July 16, 2026

Roche Molecular Systems, Inc.
Nicole Gasser
Regulatory Affairs Senior Manager
4300 Hacienda Dr.
Pleasanton, California 94588

Re: K260021
Trade/Device Name: cobas BV/CV
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
Dated: January 5, 2026
Received: January 5, 2026

Dear Nicole Gasser:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13485 clause 8.3 (Nonconforming product), and ISO 13485 clause 8.5 (Corrective and preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production and process controls (ISO 13485 clause 7.3 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

UWE SCHERF -S

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K260021

Device Name
cobas BV/CV

Indications for Use *(Describe)*
cobas BV/CV for use on the cobas 6800/8800 systems is an automated, qualitative in vitro nucleic acid diagnostic test that utilizes real-time polymerase chain reaction (PCR) for the direct detection of bacteria (Gardnerella vaginalis, Lactobacillus spp., and Atopobium vaginae) associated with bacterial vaginosis (BV) and yeast (Candida spp. listed below) associated with Candida vaginitis (CV) from self-collected vaginal swab specimens and clinician-collected vaginal swab specimens, all collected in cobas PCR Media. The assay amplifies specific DNA targets to detect organisms associated with BV (i.e., G. vaginalis, L. crispatus, L. gasseri, L. jensenii, and A. vaginae) and specific organisms associated with CV (i.e., C. albicans, C. dubliniensis, C. glabrata, C. krusei, C. tropicalis, and C. parapsilosis) but does not differentiate which BV and/or CV organism(s) is present. This test is intended as an aid in the diagnosis of BV and/or CV in symptomatic individuals with a clinical presentation consistent with vaginitis, vaginosis, or both.

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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cobas® BV/CV
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Roche Molecular Systems, Inc.
Address	4300 Hacienda Drive Pleasanton, CA 94588-2722
Contact	Nicole Gasser Phone: +41 79 567 05 32 Email: nicole.gasser@roche.com
Date Prepared	November 14, 2025
Proprietary Name	**cobas**® BV/CV
Common Name	Vaginitis and Bacterial Vaginosis Nucleic Acid Detection System
Regulation Number	21 CFR 866.3975
Regulation Name	Device that detects nucleic acid sequences from microorganisms associated with vaginitis and bacterial vaginosis
Product Code	PQA
Predicate Device	BD MAX™ Vaginal Panel (DEN160001, K191957(current))
Establishment Registration	Roche Molecular Systems, Inc. (2243471)

1. DEVICE DESCRIPTION

cobas® BV/CV for use on the **cobas**® 6800/8800 systems (**cobas**® BV/CV) is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. The **cobas**® 6800/8800 systems consist of the sample supply module, the transfer module, the processing module, and the analytic module. Automated data management is performed by **cobas**® 6800/8800 systems which assigns test results for all tests as positive, negative or invalid. Results can be reviewed directly on the system screen, exported, or printed as a report.

Nucleic acid from patient samples and added internal control DNA (DNA-IC) molecules are simultaneously extracted. In summary, nucleic acid is released by addition of proteinase and lysis reagent to the sample. The released nucleic acid binds to the silica surface of the added magnetic glass particles. Unbound substances and impurities, such as denatured protein, cellular debris and potential PCR inhibitors are removed with subsequent wash steps and purified nucleic acid is eluted from the magnetic glass particles with elution buffer at elevated temperature. External controls (positive and negative) are processed in the same way.

Selective amplification of target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for the bacteria and yeast associated with BV and CV which are selected from highly conserved regions within the respective target organism (CV: *Candida* species, BV: *Gardnerella vaginalis, Atopobium vaginae*, and *Lactobacillus* species). The bacteria and yeast associated with BV and CV, respectively, are detected by multiple sets of primers and probes. Selective amplification of DNA IC is achieved by the use of sequence-specific forward and reverse primers which are selected to have no homology with any target regions for the bacteria and yeast associated with BV and CV. A thermostable DNA polymerase enzyme is used for PCR amplification. The target and DNA-IC sequences are amplified simultaneously utilizing a universal PCR amplification profile with predefined temperature steps and number of cycles. The master mix includes deoxyuridine triphosphate (dUTP), instead of deoxythymidine triphosphate (dTTP), which is incorporated into the newly synthesized DNA (amplicon). Any contaminating amplicon from previous PCR runs is eliminated by the AmpErase enzyme, which is included in the PCR master mix, during the first thermal cycling step. However, newly formed amplicons are not eliminated since the AmpErase enzyme is inactivated once exposed to temperatures above 55°C.

The **cobas**® BV/CV master mix contains multiple probes specific for the CV associated target sequences, multiple probes specific for the BV associated target sequences and one for the DNA-IC. The probes are labeled with target specific fluorescent reporter dyes allowing simultaneous detection of CV associated targets, BV associated targets and DNA-IC in five different target channels. When not bound to the target sequence, the fluorescent signal of the intact probes is suppressed by a quencher dye. During the PCR amplification step, hybridization of the probes to the specific single-stranded DNA template results in cleavage of the probe by the 5' to 3' exonuclease activity of the DNA polymerase resulting in separation of the reporter and quencher dyes and the generation of a fluorescent signal. With each PCR cycle, increasing amounts of cleaved probes are generated and the cumulative signal of the reporter dye increases concomitantly. Real-time detection and discrimination of PCR products is accomplished by measuring the fluorescence of the released reporter dyes for the BV and CV associated targets and DNA-IC, respectively.

2. INTENDED USE

cobas® BV/CV for use on the **cobas**® 6800/8800 systems is an automated, qualitative in vitro nucleic acid diagnostic test that utilizes real-time polymerase chain reaction (PCR) for the direct detection of bacteria (*Gardnerella vaginalis*, *Lactobacillus* spp., and *Atopobium vaginae*) associated with bacterial vaginosis (BV) and yeast (*Candida* spp. listed below) associated with *Candida* vaginitis (CV) from self-collected vaginal swab specimens and clinician-collected vaginal swab specimens, all collected in **cobas**® PCR Media. The assay amplifies specific DNA targets to detect organisms associated with BV (i.e., *G. vaginalis*, *L. crispatus*, *L. gasseri*, *L. jensenii*, and *A. vaginae*) and specific organisms associated with CV (i.e., *C. albicans*, *C. dubliniensis*, *C. glabrata*, *C. krusei*, *C. tropicalis*, and *C. parapsilosis*) but does not differentiate which BV and/or CV organism(s) is present. This test is intended as an aid in the diagnosis of BV and/or CV in symptomatic individuals with a clinical presentation consistent with vaginitis, vaginosis, or both.

3. TECHNOLOGICAL CHARACTERISTICS

The primary technological characteristics and intended use of the **cobas**® BV/CV are substantially equivalent to other legally marketed nucleic acid amplification tests intended for the qualitative detection of bacteria associated with bacterial vaginosis (BV) and yeast associated with Candida vaginitis (CV).

As indicated in Table 1, **cobas**® BV/CV is substantially equivalent to significant characteristics of the identified predicate device, the currently cleared BD MAX™ Vaginal Panel (K191957).

