# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY AND INSTRUMENT

## I Background Information:

### A 510(k) Number

K223653

### B Applicant

Becton, Dickinson and Company

### C Proprietary and Established Names

BD Vaginal Panel

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| PQA | Class II | 21 CFR 866.3975 - Device That Detects Nucleic Acid Sequences From Microorganisms Associated With Vaginitis And Bacterial Vaginosis | MI - Microbiology |
| OUY | Class II | 21 CFR 866.3860 - Trichomonas vaginalis nucleic acid assay | MI - Microbiology |
| OOI | Class II | 21 CFR 862.2570 - Instrumentation for clinical multiplex test systems | CH - Clinical Chemistry |
| NSU | Class II | 21 CFR 862.2570 - Instrumentation for clinical multiplex test systems | CH - Clinical Chemistry |

## II Submission/Device Overview:

### A Purpose for Submission:

To obtain a substantial equivalence determination for the BD Vaginal Panel on the BD COR System

**B Measurand:**

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 (Results for individual organisms are not reported. Qualitative BV results are based on detection and quantitation of targeted organisms)

- *Lactobacillus spp*. (*L. crispatus and L. jensenii*)
- *Gardnerella vaginalis*
- *Atopobium vaginae*
- Bacterial Vaginosis Associated Bacteria-2 (BVAB-2)
- Megasphaera-1

• *Candida spp.* (Reported as C. group includes: *C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis*)

• *Candida glabrata*

• *Candida krusei*

• *Trichomonas vaginalis*

**C Type of Test:**

The BD Vaginal Panel is a nucleic acid-based test for the detection of the above listed bacteria, yeast and parasites in vaginal specimens obtained from symptomatic patients.

## III Intended Use/Indications for Use:

**A Intended Use(s):**

See Indications for Use below.

**B Indication(s) for Use:**

The BD Vaginal Panel is an automated qualitative in vitro diagnostic test for the direct detection of DNA targets from bacteria associated with bacterial vaginosis (qualitative results reported based on detection and quantitation of targeted organism markers), Candida species associated with vulvovaginal candidiasis, and Trichomonas vaginalis from vaginal swabs in patients who are symptomatic for vaginitis/vaginosis. The test utilizes real-time polymerase chain reaction (PCR) for the amplification of specific DNA targets and utilizes fluorogenic target-specific hybridization probes to detect and differentiate DNA from:

- Bacterial vaginosis markers (Individual markers not reported)
  - *Lactobacillus spp*. (*L. crispatus* and *L. jensenii*)
  - *Gardnerella vaginalis*
  - *Atopobium vaginae*
  - Bacterial Vaginosis Associated Bacteria-2 (BVAB-2)
  - *Megasphaera-1*

- *Candida spp*. (*C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*)
- *Candida glabrata*
- *Candida krusei*
- *Trichomonas vaginalis*

The BD 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.

The BD Vaginal Panel is available for use with the BD MAX System or the BD COR System.

**C Special Conditions for Use Statement(s):**
Rx - For Prescription Use Only

**D Special Instrument Requirements:**
BD MAX System or the BD COR System

## IV Device/System Characteristics:

**A Device Description:**
The BD COR System and the BD Vaginal Panel are comprised of an instrument with associated hardware and accessories, disposable microfluidic cartridges, master mixes, unitized reagent strips, and extraction reagents. The BD COR System consists of the combination of the BD COR MX and the BD COR PX Instruments. The system allows the user to place clinical specimens directly into designated transport racks to be loaded into the System. Once the specimens are loaded, the System will perform the pre-analytical steps such as vortexing and aliquoting into a molecular tube with the correct diluent, sorting/grouping of the secondary samples for testing by assay, pre-warming and cooling of the sample (where required), and transport of the sample into a molecular analyzer, where extraction, amplification and detection will take place. The BD COR System software automatically interprets test results. For the BD Vaginal Panel, a test result may be called as POS, NEG or UNR (Unresolved) based on the amplification status of the targets and of the Sample Processing Control. Non-reportable results due to instrument failure or warning are indicated as incomplete (INC) or indeterminate (IND).

Additionally, the steps of ordering tests on the instrument for specific samples are managed directly by the user interaction with the Laboratory Information System (LIS), which communicates directly with the instrument. Once the clinical specimens are received in the laboratory and loaded into the transport racks, the user is not required to directly handle the specimen again prior to result reporting and removal from the system.

**B Principle of Operation:**
The BD Vaginal Panel, when performed on the BD COR System is designed for use with the BD Molecular Swab Collection kit. Samples are transported to the testing laboratory in BD Molecular Swab Sample Buffer Tubes. The BD COR MX Instrument, when combined with the BD COR PX Instrument, is to be used for automated sample preparation, extraction and purification of nucleic acids from multiple specimen types, as well as the automated amplification and detection of target nucleic acid sequences by fluorescence-based real-time PCR.

The BD Vaginal Panel extraction reagents are dried in 96-well microtiter plates that contain binding magnetic affinity beads and a Sample Processing Control (SPC). Each well is capable of binding and eluting sample nucleic acids. The SPC monitors the integrity of the reagents and the process steps involved in DNA extraction, amplification and detection, as well as for the presence of potential assay inhibitors.

The BD Vaginal Panel liquid reagent plate includes Wash, Elution and Neutralization buffers. The beads (described above), together with the bound nucleic acids, are washed and the nucleic acids are eluted by a combination of heat and pH. Eluted DNA is neutralized and transferred to the Amplification reagent (described below) to rehydrate the PCR reagents. After reconstitution, the BD COR PX/MX System dispenses a fixed volume of PCR-ready solution containing extracted nucleic acids into the BD PCR Cartridge.

