the predicate device.