Table 1: Comparison of the cobas® BV/CV with the Predicate Device

Comparator	Candidate Device: cobas® BV/CV	Predicate Device: BD MAX™ Vaginal Panel DEN160001, K191957 (current)
Regulation Number	21 CFR 866.3975	Same
Regulation Name	Device that detects nucleic acid sequences from microorganisms associated with vaginitis and bacterial vaginosis	Same
Regulatory Class	Class II	Same
Product Code	PQA, Vaginitis and Bacterial Vaginosis Nucleic Acid Detection System	Same
Intended Use	**cobas**® BV/CV for use on the **cobas**® 6800/8800 systems is an automated, qualitative in vitro nucleic acid diagnostic test that utilizes real-time polymerase chain reaction (PCR) for the direct detection of bacteria (*Gardnerella vaginalis*, *Lactobacillus* spp., and *Atopobium vaginae*) and yeast (*Candida* spp. listed below) associated with bacterial vaginosis (BV) and *Candida* vaginitis (CV) from self-collected vaginal swab specimens and clinician-collected vaginal swab specimens, all collected in **cobas**® PCR Media. The assay amplifies specific DNA sequences from the *Candida* spp. *C. albicans*, *C. dubliniensis*, *C. glabrata*, *C. krusei*, *C. tropicalis*, and *C. parapsilosis* and likewise from the *Lactobacillus* spp. *L. crispatus*, *L. gasseri*, and *L. jensenii* but does not differentiate these species. This test is intended as an aid in the diagnosis of BV and/or CV in symptomatic individuals with a clinical presentation consistent with vaginitis, vaginosis, or both.	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* Bacterial Vaginosis Associated Bacteria-2 (BVAB-2) *Megasphaera-1* • *Candida* spp. (*C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*) • *Candida glabrata*

Comparator	Candidate Device: cobas® BV/CV	Predicate Device: BD MAX™ Vaginal Panel DEN160001, K191957 (current)
		• *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.
Sample Types	Vaginal swab	Same
Subject Status	Symptomatic	Same
Conditions for use	For prescription use	same
Target Organisms	BV (Bacteria): *G. vaginalis*, *Lactobacillus* spp. (*L. crispatus*, *L. gasseri*, *L. jensenii*), *A. vaginae* CV (yeast): *C. albicans, C. dubliniensis, C. glabrata, C. krusei, C. tropicalis, C. parapsilosis*	BV (Bacteria): *Lactobacillus* spp. (*L. crispatus* and *L. jensenii*), *G. vaginalis*, *A. vaginae*, BVAB-2, Megasphaera-1 CV (yeast): *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*, *C. glabrata*, *C. krusei* Other: *Trichomonas vaginalis*
Sample Preparation Procedure	Automated	Same
Technology	Nucleic Acid Amplification Technology (NAAT) / Real-Time PCR/Real Time PCR	Same
Detection Chemistry	Paired reporter and quencher fluorescence labeled probes (TaqMan Technology) using fluorescence resonance energy transfer (FRET)	Same
Controls used	Sample processing control (IC) Positive and negative control	Same
Result Analysis	Automated Software	Same

4. ANALYTICAL PERFORMANCE STUDIES (NON-CLINICAL)

4.1. Analytical sensitivity (Limit of Detection)

The limit of detection (LoD) of **cobas**® BV/CV was determined by analysis of serial dilutions of one *Atopobium vaginae*, one *Gardnerella vaginalis*, three *Lactobacillus* species in simulated vaginal matrix stabilized in **cobas**® PCR Media and six *Candida* species in clinical vaginal swab matrix. Panels of five to six concentration levels plus a blank were tested over three lots of

cobas® BV/CV test reagents, multiple runs, days, operators, and instruments. The LoD for BV and CV targets are presented in Table 2.

Table 2: Limit of Detection for individual cobas® BV/CV targets

Target	Strain / Isolate	LoD by Hit Rate ≥ 95% (CFU/mL)	95% LoD PROBIT (CFU/mL)	Mean Ct at LoD by Hit Rate ≥ 95%
Lactobacillus crispatus	*Lactobacillus crispatus* 33820 (ATCC)	1.50E+00	1.64E+00 (95% CI: 1.38E+00 – 2.09E+00)	34.90
Lactobacillus gasseri	*Lactobacillus gasseri* HM-644 (BEI Resources)	1.60E+02	1.14E+02 (95% CI: 9.12E+01 – 1.54E+02)	34.24
Lactobacillus jensenii	*Lactobacillus jensenii* HM-374 (BEI Resources)	8.70E+01	8.51E+01 (95% CI: 6.73E+01 – 1.25E+02)	34.60
Gardnerella vaginalis	*Gardnerella vaginalis* 72422 (CCUG)	5.00E+02	3.44E+02 (95% CI: 2.93E+02 – 4.32E+02)	32.14
Atopobium vaginae	*Atopobium vaginae* 55227 (CCUG)	1.50E+02	1.35E+02 (95% CI: 1.08E+02 – 1.95E+02)	34.83
Candida parapsilosis	*Candida parapsilosis* 22019 (ATCC)	1.60E+02	1.41E+02 (95% CI: 1.10E+02 – 2.00E+02)	33.24
Candida tropicalis	*Candida tropicalis* 750 (ATCC)	6.67E+01	5.66E+01 (95% CI: 4.58E+01 – 7.61E+01)	33.79
Candida dubliniensis	*Candida dubliniensis* MYA-646 (ATCC)	1.20E+03	8.19E+02 (95% CI: 6.59E+02 – 1.12E+03)	33.29
Candida krusei	*Candida krusei* 14243 (ATCC)	1.50E+02	9.39E+01 (95% CI: 7.68E+01 – 1.23E+02)	33.82
Candida albicans	*Candida albicans* 14053 (ATCC)	7.00E+02	6.77E+02 (95% CI: 5.34E+02 – 9.30E+02)	33.36
Candida glabrata	*Candida glabrata* MYA-275 (ATCC)	7.00E+02	3.52E+02 (95% CI: 2.75E+02 – 5.01E+02)	31.86

Table 3 provides a summary of LoD for BV target combinations used in various non-clinical performance studies. These combinations served as representative compositions of bacterial targets to reflect the BV LoD because the BV algorithm integrates real-time PCR signals from multiple bacterial targets to calculate the final BV result.

Table 3: LoD – BV target combinations

Strain / Isolate	LoD (CFU/mL)
Atopobium vaginae 55227 (CCUG) and *Gardnerella vaginalis* 72422 (CCUG)	*A. vaginae* = 2.01E+03 and *G. vaginalis* = 2.15E+04
Atopobium vaginae 55227 (CCUG), *Gardnerella vaginalis* 72422 (CCUG), and *Lactobacillus crispatus* 33820 (ATCC)	*A. vaginae* = 7.41E+04, *G. vaginalis* = 1.52E+06, and *L. crispatus* = 2.98E+01

4.2. Inclusivity

The inclusivity of **cobas®** BV/CV was confirmed by testing minimum of five strains of each BV target *(Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus jensenii*, *Gardnerella vaginalis*, and *Atopobium vaginae)* and five strains of each CV target (*Candida parapsilosis, Candida tropicalis, Candida dubliniensis, Candida krusei, Candida albicans, and Candida glabrata*). All BV strains were detected at approximately 3x LoD compared to the respective LoD strain. Four of the five strains of *Candida tropicalis* were detected at 4-8x LoD. All other CV strains were detected at approximately 3x LoD compared to the respective LoD strain.

4.3. Precision (within laboratory)

Within laboratory precision was examined using BV and CV cultures diluted into simulated vaginal matrix stabilized in **cobas®** PCR Media. Sources of variability were examined with a panel consisting of three concentration levels per CV strain or co-formulated BV target (three different compositions utilizing distinct concentrations of *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae*) plus simulated vaginal matrix without analytes, using three lots of **cobas®** BV/CV reagents, three instruments and three operators over six testing days days and with a total of 36 runs. Per testing day, two runs per instrument were performed with three replicates of each panel member tested per run. The study performance positivity rates are shown in Table 4. All negative panel members tested negative. Analysis of standard deviation (SD) and percent coefficient of variation (CV%) of the BV probability and CV Ct values from valid tests performed on positive panel members are presented in Table 5 and Table 6.