Microvalves in the BD PCR Cartridge are sealed by the system prior to initiating PCR to contain the amplification mixture and prevent evaporation and contamination. The amplified DNA targets are detected using hydrolysis (TaqMan) probes, labeled at one end with a fluorescent reporter dye (fluorophore), and at the other end, with a quencher moiety. Probes labeled with different fluorophores are used to detect the target analytes in different optical channels of the BD COR PX/MX System. When the probes are in their native state, the fluorescence of the fluorophore is quenched due to its proximity to the quencher. However, in the presence of target DNA, the probes hybridize to their complementary sequences and are hydrolyzed by the 5'-3' exonuclease activity of the DNA polymerase as it synthesizes the nascent strand along the DNA template. As a result, the fluorophores are separated from the quencher molecules and fluorescence is emitted. The BD COR PX/MX System monitors these signals at each cycle of the PCR and interprets the data at the end of the reaction to provide the qualitative test results for each vaginitis analyte as well as qualitative results for bacterial vaginosis, based on detection and quantitation of targeted markers.

**C Instrument Description Information:**

1. Instrument Name:
   BD COR PX/MX (BD COR)

2. Specimen Identification:

The steps of ordering tests on the instrument for specific samples will be managed directly by the user interaction with the Laboratory Information System (LIS), which communicates directly with the instrument.

3. Specimen Sampling and Handling:

The BD COR System allows the user to place clinical specimens directly into designated transport racks to be loaded into the System. Once the specimens are loaded, the System will perform the necessary pre-analytical steps such as vortexing, aliquoting into a molecular tube with the correct diluent, sorting/grouping of the secondary samples for testing by assay, pre-warming and cooling of the sample (where required), and transport of the sample into a molecular analyzer, where extraction, amplification and detection will take place.

4. Calibration:

BD COR does not require user calibration. Annual preventative maintenance is required to be performed by BD authorized service personnel

5. Quality Control:

Each Extraction Plate contains a (internal) Sample Processing Control (SPC) comprised of plasmids containing a synthetic target DNA sequence. The SPC monitors the efficiency of DNA capture, washing and elution during the sample processing steps, as well as the efficiency of DNA amplification and detection during PCR analysis. If the SPC result fails to meet the

acceptance criteria, the result of the specimen will be reported as Unresolved for the Master Mix reaction. Each Master Mix contains its own Sample Processing Control; thus, Unresolved results are determined independently for each Master Mix (MM1 and MM2). An Unresolved result is indicative of specimen-associated inhibition or reagent failure. The operator is directed to repeat any specimen reported as Unresolved.

External Control materials are not provided by BD; however, Quality Control procedures are included in the package insert. Various types of External Controls are recommended to allow the user to select the most appropriate for their laboratory quality control program including *Trichomonas vaginalis* (ATCC 30001), *Candida albicans* (ATCC 10231), *Candida glabrata* (ATCC 2001), *Candida krusei* (ATCC 6258), or other commercially available positive control materials.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):
BD MAX Vaginal Panel, BD MAX Instrument, BD MAX Vaginal Panel

### B Predicate 510(k) Number(s):
K201017

### C Comparison with Predicate(s):

| **Device & Predicate Device(s):** | K223653 | K201017 |
|---|---|---|
| Device Trade Name | The BD Vaginal Panel | The BD MAX Vaginal Panel |
| **General Device Characteristic Similarities** | | |
| Intended Use/Indications For Use | The BD Vaginal Panel 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 | 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 |

| | | |
|---|---|---|
| | chain reaction (PCR) for the amplification of specific DNA targets and utilizes fluorogenic target-specific hybridization probes to detect and differentiate DNA from:<br>•Bacterial vaginosis markers (Individual markers not reported)<br>-*Lactobacillus spp*. (*L. crispatus* and *L. jensenii*)<br>-*Gardnerella vaginalis*<br>-*Atopobium vaginae*<br>-Bacterial Vaginosis Associated Bacteria-2 (BVAB-2)<br>-Megasphaera-1<br>•*Candida spp*. (*C. albicans, C. tropicalis*, *C. parapsilosis, C. dubliniensis*)<br>•*Candida glabrata*<br>•*Candida krusei*<br>•*Trichomonas vaginalis*<br>The BD 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.<br>The BD Vaginal Panel is available for use with the BD MAX System or the BD COR System. | 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:<br>• Bacterial vaginosis markers (Individual markers not reported) - *Lactobacillus* spp. (*L. crispatus* and *L. jensenii*)<br>- *Gardnerella vaginalis*<br>- *Atopobium vaginae*<br>- Bacterial Vaginosis Associated Bacteria-2 (BVAB-2)<br>- *Megasphaera-1*<br>• *Candida* spp. (*C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*)<br>• *Candida glabrata*<br>• *Candida krusei*<br>• *Trichomonas vaginalis*<br>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. |
| Assay Controls | Same | Sample Processing Control |
| Technology | Same | PCR |
| Organisms Detected | Same | Bacterial vaginosis (BV) markers (Results for individual organisms are not |

| | | |
|---|---|---|
| | | reported. Qualitative BV results are based on detection and quantitation of targeted organisms)<br><br>•*Lactobacillus spp*. (*L. crispatus* and *L.jensenii*)<br>•*Gardnerella vaginalis*<br>•*Atopobium vaginae*<br>•Bacterial Vaginosis Associated Bacteria-2 (BVAB-2)<br>•*Megasphaera*-1<br>•*Candida spp*. (Reported as Cgroup includes *C. albicans, C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*)<br>•*Candida glabrata*<br>•*Candida krusei*<br>•*Trichomonas vaginalis* |
| Indications for use | Same | Symptomatic patients |
| Specimen type | Same | Clinician and patient-collected female vaginal swab |
| **General Device Characteristic Differences** | | |
| Sample Prep/Results | Automated by BD COR System | Partially Automated by BD MAX System |
| Collection/Transport Device | BD Molecular Swab Collection Kit | BD Molecular Swab Collection Kit |

## VI Standards/Guidance Documents Referenced:

Assay Migration Studies for In Vitro Diagnostic Devices: Guidance for Industry and FDA Staff.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

*Precision*

To evaluate within-laboratory precision, a study was conducted over 12 days that included two operators, one BD COR PX/MX system and one BD MAX system at a single internal site. A single lot of reagents and two test panels containing a known amount of target organism(s) in the presence of simulated vaginal matrix were evaluated. Each operator conducted six days of testing per panel, performing two runs per day on each platform with each run containing two replicates of each panel member, for a total of 48 runs per instrument. Analysis of precision included evaluation of within-run, between-run, and between-day components of variance for BD Vaginal Panel on both the BD COR and the BD MAX systems.