Table 4: Summary of within laboratory precision

Target	Level	Number of Positive / Valid Replicates	Positivity Rate	95% two-sided CI (Clopper-Pearson)
BV[1]	High Negative	302/ 324	93.21%	89.90 - 95.70%

Target	Level	Number of Positive / Valid Replicates	Positivity Rate	95% two-sided CI (Clopper-Pearson)
BV[1]	Low Positive	324 / 324	100.00%	98.87 - 100.00%
BV[1]	Moderate Positive	324 / 324	100.00%	98.87 - 100.00%
CV[2]	High Negative	289 / 324	89.20%	85.30 - 92.36%
CV[2]	Low Positive	324 / 324	100.00%	98.87 - 100.00%
CV[2]	Moderate Positive	324 / 324	100.00%	98.87 - 100.00%

[1] Performance for BV includes combined results from replicates of three panel members containing different BV target organism compositions (A, B and C).

[2] Performance for CV includes combined results from replicates of three panel members containing *Candida albicans*, *Candida glabrata* and *Candida krusei*.

Table 5: Overall mean, standard deviations and coefficients of variation (%) for probability, BV positive panels

Composition*	Level	Positivity Rate %	Mean Probability**	Instrument-to-Instrument SD / %CV	Lot-to-Lot SD / %CV	Day-to-Day SD / %CV	Run-to-Run SD / %CV	Within Run SD / %CV	Total SD / %CV
A	High Negative	*100.00*	*0.63*	0.03 / 4.21	0.01 / 2.17	0.02 / 2.60	0.00 / 0.69	0.04 / 6.16	0.05 / 8.22
B	High Negative	*80.56*	*0.57*	0.02 / 3.38	0.02 / 3.44	0.00 / 0.00	0.03 / 4.95	0.03 / 5.21	0.04 / 6.23
C	High Negative	*99.07*	*0.72*	0.02 / 2.90	0.00 / 0.00	0.03 / 3.83	0.00 / 0.00	0.15 / 21.43	0.16 / 21.96***
A	Low Positive	*100.00*	*0.77*	0.01 / 1.48	0.02 / 2.92	0.01 / 1.60	0.00 / 0.00	0.03 / 4.09	0.04 / 5.48
B	Low Positive	*100.00*	*0.76*	0.01 / 1.40	0.00 / 0.00	0.01 / 1.51	0.00 / 0.00	0.05 / 6.93	0.05 / 7.20
C	Low Positive	*100.00*	*0.90*	0.00 / 0.44	0.00 / 0.39	0.00 / 0.31	0.00 / 0.00	0.02 / 2.30	0.02 / 2.70
A	Moderate Positive	*100.00*	*0.96*	0.00 / 0.30	0.00 / 0.48	0.00 / 0.29	0.00 / 0.00	0.01 / 0.82	0.01 / 1.04
B	Moderate Positive	*100.00*	*0.97*	0.00 / 0.00	0.00 / 0.06	0.00 / 0.00	0.00 / 0.00	0.01 / 0.52	0.01 / 0.52
C	Moderate Positive	*100.00*	*0.99*	0.00 / 0.05	0.00 / 0.10	0.00 / 0.16	0.00 / 0.05	0.00 / 0.31	0.00 / 0.38

* BV composition A (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vagina*e, BV composition B (two microorganisms) - *Gardnerella vaginalis* and *Atopobium vaginae*, BV composition C (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae* (different ratios of the three target concentrations compared to composition A)

** Probability is calculated using the Ct values of the three BV targets (*G. vaginalis*, *A. vaginae*, *L. crispatus*). Samples with a probability score greater than 0.5 are called BV positive

*** The elevated variance is due to the intermittent detection of *L. crispatus* at the specific concentration used in this panel member, which lies at the assay's limit of detection.

Table 6: Overall mean, standard deviations and coefficients of variation (%) for cycle threshold, CV positive panels

Target	Level	Positivity Rate %	Mean Ct	Instrument-to-Instrument SD / %CV	Lot-to-Lot SD / %CV	Day-to-Day SD / %CV	Run-to-Run SD / %CV	Within Run SD / %CV	Total SD / %CV
C. albicans	High Negative	79.63	35.13	0.00 / 0.00	0.17 / 0.48	0.11 / 0.30	0.00 / 0.00	0.63 / 1.80	0.66 / 1.89
C. glabrata	High Negative	99.07	34.06	0.00 / 0.00	0.03 / 0.07	0.10 / 0.30	0.00 / 0.00	0.78 / 2.30	0.79 / 2.32
C. krusei	High Negative	88.89	34.78	0.00 / 0.00	0.00 / 0.00	0.00 / 0.00	0.00 / 0.00	0.65 / 1.86	0.65 / 1.86
C. albicans	Low Positive	100.00	32.67	0.00 / 0.00	0.11 / 0.34	0.08 / 0.25	0.19 / 0.58	0.50 / 1.53	0.55 / 1.69
C. glabrata	Low Positive	100.00	31.43	0.00 / 0.00	0.12 / 0.39	0.00 / 0.00	0.00 / 0.00	0.62 / 1.99	0.64 / 2.02
C. krusei	Low Positive	100.00	33.21	0.00 / 0.00	0.06 / 0.18	0.00 / 0.00	0.01 / 0.04	0.48 / 1.44	0.48 / 1.45
C. albicans	Moderate Positive	100.00	30.97	0.00 / 0.00	0.00 / 0.00	0.13 / 0.43	0.22 / 0.70	0.31 / 1.01	0.40 / 1.30
C. glabrata	Moderate Positive	100.00	29.41	0.18 / 0.62	0.00 / 0.00	0.20 / 0.67	0.23 / 0.79	0.78 / 2.67	0.86 / 2.93
C. krusei	Moderate Positive	100.00	31.96	0.00 / 0.00	0.00 / 0.00	0.00 / 0.00	0.00 / 0.00	0.51 / 1.61	0.51 / 1.61

4.4. Cross reactivity and Microbial Interference

A panel of 109 bacteria, fungi, viruses, parasites and plasmids were tested with **cobas**® BV/CV to assess analytical specificity. The organisms listed in Table 7 were spiked at concentrations of approximately 1 x 10^6 units/mL for bacteria, fungi, parasites and plasmid and approximately 1 x 10^5 units/mL for viruses into simulated vaginal matrix stabilized in **cobas**® PCR Media. Testing was performed with each potential interfering organism in absence and presence of BV and CV target (spiked at approximately 3x LoD). *Candida orthopsilosis*, *Lactobacillus acidophilus*, *Lactobacillus helveticus* and *Lactobacillus johnsonii* were detected by **cobas**® BV/CV as predicted based on the *Lactobacillus spp*. and *Candida spp.* target oligo design. The other tested microorganisms did not interfere with **cobas**® BV/CV.

Table 7: Microorganism tested for analytical specificity/cross reactivity

Microorganism	Concentration Tested	Microorganism	Concentration Tested
Acinetobacter baumannii	1.00E+06 CFU/mL	*Kodamaea ohmeri*	6.00E+05 CFU/mL
Acinetobacter calcoaceticus	1.00E+06 CFU/mL	*Lactobacillus acidophilus**	1.00E+06 CFU/mL
Actinomyces israelii	1.00E+06 CFU/mL	*Lactobacillus helveticus**	1.00E+06 CFU/mL
Aerococcus viridans	1.00E+06 CFU/mL	*Lactobacillus iners*	1.00E+06 CFU/mL
Alcaligenes faecalis	1.00E+06 CFU/mL	*Lactobacillus johnsonii**	1.00E+06 CFU/mL
Anaerococcus tetradius	1.00E+06 CFU/mL	*Legionella pneumophila*	1.00E+06 CFU/mL
Atopobium minutum	1.00E+06 CFU/mL	*Mageeibacillus indolicus*	1.00E+06 CFU/mL
Atopobium parvulum	1.00E+06 CFU/mL	*Megasphaera elsdenii*	1.00E+06 CFU/mL
Atopobium rimae	1.00E+06 CFU/mL	*Mobiluncus curtisii*	1.00E+06 CFU/mL
Bacillus subtilis	1.00E+06 CFU/mL	*Mobiluncus mulieris*	1.00E+06 CFU/mL
Bacteroides caccae	1.00E+06 CFU/mL	*Moraxella catarrhalis*	1.00E+06 CFU/mL
Bacteroides fragilis	1.00E+06 CFU/mL	*Morganella morganii*	1.00E+06 CFU/mL
Bacteroides stercoris	1.00E+06 CFU/mL	*Mycobacterium smegmatis*	1.00E+06 CFU/mL
Bacteroides ureolyticus / Campylobacter ureolyticus	1.00E+06 CFU/mL	*Mycoplasma genitalium*	1.00E+06 CFU/mL
Bifidobacterium adolescentis	1.00E+06 CFU/mL	*Mycoplasma hominis*	1.00E+06 CFU/mL
Bifidobacterium breve	1.00E+06 CFU/mL	*Neisseria gonorrhoeae*	1.00E+06 CFU/mL
Bifidobacterium longum	1.00E+06 CFU/mL	*Olsenella uli*	1.00E+06 CFU/mL
Brevibacterium linens	1.00E+06 CFU/mL	*Pantoea agglomerans*	1.00E+06 CFU/mL
Burkholderia cepacia	1.00E+06 CFU/mL	*Pentatrichomonas hominis*	1.00E+06 CFU/mL
BVAB1 plasmid	1.00E+06 cp/mL	*Peptoniphilus asaccharolyticus*	1.00E+06 CFU/mL
Campylobacter jejuni	1.00E+06 CFU/mL	*Peptostreptococcus anaerobius*	1.00E+06 CFU/mL

Microorganism	Concentration Tested	Microorganism	Concentration Tested
Candida catenulata / Diutina catenulata	1.00E+06 CFU/mL	*Pichia fermentans*	5.60E+05 CFU/mL
Candida famata	1.00E+06 CFU/mL	*Pichia norvegensis*	1.00E+06 CFU/mL
Candida haemulonii	1.00E+06 CFU/mL	*Pichia occidentalis*	1.00E+06 CFU/mL
Candida inconspicua	1.00E+06 CFU/mL	*Plesiomonas shigelloides*	1.00E+06 CFU/mL
Candida intermedia	1.00E+06 CFU/mL	*Porphyromonas asaccharolytica*	1.00E+06 CFU/mL
Candida kefyr	1.00E+06 CFU/mL	*Prevotella bivia*	1.00E+06 CFU/mL
Candida lusitaniae	1.00E+06 CFU/mL	*Prevotella melaninogenica*	1.00E+06 CFU/mL
Candida norvegica	1.00E+06 CFU/mL	*Prevotella oralis / Hoylesella oralis*	1.00E+06 CFU/mL
*Candida orthopsilosis**	1.00E+06 CFU/mL	*Propionibacterium acnes*	1.00E+06 CFU/mL
Candida rugosa / Diotima rugosa	1.00E+06 CFU/mL	*Proteus mirabilis*	1.00E+06 CFU/mL
Candida utilis	1.00E+06 CFU/mL	*Providencia stuartii*	1.00E+06 CFU/mL
Chlamydia trachomatis	1.00E+06 CFU/mL	*Pseudomonas aeruginosa*	1.00E+06 CFU/mL
Citrobacter freundii	1.00E+06 CFU/mL	*Saccharomyces cerevisiae*	1.00E+06 CFU/mL
Clostridium perfringens	1.00E+06 CFU/mL	*Salmonella typhimurium*	1.00E+06 CFU/mL
Corynebacterium genitalium	1.00E+06 CFU/mL	*Serratia marcescens*	1.00E+06 CFU/mL
Dialister micraerophilus	1.00E+06 CFU/mL	*Shigella flexneri*	1.00E+06 CFU/mL
Eikenella corrodens	1.00E+06 CFU/mL	*Sneathia sanguinegens*	1.00E+06 CFU/mL
Enterobacter aerogenes	1.00E+06 CFU/mL	*Sneathia vaginalis*	1.00E+06 CFU/mL
Enterococcus faecalis	1.00E+06 CFU/mL	*Staphylococcus aureus*	1.00E+06 CFU/mL
Enterococcus faecium	1.00E+06 CFU/mL	*Staphylococcus epidermidis*	1.00E+06 CFU/mL
Erysipelothrix rhusiopathiae	1.00E+06 CFU/mL	*Streptococcus agalactiae*	1.00E+06 CFU/mL
Escherichia coli	1.00E+06 CFU/mL	*Streptococcus mitis*	1.00E+06 CFU/mL
Finegoldia magna	1.00E+06 CFU/mL	*Streptococcus mutans*	1.00E+06 CFU/mL
Fusobacterium nucleatum	1.00E+06 CFU/mL	*Streptococcus salivarius*	1.00E+06 CFU/mL
Gemella haemolysans	1.00E+06 CFU/mL	*Treponema pallidum*	1.00E+06 CFU/mL
Hepatitis B virus	1.00E+05 IU/mL	*Trichomonas tenax*	1.00E+06 CFU/mL
Hepatitis C virus	1.00E+05 IU/mL	*Trichomonas vaginalis*	2.30E+05 CFU/mL
Herpes simplex virus I / HSV type 1	1.00E+05 IU/mL	*Trueperella pyogenes / Actinomyces pyogenes / Corynebacterium pyogenes*	1.00E+06 CFU/mL
Herpes simplex virus II / Human herpesvirus 2	1.00E+05 IU/mL	*Varicella-zoster virus*	1.00E+05 IU/mL
HIV-1	1.00E+05 IU/mL	*Veillonella atypica*	1.00E+06 CFU/mL
Human papilloma virus	1.00E+05 IU/mL	*Veillonella parvula*	1.00E+06 CFU/mL
Kingella denitrificans	1.00E+06 CFU/mL	*Vibrio parahaemolyticus*	1.00E+06 CFU/mL

Microorganism	Concentration Tested	Microorganism	Concentration Tested
Klebsiella pneumoniae	1.00E+06 CFU/mL	*Yersinia enterocolitica*	1.00E+06 CFU/mL
Kocuria rhizophila	1.00E+06 CFU/mL	-	-

* *Candida orthopsilosis*, *Lactobacillus acidophilus*, *Lactobacillus helveticus* and *Lactobacillus johnsonii* were detected by the test due to oligo design. The detection of these organisms by **cobas**® BV/CV does not compromise the final BV or CV result.

4.5. Interfering substances

The effect of over-the-counter and prescription products that may be present in vaginal swab specimens (Table 8) were evaluated with **cobas**® BV/CV. Testing was done using simulated vaginal matrix stabilized in **cobas**® PCR media and spiked with potential interferents at levels expected from normal patient usage and in absence and presence of BV and CV target (spiked at approximately 3x LoD).