To prepare the panels, target organisms (or plasmid DNA for *Megasphaera-1* and BVAB-2) were spiked in simulated vaginal matrix. The panels for Bacterial Vaginosis (Master Mix 1, MM1) organisms were prepared at varying concentrations of multiple targeted species with sample compositions designed to generate low positive, moderate positive, high negative, or negative results for bacterial vaginosis. For panel members for *Candida* and *Trichomonas vaginalis* (Master Mix 2, MM2), the target organisms were spiked at concentrations based on the assay LoD. Table 1 lists the panel members evaluated and their approximate concentrations based on the percentage of positive results expected with each concentration. Panel 1 was composed of targets for vaginosis and vaginitis (MM1 and MM2), whereas Panel 2 was only composed of vaginosis targets (MM2). Panel 1 was also used for Reproducibility testing described below.

**Table 1: Microorganism Concentration Levels for Panel Design for Precision Study**

| Concentration Designation | Bacterial Vaginosis | *Candida* and *Trichomonas vaginalis* |
|---|---|---|
| | (% of Positive Results expected, based on the organism composition) | (x LoD) |
| Moderate Positive | ~100 | ≥ 2 to ≤ 5 |
| Low Positive | ~95 | < 2 |
| High BV Negative | ~20 -~80 | |
| BV Negative | ~5 | |
| True Negative | 0 (No Target) | No Target |

The quantitative summaries of the precision study for the two instruments, using the mean Second Derivative Peak Abscissa (SDPA) values with variance components (SD and % CV) for Vaginitis targets are presented in Table 2 and Table 3 below. Additionally, the summary of the results for the precision study, comparing the precision of the qualitative results for BD COR and BD MAX Systems is presented in Table 4 below.

**Table 2: Quantitative Precision Summary of Variance Components by Vaginitis Target for BD COR System**

| Target | Level | N | Mean SDPA | Within Run (Residual) | | Between Run | | Between Day | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| *Candida glabrata* | Low Positive | 48 | 30.88 | 0.83 | 2.68 | 1.00 | 3.23 | 0 | 0 | 1.30 | 4.20 |
| *Candida krusei* | Low Positive | 48 | 28.87 | 0.23 | 0.79 | 0.13 | 0.45 | 0 | 0 | 0.26 | 0.91 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Candida albicans* | Low Positive | 48 | 27.87 | 0.26 | 0.94 | 0 | 0 | 0.10 | 0.35 | 0.28 | 1.00 |
| | Moderate Positive | 48 | 27.12 | 0.20 | 0.75 | 0.32 | 0.32 | 0 | 0 | 0.22 | 0.82 |
| *Trichomonas vaginalis* | Low Positive | 48 | 32.70 | 0.34 | 1.04 | 0.60 | 0.60 | 0 | 0 | 0.39 | 1.20 |
| | Moderate Positive | 48 | 31.63 | 0.30 | 0.96 | 0.15 | 0.15 | 0 | 0 | 0.31 | 0.98 |

**Table 3: Quantitative Precision Summary of Variance Components by Vaginitis Target for BD MAX System**

| Target | Level | N | Mean SDPA | Within Run (Residual) | | Between Run | | Between Day | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| *Candida glabrata* | Low Positive | 48 | 31.33 | 0.88 | 2.81 | 0.73 | 2.34 | 0.36 | 1.15 | 1.20 | 3.83 |
| *Candida krusei* | Low Positive | 48 | 28.87 | 0.32 | 1.11 | 0.16 | 0.56 | 0.17 | 0.58 | 0.40 | 1.37 |
| *Candida albicans* | Low Positive | 48 | 28.24 | 0.25 | 0.90 | 0.09 | 0.33 | 0 | 0 | 0.27 | 0.96 |
| | Moderate Positive | 48 | 27.26 | 0.26 | 0.95 | 0 | 0 | 0.17 | 0.62 | 0.31 | 1.14 |
| *Trichomonas vaginalis* | Low Positive | 48 | 32.64 | 0.46 | 1.42 | 0 | 0 | 0 | 0 | 0.46 | 1.42 |
| | Moderate Positive | 48 | 31.63 | 0.24 | 0.76 | 0 | 0 | 0 | 0 | 0.24 | 0.76 |

**Table 4: Qualitative Precision Study Results Summary for Vaginosis and Vaginitis Targets for BD COR and BD MAX Systems**

| Concentration | BDCOR System Percent Agreement with Expected Result [95 % Confidence Interval] | | | | | BDMAX System Percent Agreement with Expected Result [95 % Confidence Interval] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Bacterial Vaginosis** | ***Trichomonas vaginalis*** | ***Candida albicans*** | ***Candida glabrata*** | ***Candida krusei*** | **Bacterial Vaginosis** | ***Trichomonas vaginalis*** | ***Candida albicans*** | ***Candida glabrata*** | ***Candida krusei*** |
| True Negative[a] | 288/288 100% [98.7-100] | 720/720 100% [99.5-100] | 720/720 100% [99.5-100] | 720/720 100% [99.5-100] | 720/720 100% [99.5-100] | 288/288 100% [98.7-100] | 719/720 99.9% [99.2-100] | 718/720 99.7% [99-100] | 719/720 99.9% [99.2-100] | 720/720 100% [99.5-100] |
| Low Positive[c] | 285/288 99% [97-99.6] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] | 288/288 100% [98-100] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] |
| Moderate Postive[d] | 191/192 99.5% [97.1-99.9] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] | | | 192/192 100% [98-100] | 48/48 100% [92.6-100] | 48/48 100% [92.6-100] | | |
| BV Negative[a] | 48/48 100% [92.6-100] | | | | | 48/48 100% [92.6-100] | | | | |
| BV High Negative[b] | 153/192 79.7% [73.4-84.8] | | | | | 168/192 87.5% [82.1-91.5] | | | | |

[a] For the true negative and BV Negative agreements, the reported agreement indicates the percent of negative results.

[b] For the high Negative, the reported percent agreement corresponds to the positive results.
[c] Performance includes combined results from replicates of six panel members containing different organism compositions.
[d] Performance includes combined results from replicates of four panel members containing different organism compositions.