Of the products tested, Crinone® 8% Vaginal Gel, Gynaedron®, Metronidazole Vaginal Gel, NUVESSA®, RepHresh™ Odor Eliminating Gel and Vagisil produced false negative or invalid results at levels that may be present in vaginal swab specimens. These products contain carbomer(s) or polycarbophil. Products containing carbomer(s) or polycarbophil(s) have been shown to generate false negative and invalid results. Utrogestan® interfered with **cobas**® BV/CV and generated false positive results for CV. Table 8 lists the substances tested for interference and is not intended to be a comprehensive list of carbomer or polycarbophil containing products.

Table 8: List of substances tested for interference with cobas® BV/CV

Exogenous Product or Substance	Ingredient	Testing Concentration [mg/mL]	Concentration of Active Ingredient Tested [mg/mL]
Acyclovir Cream	Acyclovir	33.64	1.68
AFI LactoSpore®	*Bacillus coagulans*	123.13	1.16E+09 CFU/mL
Arilin®[2]	Metronidazole	63.60	26.07
Clindamycin Phosphate Vaginal Cream	Clindamycin Phosphate	41.54	0.83
7 Day Vaginal Cream	Clotrimazole	37.82	0.38
Crinone® 8% Vaginal Gel[1]	Progesterone	33.72	2.70
Daktarin®	Miconazole Nitrate	38.56	0.77

Exogenous Product or Substance	Ingredient	Testing Concentration [mg/mL]	Concentration of Active Ingredient Tested [mg/mL]
Estradiol Vaginal Cream	Estradiol	46.64	0.01
Globe® Hemorrhoidal Cream	Glycerol	47.22	6.80
Globe® Hemorrhoidal Cream	Pramoxine HCl	47.22	0.47
Globe® Hemorrhoidal Cream	Phenylephrine HCl	47.22	0.12
Globe® Hemorrhoidal Cream	Petrolatum	47.22	7.08
Gynaedron®[1]	Dexpanthenol	36.01	0.72
Gynaedron®[1]	Lactic acid	36.01	0.29
Gynaedron®[1]	Carbomer	36.01	N/A[3]
Gynofit®	Glycerin, Hydroxyethyl Cellulose	48.24	N/A[3]
Imiquimod Cream	Imiquimod	39.72	1.99
K-Y Ultragel®	Propylene Glycol	75.01	N/A[3]
Lactacyd®	Glycerin, Propylene Glycol	57.07	N/A[3]
Monistat®	Hydrocortisone	36.39	0.36
Metronidazole Vaginal Gel[1]	Metronidazole	41.93	0.31
NutraBlast Boric Acid Vaginal Supp.	Boric Acid	138.99	139.53
Norforms®	Benzethonium Chloride	490.66	N/A[3]
NUVESSA®[1]	Metronidazole	61.14	0.79
Premarin®	Conjugated Estrogens	33.76	0.02
Progesterone	N/A	1.57	1.57[4]
RepHresh™ Odor Eliminating Gel[1]	Glycerin; Sodium Hydroxide; Carbomer	51.76	N/A[3]
Summer's Eve® Ultimate Odor Protection Spray	Isobutane, Isopropyl M Myristate	28.14	N/A[3]
Tioconazole 1 Ointment	Tioconazole	56.06	3.65
Utrogestan®[1]	Progesterone	170.92	46.51
VCF® Vaginal Contraceptive Gel	Nonoxynol-9	71.18	2.85
Vagisan®	Povidone-iodine	55.92	5.90
Vagisil®[1]	Benzocaine	40.12	8.02
Vagisil®[1]	Resorcinol	40.12	1.20

Exogenous Product or Substance	Ingredient	Testing Concentration [mg/mL]	Concentration of Active Ingredient Tested [mg/mL]
YeastGard Advanced™	*Candida albicans, Candida parapsilosis, Pulsatilla, Bacillus coagulans*	495.46	N/A[3]

[1] Products that showed interference at levels that may be present in vaginal swab specimens.

[2] Product containing metronidazole which did not show interference.

[3] Concentrations of the ingredients not available from the manufacturer.

[4] Progesterone was tested as a pure active ingredient dissolved in DMSO along with DMSO solvent alone. Both yielded 100% expected results, demonstrating no interference from progesterone at the tested concentration.

Endogenous substances which may be present in vaginal specimens were tested for interference. Testing was done using simulated vaginal matrix stabilized in **cobas**® PCR media and spiked with potential interferents at elevated levels and in the absence and presence of BV and CV target (spiked at approximately 3x LoD).

None of the tested substances interfered with **cobas**® BV/CV performance by generating false-negative or false-positive results. The levels of endogenous substances tolerated by the assay are shown in Table 9.

Table 9: Summary of endogenous substance concentrations that do not show interference

Interferent	Concentration Tested
Whole Blood	44.86 mg/mL*
Leukocytes	36.50 mg/mL*
Mucin	0.20% - 0.50%
Seminal fluid	42.32 mg/mL*

*Concentration is equivalent to a fully covered swab stabilized into 4.3 mL of **cobas**® PCR media

4.6. Competitive inhibition

To assess competitive inhibition between BV and CV targets, low and moderate concentrations of one target were mixed with very high concentrations of the other target. Low and moderate concentrations were defined as approximately 1x LoD and approximately 3x LoD, respectively, and high concentrations were defined at approximately 1E+06 CFU/mL. The study samples were prepared in simulated vaginal matrix stabilized in **cobas**® PCR Media.

Testing results indicated that when BV targets were present at a high concentration, CV was detected at both low and moderate levels. Results also indicated that when CV was present at a high concentration, BV was detected at both low and moderate levels. The specificity of CV was not affected by the presence of high concentrations of BV and the specificity of BV was not affected by the presence of high concentrations of CV.

4.7. Cross contamination

Cross-contamination can cause false positive results. The sample-to-sample cross-contamination rate of **cobas®** BV/CV was determined by testing alternating very high positive and negative samples over multiple runs. Testing was done using samples prepared with simulated vaginal matrix stabilized in **cobas®** PCR Media. High positive samples in the study were co-formulated with *Gardnerella vaginalis* and *Candida albicans* to a concentration that generated Ct values ~14 and ~24 cycles, respectively, representing the Ct value lower than that observed in 95% of positive results in the intended use population. Negative samples consisted of simulated vaginal matrix stabilized in **cobas®** PCR Media without the analytes.

Positive and negative samples were processed in a checkerboard configuration in five runs on **cobas®** 8800 system for a total of 470 samples (46 high positive samples and 48 negative samples per run). Study results included 240 negative samples correctly reported as negative and 230 positive samples correctly reported as positive for each of the tested **cobas®** BV/CV analyte demonstrating no cross-contamination (0%; 0/240) when tested with **cobas®** BV/CV on the **cobas®** 6800/8800 systems.

4.8. Reproducibility

A reproducibility study was performed across different sites, reagent lots, operators, and days, for **cobas®** BV/CV. Testing was performed at two external sites and one internal site. There were 13 panel members formulated with simulated vaginal matrix stabilized in **cobas®** PCR media. A reproducibility panel included 1 negative panel member, 3 low-positive, 3 moderate-positive, and 3 high-negative members that were representative of a BV infection (i.e., *G. vaginalis*, *L. crispatus*, and/or *A. vaginae*). The reproducibility panel also included 1 low-positive, 1 moderate-positive, and 1 high-negative *C. albicans* member.

Overall, there were 3744 tests, run across 3 reagent lots and over 6 testing days. Of the 3744 tests, there were 3729 (99.6%) valid and 15 (0.4%) invalid test results. Nine operators participated across the three study sites.

Table 10 below shows the percent agreement of **cobas®** BV/CV test results with the expected result, along with the corresponding 95% CIs, by target pathogen and level of infection.