*Reproducibility*

A reproducibility study was conducted over eight days using two operators, one BD COR PX/MX System and one BD MAX system for each of three sites (two external and one internal). Each operator conducted four days of testing, performing two runs per day on each platform with each run containing two replicates of each panel member, for a total of 96 runs. A single lot of reagents and one test panel containing a known amount of target organism(s) in the presence of simulated vaginal matrix was evaluated.

The quantitative summaries of reproducibility for the two instruments, using the mean SDPA values with variance components (SD and % CV) for Vaginitis targets are presented in Table 5 and Table 6 below. Additionally, Table 7 presents a summary comparison of the qualitative result reproducibility across both BD COR and BD MAX Systems

**Table 5: Quantitative Reproducibility Site-to-Site Summary by Vaginitis Target for BD COR System**

| Target | Level | N | Mean SDPA | Within Run (Residual) | | Between Run | | Between Day | | Between Site | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| *Candida glabrata* | Low Positive | 96 | 30.30 | 0.53 | 1.76 | 0 | 0 | 0 | 0 | 0.26 | 0.87 | 0.59 | 1.96 |
| *Candida krusei* | Low Positive | 96 | 28.93 | 0.20 | 0.71 | 0.07 | 0.23 | 0 | 0 | 0 | 0 | 0.21 | 0.74 |
| *Candida albicans* | Low Positive | 96 | 26.69 | 0.38 | 1.44 | 0 | 0 | 0.16 | 0.59 | 0.07 | 0.25 | 0.42 | 1.57 |
| | Moderate Positive | 96 | 26.08 | 0.30 | 1.14 | 0.04 | 0.17 | 0.06 | 0.24 | 0.12 | 0.48 | 0.33 | 1.27 |
| *Trichomonas vaginalis* | Low Positive | 96 | 32.85 | 0.38 | 1.17 | 0 | 0 | 0 | 0 | 0.15 | 0.45 | 0.41 | 1.25 |
| | Moderate Positive | 96 | 31.66 | 0.30 | 0.93 | 0 | 0 | 0.04 | 0.13 | 0 | 0 | 0.30 | 0.94 |

**Table 6: Quantitative Reproducibility Site-to-Site Summary by Vaginitis Target for BD MAX System**

| Target | Level | N | Mean SDPA | Within Run (Residual) | | Between Run | | Between Day | | Between Site | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| *Candida glabrata* | Low Positive | 96 | 30.95 | 0.71 | 2.28 | 0 | 0 | 0.20 | 0.64 | 0.51 | 1.66 | 0.89 | 2.89 |
| *Candida krusei* | Low Positive | 96 | 29.09 | 0.42 | 1.44 | 0.15 | 0.53 | 0 | 0 | 0 | 0 | 0.45 | 1.54 |
| *Candida albicans* | Low Positive | 96 | 27.34 | 0.42 | 1.55 | 0.20 | 0.72 | 0 | 0 | 0 | 0 | 0.47 | 1.71 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Moderate Positive | 96 | 26.49 | 0.42 | 1.59 | 0 | 0 | 0.05 | 0.18 | 0 | 0 | 0.43 | 1.60 |
| *Trichomonas vaginalis* | Low Positive | 96 | 32.73 | 0.46 | 1.40 | 0 | 0 | 0.21 | 0.65 | 0.24 | 0.73 | 0.56 | 1.71 |
| | Moderate Positive | 96 | 31.69 | 0.42 | 1.31 | 0 | 0 | 0 | 0 | 0.08 | 0.25 | 0.42 | 1.34 |

## Table 7: Qualitative Reproducibility by Target and Site for BD COR System and BD MAX System

| Concentration | Site | BD COR System Percent Agreement with Expected Result [95 % Confidence Interval] | | | | | BD MAX System Percent Agreement with Expected Result [95 % Confidence Interval] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Bacterial Vaginosis** | ***Trichomonas vaginalis*** | ***Candida albicans*** | ***Candida glabrata*** | ***Candida krusei*** | **Bacterial Vaginosis** | ***Trichomonas vaginalis*** | ***Candida albicans*** | ***Candida glabrata*** | ***Candida krusei*** |
| True Negative[a] | 1 | 192/192 100% [98-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 192/192 100% [98-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] |
| | 2 | 192/192 100% [98-100] | 160/160 100% [97.7-100] | 159/160 99.4% [96.5-99.9] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 192/192 100% [98-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] | 160/160 100% [97.7-100] |
| | 3 | 192/192 100% [98-100] | 159/159 100% [97.6-100] | 158/159 99.4% [96.5-99.9] | 159/159 100% [97.6-100] | 159/159 100% [97.6-100] | 192/192 100% [98-100] | 159/159 100% [97.6-100] | 156/159 98.1% [94.6-99.4] | 155/159 97.5% [93.7-99] | 159/159 100% [97.6-100] |
| Low Positive[c] | 1 | 64/64 100% [94.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 63/64 98.4% [91.7-99.7] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] |
| | 2 | 64/64 100% [94.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 62/64 96.9% [89.3-99.1] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100 |
| | 3 | 63/63 100% [94.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 63/63 100% [94.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100 |
| Moderate Postive[d] | 1 | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | | | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | | |
| | 2 | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | | | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | | |
| | 3 | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | | | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | 32/32 100% [89.3-100] | | |
| BV Negative[a] | 1 | 32/32 100% [89.3-100] | | | | | 32/32 100% [89.3-100] | | | | |
| | 2 | 32/32 100% [89.3-100] | | | | | 32/32 100% [89.3-100] | | | | |
| | 3 | 32/32 100% [89.3-100] | | | | | 32/32 100% [89.3-100] | | | | |
| BV High Negative[b] | 1 | 25/32 78.1% [61.2-89] | | | | | 13/32 40.6% [25.5-57.7] | | | | |
| | 2 | 17/32 53.1% [36.4-69.1] | | | | | 29/32 90.6% [75.8-96.8] | | | | |
| | 3 | 28/32 87.5% [71.9-95] | | | | | 30/32 93.8% [79.9-98.3] | | | | |

[a] For the true negative and BV Negative agreements, the reported agreement indicates the percent of negative results.
[b] For the high Negative, the reported percent agreement corresponds to the positive results.
[c] Performance includes combined results from replicates of six panel members containing different organism compositions.
[d] Performance includes combined results from replicates of four panel members containing different organism compositions.