Table 10: Percentage of Agreement of cobas® BV/CV Test with the Expected Result, Presented by Pathogen and Level of Infection on cobas® 6800/8800

Pathogen	Level of Infection	Valid Replicates Tested (N)	Tests with Expected Results (n)	Percent Agreement (n/N) 100%	95% CI[a]
BV	Negative	288	288	100.0	(98.7 %, 100.0 %)
BV[1]	High Negative	856	618	72.2	(69.1 %, 75.1 %)
BV[1]	Low Positive	862	862	100.0	(99.6 %, 100.0 %)
BV[1]	Moderate Positive	861	861	100.0	(99.6 %, 100.0 %)
CV	Negative*	288	286	99.3	(97.5 %, 99.8 %)
CV	High Negative	288	40	13.9	(10.4 %, 18.4 %)
CV	Low Positive	286	286	100.0	(98.7 %, 100.0 %)
CV	Moderate Positive	288	288	100.0	(98.7 %, 100.0 %)

[1] Performance for BV includes combined results from replicates of three panel members containing different BV target organism compositions (A, B and C).

* Two samples were unexpectedly positive with high Ct-values suggesting contamination at the testing site

[a] Confidence Intervals are calculated using Clopper-Pearson's exact method

Note: CI= Confidence interval; N/A = Not Applicable.

Table 11 and Table 12 show the variance component analysis for BV and CV respectively.

Table 11: Standard Deviations and Coefficients of Variation of Probability Values across Testing Site, Reagent Lot, Days, and Runs, Presented by Positive Panel Member on cobas® 6800/8800 - BV

Panel Member[a]	(n/N)[b]	Positivity Rate%	Overall Mean / SD / %CV	Between – Site SD / %CV	Between – Lot SD / %CV	Between – Day SD / %CV	Between – Run SD / %CV	Within – Run SD / %CV
BV/High negative/ Composition A	228/286	79.72	0.59 / 0.05 / 8.69	0.02 / 3.15	0.02 / 3.07	0.01 / 2.55	0.01 / 1.86	0.04 / 6.79
BV/High negative/ Composition B	131/286	45.80	0.57 / 0.06 / 10.00	0.00 / 0.00	0.01 / 2.27	0.01 / 2.10	0.00 / 0.00	0.05 / 9.51
BV/High negative/ Composition C	259/284	91.20	0.84 / 0.20 / 24.31[c]	0.00 / 0.00	0.01 / 1.17	0.00 / 0.00	0.00 / 0.00	0.20 / 24.29

Panel Member[a]	(n/N)[b]	Positivity Rate%	Overall Mean / SD / %CV	Between – Site SD / %CV	Between – Lot SD / %CV	Between – Day SD / %CV	Between – Run SD / %CV	Within – Run SD / %CV
BV/Low positive/ Composition A	288/288	100.00	0.80 / 0.05 / 6.25	0.03 / 3.83	0.01 / 1.25	0.02 / 2.87	0.01 / 1.69	0.03 / 3.43
BV/Low positive/ Composition B	288/288	100.00	0.79 / 0.06 / 7.11	0.02 / 2.66	0.00 / 0.00	0.02 / 2.03	0.02 / 2.28	0.05 / 5.85
BV/Low positive/ Composition C	286/286	100.00	0.87 / 0.07 / 8.15	0.03 / 3.02	0.02 / 1.74	0.02 / 1.93	0.00 / 0.00	0.06 / 7.11
BV/moderate positive/ Composition A	287/287	100.00	0.96 / 0.01 / 1.22	0.01 / 0.57	0.00 / 0.46	0.01 / 0.57	0.00 / 0.40	0.01 / 0.69
BV/moderate positive/ Composition B	287/287	100.00	0.98 / 0.00 / 0.48	0.00 / 0.10	0.00 / 0.05	0.00 / 0.11	0.00 / 0.11	0.00 / 0.44
BV/moderate positive/ Composition C	287/287	100.00	0.99 / 0.00 / 0.24	0.00 / 0.15	0.00 / 0.03	0.00 / 0.08	0.00 / 0.04	0.00 / 0.16

[a] BV composition A (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae*, BV composition B (two microorganisms) - *Gardnerella vaginalis* and *Atopobium vaginae*, BV composition C (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae* (different ratios of the three target concentrations compared to composition A)

[b] n is the number of positive tests, which contribute probability values to the analysis. N is the total number of valid tests for the panel member.

[c] The elevated variance is due to the intermittent detection of *L. crispatus* at the specific concentration used in this panel member, which lies at the assay's limit of detection.

Note: Probability is calculated using the Ct values of the three BV targets (*G. vaginalis*, *A. vaginae*, *L. crispatus*). Samples with a probability score greater than 0.5 are called BV positive. CV = coefficient of variation; N = Number; SD = standard deviation.

Table 12: Standard Deviations and Coefficients of Variation of Cycle Threshold (Ct) Values across Testing Site, Reagent Lot, Days, and Runs, Presented by Positive Panel Member on cobas® 6800/8800 - CV

Panel Member	(n/N)[a]	Positivity Rate%	Overall Mean / SD / %CV	Between – Site SD / %CV	Between – Lot SD / %CV	Between – Day SD / %CV	Between – Run SD / %CV	Within – Run SD / %CV
CV/High negative	40/288	13.89	35.48 / 0.44 / 1.25	0.13 / 0.37	0.00 / 0.00	0.22 / 0.62	0.34 / 0.95	0.13 / 0.38
CV/Low positive	286/286	100.00	34.40 / 0.48 / 1.38	0.23 / 0.68	0.00 / 0.00	0.08 / 0.23	0.16 / 0.45	0.38 / 1.09

Panel Member	(n/N)[a]	Positivity Rate%	Overall Mean / SD / %CV	Between – Site SD / %CV	Between – Lot SD / %CV	Between – Day SD / %CV	Between – Run SD / %CV	Within – Run SD / %CV
CV/moderate positive	288/288	100.00	32.79 / 0.44 / 1.35	0.30 / 0.90	0.00 / 0.00	0.14 / 0.41	0.08 / 0.24	0.29 / 0.88

[a] n is the number of positive tests, which contribute Ct values to the analysis. N is the total number of valid tests for the panel member.

Note: CV = coefficient of variation; N = Number; SD = standard deviation.

Table 13 to Table 15 show the variance component analysis for individual BV organisms on the Ct values (*Gardnerella vaginalis*, *Lactobacillus crispatus*, and *Atopobium vaginae*) for all BV panel members.

Table 13: Standard Deviations and Coefficients of Variation of Ct Values across Testing Site, Reagent Lot, Days, and Runs, Presented by Positive Panel Member on cobas® 6800/8800 – BV (*Gardnerella vaginalis target only*)

Panel Member[a]	(n/N)[b]	Positivity Rate %	Overall Mean / SD / %CV	Between - Site SD / %CV	Between - Lot SD / %CV	Between - Day SD / %CV	Between - Run SD / %CV	Within - Run SD / %CV
BV/High negative/ Composition A	286/286	100.00	21.07 / 0.23 / 1.07	0.07 / 0.32	0.06 / 0.30	0.06 / 0.29	0.13 / 0.61	0.15 / 0.70
BV/High negative/ Composition B	286/286	100.00	27.73 / 0.22 / 0.79	0.07 / 0.24	0.06 / 0.23	0.06 / 0.20	0.12 / 0.42	0.15 / 0.54
BV/High negative/ Composition C	284/284	100.00	23.23 / 0.21 / 0.90	0.00 / 0.00	0.06 / 0.25	0.11 / 0.45	0.12 / 0.52	0.12 / 0.52
BV/Low positive/ Composition A	288/288	100.00	20.35 / 0.23 / 1.12	0.07 / 0.34	0.06 / 0.29	0.11 / 0.54	0.14 / 0.70	0.11 / 0.52
BV/Low positive/ Composition B	288/288	100.00	26.45 / 0.19 / 0.73	0.00 / 0.00	0.06 / 0.24	0.05 / 0.20	0.14 / 0.52	0.11 / 0.40
BV/Low positive/ Composition C	286/286	100.00	22.23 / 0.20 / 0.89	0.00 / 0.00	0.03 / 0.13	0.09 / 0.42	0.12 / 0.56	0.12 / 0.53

Panel Member[a]	(n/N)[b]	Positivity Rate %	Overall Mean / SD / %CV	Between - Site SD / %CV	Between - Lot SD / %CV	Between - Day SD / %CV	Between - Run SD / %CV	Within - Run SD / %CV
BV/moderate positive/ Composition A	287/287	100.00	18.54 / 0.22 / 1.19	0.05 / 0.24	0.06 / 0.32	0.09 / 0.47	0.13 / 0.69	0.14 / 0.74
BV/moderate positive/ Composition B	287/287	100.00	24.83 / 0.17 / 0.69	0.03 / 0.13	0.02 / 0.07	0.07 / 0.26	0.11 / 0.44	0.11 / 0.44
BV/moderate positive/ Composition C	287/287	100.00	19.71 / 0.18 / 0.91	0.03 / 0.17	0.04 / 0.19	0.07 / 0.35	0.09 / 0.47	0.13 / 0.65

[a] BV composition A (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae*, BV composition B (two microorganisms) - *Gardnerella vaginalis* and *Atopobium vaginae*, BV composition C (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae* (different ratios of the three target concentrations compared to composition A)

[b] n is the number of positive tests, which contribute Ct values to the analysis. N is the total number of valid tests for the panel member.

Note: CV = coefficient of variation; N = Number; SD = standard deviation-

Table 14: Standard Deviations and Coefficients of Variation of Ct Values across Testing Site, Reagent Lot, Days, and Runs, Presented by Positive Panel Member on cobas® 6800/8800 – BV (*Lactobacillus crispatus target only*)

Panel Member[a]	(n/N)[b]	Positivity Rate %	Overall Mean / SD / %CV	Between - Site SD / %CV	Between - Lot SD / %CV	Between - Day SD / %CV	Between - Run SD / %CV	Within - Run SD / %CV
BV/High negative/ Composition A	286/286	100.00	27.85 / 0.21 / 0.74	0.08 / 0.28	0.00 / 0.00	0.07 / 0.26	0.11 / 0.40	0.14 / 0.49
BV/High negative/ Composition B[c]	0/286	0.00	n/a	n/a	n/a	n/a	n/a	n/a
BV/High negative/ Composition C	122/284	42.96	35.56 / 0.30 / 0.83	0.05 / 0.15	0.00 / 0.00	0.05 / 0.13	0.00 / 0.00	0.29 / 0.81

Panel Member[a]	(n/N)[b]	Positivity Rate %	Overall Mean / SD / %CV	Between - Site SD / %CV	Between - Lot SD / %CV	Between - Day SD / %CV	Between - Run SD / %CV	Within - Run SD / %CV
BV/Low positive/ Composition A	288/288	100.00	27.09 / 0.20 / 0.73	0.08 / 0.31	0.00 / 0.00	0.10 / 0.36	0.11 / 0.40	0.10 / 0.37
BV/Low positive/ Composition B[c]	0/288	0.00	n/a	n/a	n/a	n/a	n/a	n/a
BV/Low positive/ Composition C	242/286	84.62	35.22 / 0.47 / 1.34	0.13 / 0.36	0.01 / 0.04	0.14 / 0.41	0.00 / 0.00	0.43 / 1.22
BV/moderate positive/ Composition A	287/287	100.00	25.26 / 0.21 / 0.83	0.10 / 0.41	0.00 / 0.00	0.10 / 0.39	0.12 / 0.46	0.10 / 0.41
BV/moderate positive/ Composition B[c]	0/287	0.00	n/a	n/a	n/a	n/a	n/a	n/a
BV/moderate positive/ Composition C	287/287	100.00	33.11 / 0.39 / 1.17	0.23 / 0.70	0.00 / 0.00	0.13 / 0.39	0.01 / 0.02	0.28 / 0.84

[a] BV composition A (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae*, BV composition B (two microorganisms) - *Gardnerella vaginalis* and *Atopobium vaginae*, BV composition C (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae* (different ratios of the three target concentrations compared to composition A)

[b] n is the number of positive tests, which contribute Ct values to the analysis. N is the total number of valid tests for the panel member.

[c] Composition B does not contain *Lactobacillus crispatus* and can therefore not be evaluated for these panel members

Note: CV = coefficient of variation; N = Number; SD = standard deviation; n/a = not applicable.

Table 15: Standard Deviations and Coefficients of Variation of Ct Values across Testing Site, Reagent Lot, Days, and Runs, Presented by Positive Panel Member on cobas® 6800/8800 – BV (*Atopobium vaginae target only*)

Panel Member[a]	(n/N)[b]	Positivity Rate%	Overall Mean / SD / %CV	Between - Site SD / %CV	Between - Lot SD / %CV	Between - Day SD / %CV	Between - Run SD / %CV	Within - Run SD / %CV
BV/High negative/ Composition A	286/286	100.00	26.93 / 0.19 / 0.71	0.06 / 0.21	0.00 / 0.00	0.00 / 0.00	0.11 / 0.43	0.14 / 0.52
BV/High negative/ Composition B	286/286	100.00	32.81 / 0.31 / 0.95	0.06 / 0.18	0.00 / 0.00	0.00 / 0.00	0.13 / 0.39	0.28 / 0.85
BV/High negative/ Composition C	284/284	100.00	29.16 / 0.23 / 0.80	0.07 / 0.25	0.00 / 0.00	0.11 / 0.38	0.09 / 0.30	0.17 / 0.59
BV/Low positive/ Composition A	288/288	100.00	26.25 / 0.18 / 0.69	0.03 / 0.11	0.00 / 0.00	0.07 / 0.26	0.12 / 0.45	0.12 / 0.44
BV/Low positive/ Composition B	288/288	100.00	31.54 / 0.25 / 0.80	0.01 / 0.03	0.05 / 0.14	0.04 / 0.13	0.15 / 0.48	0.19 / 0.61
BV/Low positive/ Composition C	286/286	100.00	28.04 / 0.22 / 0.79	0.06 / 0.20	0.00 / 0.00	0.06 / 0.21	0.15 / 0.53	0.14 / 0.50
BV/moderate positive/ Composition A	287/287	100.00	24.45 / 0.18 / 0.73	0.04 / 0.16	0.02 / 0.09	0.05 / 0.22	0.11 / 0.44	0.13 / 0.51
BV/moderate positive/ Composition B	287/287	100.00	30.16 / 0.22 / 0.74	0.06 / 0.21	0.03 / 0.09	0.08 / 0.26	0.10 / 0.34	0.17 / 0.57
BV/moderate positive/ Composition C	287/287	100.00	25.34 / 0.19 / 0.74	0.05 / 0.20	0.00 / 0.00	0.08 / 0.33	0.09 / 0.36	0.13 / 0.52

[a] BV composition A (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae*, BV composition B (two microorganisms) - *Gardnerella vaginalis* and *Atopobium vaginae*, BV composition C (three microorganisms) - *Lactobacillus crispatus*, *Gardnerella vaginalis*, and *Atopobium vaginae* (different ratios of the three target concentrations compared to composition A)

Panel Member[a]	(n/N)[b]	Positivity Rate%	Overall Mean / SD / %CV	Between - Site SD / %CV	Between - Lot SD / %CV	Between - Day SD / %CV	Between - Run SD / %CV	Within - Run SD / %CV

[b] n is the number of positive tests, which contribute Ct values to the analysis. N is the total number of valid tests for the panel member.