The precision and reproducibility results described above across both the BD Max and BD COR instruments are comparable and thus establish equivalent performance of the BD Vaginal panel between both instruments.

2. Linearity and Reportable Range:

Not applicable

3. Analytical Specificity/Interference:

The BD Vaginal Panel was originally reviewed under DEN160001. Please refer to additional information contained in the published decision summary for DEN160001regarding Analytical Specificity/Cross-reactivity Study performance. No additional testing was conducted as part of this submission.

4. Assay Reportable Range:

Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

The BD Vaginal Panel was originally reviewed under DEN160001. There are no changes to the traceability, stability, or expected values.

On-Deck Specimen Stability Study:

A study was conducted to evaluate the stability of the BD Vaginal Panel Bacterial Vaginosis (Master Mix-1) and Vaginitis (Master Mix-2) targets in Swab Sample Buffer Tubes capped with Reclosing Septum Caps (RSCs) at 2 - 33 °C, inclusive for 4 days after initial testing. Specifically, prepared positive and negative samples were stored at specified temperatures, before being evaluated with BD Vaginal Panel on the BD MAX System at various time points. Testing was conducted on the BD MAX System and results were extrapolated to the BD COR System, given the similar performance between both systems.

The study was designed to test sample stability of each target in MM1 and MM2 in an in-use Sample Buffer Tube (SBT) previously stored at 2 - 8 °C and 33 ± 2 °C. Bacterial Vaginosis (BV) analyte stability was tested using multiple unique panel members containing Low Positive, High Negative, and Negative concentrations. Due to the presence of *Lactobacillus* (normal healthy flora) in clinical matrix, BV panel members were prepared in simulated vaginal matrix. Vaginosis organisms were spiked at specified concentrations into swab buffer in an SBT containing SVM. C. group and TV specimen stability were tested using clinical specimens with approximately 50% of the samples at challenging organism concentrations. Clinical C. group specimens were representative of all *Candida* spp claims for the BD Vaginal Panel (*C. albicans*, *C. parapsilosis*, *C. tropicalis*, *C. dubliniensis*, *C. glabrata* and *C. krusei*). Clinical samples for C. group and TV were collected externally and screened internally using the BD MAX Vaginal Panel. Clinical samples used for this verification were approximately 2-5X the LoD for C. group or TV during the screening event. This LoD range was based on a statistical analysis of the analytical LoD of the BD MAX Vaginal Panel (predicate device), as well as clinical Repeatability and Reproducibility studies. A summary of Bacterial Vaginosis (MM-1) and

Bacterial Vaginitis (MM-2) testing results and disposition are shown in Table 8 and Table 9 and respectively.

**Table 8: Bacterial Vaginosis (MM-1) Summary of Stability Testing Results**

| Test Point | In SBT | | Low POS | High NEG | NEG | Total Days |
|---|---|---|---|---|---|---|
| 1 | Baseline | | 35/36 | 22/36 | 36/36 | 0 |
| 2 | 4 days | 2-8°C | 34/36 | 10/36 | 36/36 | 4 |
| 3 | 4 days | 2-8°C | 36/36 | 13/36 | 36/36 | 8 |
| 4 | 5 days | 2-8°C | 35/36 | 12/36 | 36/36 | 9 |
| 5 | 4 days | 2-8°C | 36/36 | 8/36 | 36/36 | 14 |
| 6 | 5 days | 2-8°C | 36/36 | 8/36 | 36/36 | 15 |
| 7 | 4 days | 2-8°C | 36/36 | 7/36 | 36/36 | 21 |
| 8 | 5 days | 2-8°C | 36/36 | 8/36 | 36/36 | 22 |
| 9 | Baseline | | 36/36 | 22/36 | 36/36 | 0 |
| 10 | 4 days | 33°C | 35/36 | 3/36 | 36/36 | 4 |
| 11 | 5 days | 33°C | 36/36 | 7/36 | 36/36 | 8 |
| 12 | 4 days | 33°C | 36/36 | 5/36 | 36/36 | 9 |
| 13 | 5 days | 33°C | 36/36 | 0/36 | 36/36 | 14 |
| 14 | 4 days | 33°C | 36/36 | 1/36 | 36/36 | 15 |
| 15 | 5 days | 33°C | 36/36 | 5/36 | 36/36 | 21 |
| 16 | 4 days | 33°C | 36/36 | 6/36 | 36/36 | 22 |

**Table 9: Bacterial Vaginitis (MM-2) Summary of Stability Testing Results**

| Test Point | In SBT | | C. group | TV | NEG | Total Days |
|---|---|---|---|---|---|---|
| 1 | Baseline | | 20/20 | 20/20 | 4/4 | 0 |
| 2 | 4 days | 2-8°C | 20/20 | 19/20 | 4/4 | 4 |
| 3 | 4 days | 2-8°C | 20/20 | 20/20 | 4/4 | 8 |
| 4 | 5 days | 2-8°C | 20/20 | 20/20 | 4/4 | 9 |
| 5 | 4 days | 2-8°C | 20/20 | 20/20 | 4/4 | 14 |
| 6 | 5 days | 2-8°C | 20/20 | 20/20 | 4/4 | 15 |
| 7 | 4 days | 2-8°C | 20/20 | 20/20 | 4/4 | 21 |
| 8 | 5 days | 2-8°C | 20/20 | 20/20 | 4/4 | 22 |
| 9 | Baseline | | 36/36 | 20/20 | 4/4 | 0 |
| 10 | 4 days | 33°C | 20/20 | 20/20 | 4/4 | 4 |
| 11 | 5 days | 33°C | 20/20 | 20/20 | 4/4 | 8 |
| 12 | 4 days | 33°C | 20/20 | 20/20 | 4/4 | 9 |
| 13 | 5 days | 33°C | 20/20 | 20/20 | 4/4 | 14 |
| 14 | 4 days | 33°C | 20/20 | 20/20 | 4/4 | 15 |
| 15 | 5 days | 33°C | 20/20 | 20/20 | 4/4 | 21 |
| 16 | 4 days | 33°C | 20/20 | 20/20 | 4/4 | 22 |

Results met the acceptance criteria for all time points at each storage condition except the for Bacterial Vaginosis (Master Mix 1) at baseline (35/36) and at day 4 (34/35). The MM1-Baseline deviation was determined to be related to a bubble in the PCR chamber that resulted in a negative result. Repeat testing of the same sample with a properly filled PCR chamber yielded a positive result, indicating the negative baseline result was an aberrant event and the stability study continued with subsequent timepoints meeting acceptance criteria. The MM1-Day4 timepoint did not meet the acceptance criteria. Investigation into sample builds, allocation, consumables, and instrument did not indicate the reason behind the dropouts only that the data was variable at this timepoint. A decision was made to continue with the study to ascertain whether this was an aberrant event or a stability issue. Subsequent time points were positive and met the acceptance criteria.

The study data was considered acceptable since subsequent timepoints for those same samples met acceptance criteria out to day 22. Prior failures were attributed to aberrant events and not an indicator of target stability. Additionally, the trending reports indicated that neither of the storage temperature conditions tested induced stability failure by degradation of Ct. Score/SDPA or cycEP out to Day 22.

6. Detection Limit:

The limit of detection for the BD Vaginal Panel on the BD MAX System was originally established in DEN160001.

To establish equivalent limits of detection for the BD Vaginal Panel on the BD COR and the BD MAX Systems, 20 panels of Vaginosis and/or Vaginitis targets at varying concentration levels were evaluated (Table 10). These panels were created using the LoD previously determined on the BD MAX System at the target levels identified in Table 8. The samples were prepared by spiking representative vaginosis target and/or vaginitis targets in the presence of simulated vaginal matrix (SVM). Testing was conducted over more than three days using BD Vaginal Panel reagents, two BD COR PX/MX Systems and four BD MAX Systems.

A Two, One-Sided Test (TOST) of Equivalence was performed for the low positive (1.99x LoD) and moderate positive (5x LoD) target levels for each strain. The 90% confidence intervals for the difference in mean Ct.score (Vaginosis targets) and SDPA (Vaginitis targets) between the BD COR System and BD MAX Systems were determined for each strain of at each Vaginosis (Table 11) and Vaginitis (Table 12) target levels. Equivalence between the two systems was established when the difference was contained within the equivalence margin of [-6% of the reference mean, +6% of the reference mean]. TOST analysis was not performed on High Negative (C5) *Candida spp*. panel members based on the proportion positivity being less than 95% at C5, a predicate requirement. Equivalence between the BD COR System and BD MAX™ Systems was demonstrated at the High Negative level by overlapping 95% confidence intervals.

**Table 10: Panel Members for Limit of Detection Study**

| Low Positive (1.99x C95) | | | Moderate Positive (5x C95) | | | High Negative (C5) | | |
|---|---|---|---|---|---|---|---|---|
| **Panel** | **Target** | **Concentration** | **Panel** | **Target** | **Concentration** | **Panel** | **Target** | **Concentration** |
| 1 | Cgla | 402 CFU/mL | 8 | Cgla | 1010 CFU/mL | 15 | Cgla | 10 CFU/mL |
| 2 | GV | 1914 CFU/mL | 9 | GV | 4810 CFU/mL | 16 | Ckru | 6 CFU/mL |
| | Ckru | 2060 CFU/mL | | Ckru | 5175 CFU/mL | | | |
| 3 | BVAB | 923 Copies/mL | 10 | BVAB | 2320 Copies/mL | 17 | Calb | 53 CFU/mL |
| | Calb | 35396 CFU/mL | | Calb | 88935 CFU/mL | | | |
| 4 | Mega | 4507 Copies/mL | 11 | Mega | 11325 Copies/mL | 18 | Cpara | 399 CFU/mL |
| | Cpara | 61013 CFU/mL | | Cpara | 153300 CFU/mL | | | |
| 5 | Ljens | 1015 CFU/mL | 12 | Ljens | 2550 CFU/mL | 19 | Cdub | 52 CFU/mL |
| | Cdub | 7964 CFU/mL | | Cdub | 20010 CFU/mL | | | |
| 6 | Lcrisp | 109 CFU/mL | 13 | Lcrisp | 275 CFU/mL | 20 | Ctrop | 16 CFU/mL |
| | Ctrop | 623 CFU/mL | | Ctrop | 1565 CFU/mL | | | |
| 7 | Ato | 253 CFU/mL | 14 | Ato | 635 CFU/mL | | | |
| | TV | 44 Cells/mL | | TV | 110 Cells/mL | | | |