Note: CV = coefficient of variation; N = Number; SD = standard deviation.

5. CLINICAL PERFORMANCE EVALUATION

5.1. Clinical Study Design

The clinical performance of **cobas**® BV/CV was established in a prospective clinical study performed at eight geographically diverse sites in the U.S. and one site in Europe.

716 total subjects were screened for inclusion in this study, with 711 subjects included in the final data set. Among the 711 subjects included, 552 were symptomatic and 159 were asymptomatic subjects. Symptomatic patients had a clinical presentation consistent with vaginitis, vaginosis, or both.

Each symptomatic subject had multiple vaginal swabs collected.

- One self-collected vaginal swab for **cobas**® BV/CV testing
- Three clinician-collected vaginal swabs (randomized in collection sequence) for BV and CV comparator testing
- One clinician-collected vaginal swab for **cobas**® BV/CV testing

Each asymptomatic subject had 1 clinician-collected vaginal swab for **cobas**® BV/CV testing only.

The **cobas**® BV/CV performance in symptomatic subjects was compared to BV and CV status determined by comparator algorithms based on a combination of 3 FDA-cleared NAATs. A positive status was determined when at least 2 of the comparator NAATs were positive. A negative status was determined when at least 2 of the comparator NAATs were negative. When the results from the comparator algorithm were inconclusive, the final result was excluded from the final performance calculations.

Of the 711 subjects enrolled in the study, 17 symptomatic subjects and 5 asymptomatic subjects were non-evaluable due to invalid or missing results due to protocol deviations on **cobas**®

BV/CV and/or comparator tests. The remaining 689 subjects (535 symptomatic and 154 asymptomatic) were evaluable on either BV and/or CV.

5.2. Clinical Performance: Bacterial Vaginosis (BV)

After excluding specimens without the results from comparator method and/or **cobas**® BV/CV, 530 clinician-collected and 528 self-collected vaginal swab specimens from symptomatic subjects were included in BV performance calculations.

Table 16 shows the clinical performance of **cobas**® BV/CV for detecting BV in symptomatic subjects, stratified by clinician- and self-collected vaginal swab samples. Of the 530 evaluable clinician-collected specimens, 213 (40.2%; 213/530) were detected on **cobas**® BV/CV with concordant comparator method results. The sensitivity was 95.9% (213/222: 92.5%, 97.9%). The specificity was 93.8% (289/308: 90.6%, 96.0%). PPV and NPV were reported as 91.8% (213/232: 87.6%, 94.7%) and 97.0% (289/298: 94.4%, 98.4%) respectively.

Of the 528 evaluable self-collected specimens, 214 (40.5%; 214/528) were detected on **cobas**® BV/CV with concordant comparator method results. The sensitivity was 96.8% (214/221: 93.6%, 98.5%). The specificity was 92.8% (285/307: 89.4%, 95.2%). PPV and NPV were reported as 90.7% (214/236: 86.3%, 93.8%) and 97.6% (285/292: 95.1%, 98.8%) respectively.

Table 16: Summary of cobas® BV/CV Performance for BV in symptomatic subjects by collection method

Collection Method	Total N	SENS	95% Score CI	SPEC	95% Score CI	PPV	95% Score CI	NPV	95% Score CI
CC	530	95.9% (213/222)	(92.5%, 97.9%)	93.8% (289/308)	(90.6%, 96.0%)	91.8% (213/232)	(87.6%, 94.7%)	97.0% (289/298)	(94.4%, 98.4%)
SC	528	96.8% (214/221)	(93.6%, 98.5%)	92.8% (285/307)	(89.4%, 95.2%)	90.7% (214/236)	(86.3%, 93.8%)	97.6% (285/292)	(95.1%, 98.8%)

Note: N is the total number of evaluable subjects; CC = Clinician-collected; SC = self-collected.

CI = confidence interval, NAAT= nucleic acid amplification test, NPV = negative predictive value

PPV = positive predictive value, SENS = sensitivity, SPEC = specificity

Note: The predictive values shown above reflect performance specific to the clinical study population and may not be applicable to all individuals in the intended use population.

5.3. Clinical Performance: Candida Vaginitis (CV)

After excluding specimens without the results from comparator and/or **cobas**® BV/CV, 529 clinician-collected and 526 self-collected vaginal swab specimens from symptomatic subjects were included in CV performance calculations.

Table 17 shows the clinical performance of **cobas**® BV/CV for detecting CV in symptomatic subjects, stratified by clinician- and self-collected vaginal swab samples. Of the 529 evaluable clinician – collected specimens, 119 (22.5%; 119/529) were detected on **cobas**® BV/CV with concordant comparator method results. The PPA was 93.0% (119/128: 87.2%, 96.3%). The NPA was 97.8% (392/401: 95.8%, 98.8%).

Of the 526 evaluable self – collected specimens, 120 (22.8%; 120/526) were detected on **cobas**® BV/CV with concordant comparator method results. The PPA was 94.5% (120/127: 89.1%, 97.3%). The NPA was 93.0% (371/399: 90.0%, 95.1%).

Table 17: Summary of cobas® BV/CV Performance for CV in symptomatic subjects by collection method

Collection Method	Total N	PPA	95% Score CI	NPA	95% Score CI
CC	529	93.0% (119/128)	(87.2%, 96.3%)	97.8% (392/401)	(95.8%, 98.8%)
SC	526	94.5% (120/127)	(89.1%, 97.3%)	93.0% (371/399)	(90.0%, 95.1%)

Note: N is the total number of evaluable subjects; CC = Clinician-collected; SC = self-collected.
CI = confidence interval, NAAT= nucleic acid amplification test, PPA= positive percent agreement, NPA= negative percent agreement.

5.4. Performance in Asymptomatic Population

To provide context on organism positivity rate in individuals without symptoms, 159 subjects were enrolled, that were tested only in the **cobas**® BV/CV assay using clinician-collected swabs. Of the 159 subjects, 154 were evaluable. This testing is outside the specific Intended Use (which is for symptomatic individuals). The BV and CV organisms that are detected by **cobas**® BV/CV are also considered part of the normal vaginal microbiome. The development of BV and CV is a result of a microbiome imbalance, and the organism loads can increase in a diseased state

compared to normal, healthy levels. The detection of these organisms by any highly sensitive and specific NAAT represents an inherent challenge. It is therefore important to understand how any diagnostic NAAT performs in an asymptomatic patient population. The diagnostic utility is highest for any BV and CV NAAT when testing individuals that are presenting with vaginitis/vaginosis symptoms.

The positivity rate of BV and CV in the asymptomatic population is presented overall in (Table 18).

Table 18: cobas® BV/CV Overall positivity rate in asymptomatic population

Target	cobas® BV/CV Positive	Positivity Rate (95% CI)
BV	50 / 154	32.5% (25.6% - 40.2%)
CV	19 / 154	12.3% (8.0% - 18.5%)

6. CONCLUSIONS

A comparison of the intended use, technological characteristics, and the results of analytical (non-clinical) and clinical performance studies demonstrates that the **cobas®** BV/CV for use on the **cobas®** 6800/8800 systems is substantially equivalent to the predicate device.