**Table 11: Analytical Sensitivity Confirmation in Vaginal Swab for BD COR System for the Vaginosis Targets**

| Target | Target level | System | N | Proportion Positivity | Mean Ct Score | Difference in Mean CtScore [COR-MAX] and 90% CI | Equivalence Interval |
|---|---|---|---|---|---|---|---|
| *Atopobium vaginae* | Low Positive | COR | 48 | 100% | 26.23 | 0.21 (0.11,0.31) | (-1.56, 1.56) |
| | | MAX | | 100% | 26.02 | | |
| | Moderate Positive | COR | 48 | 100% | 25.02 | 0.12 (-0.02, 0.26) | (-1.49, 1.49) |
| | | MAX | | 100% | 24.90 | | |
| BVAB-2* | Low Positive | COR | 48 | 100% | 29.79 | 0.19 (0.06, 0.33) | (-1.78, 1.78) |
| | | MAX | | 100% | 29.60 | | |
| | Moderate Positive | COR | 48 | 100% | 28.52 | 0.21 (0.10, 0.32) | (-1.70, 1.70) |
| | | MAX | | 100% | 28.31 | | |
| *Megasphaera-1** | Low Positive | COR | 48 | 100% | 30.35 | 0.34 (0.15, 0.52) | (-1.80, 1.80) |
| | | MAX | | 100% | 30.01 | | |
| | Moderate Positive | COR | 48 | 100% | 29.18 | 0.27 (0.13, 0.41) | (-1.73, 1.73) |
| | | MAX | | 100% | 28.91 | | |
| *Gardnerella vaginallis* | Low Positive | COR | 48 | 100% | 28.69 | 0.23 (0.12, 0.34) | (-1.71, 1.71) |
| | | MAX | | 98% | 28.45 | | |
| | Moderate Positive | COR | 48 | 100% | 27.47 | 0.20 (0.10, 0.30) | (-1.64, 1.64) |
| | | MAX | | 100% | 27.27 | | |
| *Lactobacillus jensenii* | Low Positive | COR | 48 | 100% | 24.65 | 0.50 (0.39, 0.61) | (-1.45, 1.45) |
| | | MAX | | 100% | 24.15 | | |
| | Moderate Positive | COR | 48 | 100% | 23.41 | 0.48 (0.39, 0.57) | (-1.38, 1.38) |
| | | MAX | | 100% | 22.93 | | |
| *Lactobacillus crispatus* | Low Positive | COR | 48 | 100% | 26.52 | 0.40 (0.24, 0.56) | (-1.57, 1.57) |
| | | MAX | | 100% | 26.12 | | |
| | Moderate Positive | COR | 48 | 100% | 25.18 | 0.27 (0.15, 0.39) | (-1.49, 1.49) |
| | | MAX | | 100% | 24.91 | | |

* Plasmids were used for BVAB and *Megasphera* for these are non-cultivable microorganisms.

**Table 12: Analytical Sensitivity Confirmation in Vaginal Swab for BD COR System for the Vaginitis Targets**

| Target | Target level | System | N | Proportion Positivity (95% CI for High Negatives) | Mean SDPA | Difference in Mean SDPA [COR-MAX] and 90% CI | Equivalence Interval |
|---|---|---|---|---|---|---|---|
| *Trichomonas vaginalis* | Low Positive | COR | 48 | 100% | 32.31 | 0.17 (0.06, 0.28) | (-1.93, 1.93) |
| | | MAX | 48 | 100% | 32.14 | | |
| | Moderate Positive | COR | 48 | 100% | 31.34 | - 0.10 (- 0.21, 0.01) | (-1.89, 1.89) |
| | | MAX | 48 | 100% | 31.44 | | |
| *Candida albicans* | High Negative | COR | 48 | 90% (78, 95) | 34.33 | | |
| | | MAX | 48 | 90% (78, 95) | 34.30 | | |
| | Low Positive | COR | 48 | 100% | 27.75 | 0.15 0.00 – 0.29 | (-1.66, 1.66) |
| | | MAX | 48 | 100% | 27.61 | | |
| | Moderate Positive | COR | 48 | 100% | 26.89 | 0.07 (- 0.12, 0.26) | (-1.61, 1.61) |
| | | MAX | 48 | 100% | 26.82 | | |
| *Candida parapsilosis* | High Negative | COR | 48 | 71% (57, 82) | 35.39 | | |
| | | MAX | 48 | 67% (53, 78) | 35.17 | | |
| | Low Positive | COR | 48 | 100% | 29.39 | 0.43 (0.21, 0.065) | (-1.74, 1.74) |
| | | MAX | 48 | 100% | 28.96 | | |
| | Moderate Positive | COR | 48 | 100% | 28.15 | 0.31 (0.08, 0.53) | (-1.67, 1.67) |
| | | MAX | 48 | 100% | 27.85 | | |
| *Candida tropicalis* | High Negative | COR | 48 | 85% (73, 93) | 37.69 | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | MAX | 48 | 85%<br>(73, 93) | 34.45 | | |
| | Low Positive | COR | 48 | 100% | 30.83 | 0.28<br>(0.12, 0.44) | (-1.83, 1.83) |
| | | MAX | 48 | 100% | 30.55 | | |
| | Moderate Positive | COR | 48 | 100% | 29.92 | 0.22<br>(0.06, 0.37) | (-1.78, 1.78) |
| | | MAX | 48 | 100% | 29.70 | | |
| *Candida dubliniensis* | High Negative | COR | 48 | 58%<br>(44, 71) | 34.20 | | |
| | | MAX | 48 | 65%<br>(50, 77) | 34.54 | | |
| | Low Positive | COR | 48 | 100% | 28.92 | 0.39<br>(0.19, 0.59) | (-1.71, 1.71) |
| | | MAX | 48 | 100% | 28.53 | | |
| | Moderate Positive | COR | 48 | 100% | 27.66 | 0.22<br>(0.02, 0.43) | (-1.65, 1.65) |
| | | MAX | 48 | 100% | 27.43 | | |
| *Candida glabrata* | High Negative | COR | 48 | 73%<br>(59, 83) | 36.04 | | |
| | | MAX | 48 | 69%<br>(55, 80) | 37.83 | | |
| | Low Positive | COR | 48 | 100% | 29.64 | 0.05<br>(-0.12, 0.22) | (-1.78, 1.78) |
| | | MAX | 48 | 100% | 29.59 | | |
| | Moderate Positive | COR | 48 | 100% | 28.59 | 0.26<br>(0.12, 0.40) | (-1.70, 1.70) |
| | | MAX | 48 | 100% | 28.33 | | |
| *Candida krusei* | High Negative | COR | 48 | 44%<br>(31, 58) | 36.48 | | |
| | | MAX | 48 | 54%<br>(40, 67) | 36.55 | | |
| | Low Positive | COR | 48 | 100% | 29.35 | 0.32<br>(0.14, 0.50) | (-1.74, 1.74) |
| | | MAX | 48 | 100% | 29.04 | | |
| | Moderate Positive | COR | 48 | 100% | 28.17 | 0.28<br>(0.16, 0.40) | (-1.67, 1.67) |
| | | MAX | 48 | 100% | 27.89 | | |

7. Assay Cut-Off:

   The BD Vaginal panel was originally reviewed under DEN160001. The assay cut offs for the analytes in this assay were not modified as part of this submission.

8. Accuracy (Instrument):

   Not applicable

9. Carry-Over:

A cross-contamination (Carry-over) study was conducted using one high positive and one negative panels. The positive panel included a combination of vaginitis (MM1) and vaginosis (MM2) analytes in simulated vaginal matrix. Specifically, *L. jensenii* (5.57E+07 CFU/mL), *G. vaginalis* (4.29E+07 CFU/mL), *A. vaginae* (1.65E+08 CFU/mL), BVAB-2 (1.00E+09 copies/mL), and *T. vaginalis* (8.0 x 103 cells/mL) were included. The negative panel did not contain any target analyte and was prepared using swab buffer free of matrix. Both panels were run an alternating order to simulate the most sensitive case for cross-contamination.

The testing consisted of a total of at least 90 runs performed on a minimum of three BD COR PX/MX systems conducted over at least five days. Each sample was processed once in an alternating POS-NEG/NEG-POS pattern in the instrument. Each run had alternating six positive and six negative panel samples. A total of 547 positive and 543 negative replicates were run,

with any replicates beyond 540 as an extra sample run with a repeat to keep 50% positive prevalence during a run. Less than 1% cross contamination (false positive results) was observed in the study, and all analytes were correctly detected from the positive samples evaluated. A summary of the results is shown in Table 13. The BD COR System met acceptance criteria of ≤1% cross-contamination.

**Table 13: Cross-Contamination Results**

| Test Level | Number of Positive Panels Percentage [Negative 95% CI] |
|---|---|
| Positive | 547/547<br>100% |
| Negative | 1/543<br>0.18%<br>[0.03, 1.04] |

## B Comparison Studies:

The BD Vaginal Panel was originally reviewed under DEN160001. Additional details on clinical validation of the panel are available in the published decision summary for DEN160001.

1. Method Comparison with Predicate Device:

The clinical comparison study for BD Vaginal Panel on the BD COR System utilized previously collected clinical specimens. Specifically, the sponsor pooled previously collected clinical specimens and, where necessary, spiked in a high positive clinical specimen or pooled positive specimens to reach the necessary analyte level(s) for analytes of the *Candida* group (Cgroup) and *Trichomonas vaginalis* (TV). Contrived samples were also evaluated by spiking organisms into simulated matrix. For *C. glabrata* and *C. krusei*, contrived samples were created by spiking organisms into negative vaginal matrix or in simulated vaginal matrix because of their very low prevalence. For BV analytes, contrived panel members with different BV marker combinations were prepared using the simulated vaginal matrix. Additionally, the Cgroup, TV, and negative vaginitis panel members in natural vaginal matrix were analyzed for BV targets. Three aliquots were made for each panel member and each aliquot was tested on both BD MAX and BD COR systems at each testing site. Testing was conducted at one internal study site and at two external sites and a replicate of all evaluated samples was tested at each of the three testing sites.

Specimen panel levels for each organism included true negative, low positive (close to LoD), moderate positive, and high positive panel members. Panel members for each organism were built such that 60-80% are at ranges close to the cut off (with ~50% close to the LoD and the other ~50% moderate positives) and 20 - 40% will cover the remaining positive range (high positives). The positive panels were comprised of specimens that were positive for BV, Cgroup, TV, *C. glabrata*, or *C. krusei*. The negative panels were comprised of specimens that are negative for BV or for all the vaginitis organisms (Cgroup, TV, *C. glabrata*, and *C. krusei*).

Positive and negative panels of specimens were provided to investigators for testing on three BD MAX and on BD COR (PX/MX) Systems. The panels were randomized in such a way so that each test site would follow the same scheme. The study tested 700 panel members, with each

panel member tested once in each instrument, in each site. Three replicates of each panel member were tested (three on COR instruments and the same on comparable MAX instrument(s), which allowed for data analysis.

The percent agreement of BD Vaginal Panel results from the BD COR instrument versus the BD MAX instrument for each target was calculated using composite reference method. The reference results are defined by the result obtained with ≥ 2/3 BD MAX results seen with the three evaluable replicates. A specimen which generates positive BD MAX results by at least 2 of the 3 evaluable replicates is classified as positive. When three BD MAX results are all different from each other (positive, negative non-evaluable), the final BD MAX result is considered "Equivocal" in the agreement table. Overall positive percent agreement (PPA) and Negative Percent Agreement (NPA) values are provided for each target (Table 14) and stratified by BD COR System analyte level (Table 15, Table 16). PPA/NPA and 95% CI meet the pre-specified acceptance criteria of 95%-point estimate and the lower end of 95% CI, to not be less than 90% for each target (organism).

**Table 14: Overall Positive and Negative Percent Agreement for each Analyte Across BD MAX and BD COR Instrument Systems.**

| **BD COR/BDMAX Systems Results<br>Percent Agreement<br>[Bootstrap 95 % Confidence Interval]** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Bacterial Vaginosis Contrived** | | **Bacterial Vaginosis Natural** | | ***Candida group*** | | ***Candida glabrata*** | | ***Candida krusei*** | | ***Trichomonas vaginalis*** | |
| **Positive** | **Negative** | **Positive** | **Negative** | **Positive** | **Negative** | **Positive** | **Negative** | **Positive** | **Negative** | **Positive** | **Negative** |
| 215/216<br>99.5%<br>[98.4-100] | 300/300<br>100%<br>[99.3-100] | 682/697<br>97.8%<br>[96.3-99.1] | 343/358<br>95.8%<br>[93.1-98.2][1] | 350/352<br>99.4%<br>[98.5-100] | 368/372<br>98.9%<br>[97.4-100][4] | 172/172<br>100%<br>[N/A] | 372/372<br>100%[2]<br>[N/A] | 150/150<br>100%<br>[N/A] | 372/372<br>100%[3]<br>[N/A] | 329/330<br>99.7%<br>[99-100][5] | 372/372<br>100%<br>[N/A] |

[1]There were 7 non evaluable samples with the BD COR
[2] There were 8 non evaluable samples with the BD COR
[3] There were 9 non-evaluable samples with the BD COR
[4] There were 8 non-evaluable samples with the BD COR
[5] There were 6 non-evaluable samples with the BD COR

**Table 15: Percent Agreement of the BD Vaginal Panel Result Across BD COR and BD MAX Instrument Systems Stratified by Analyte Level**

| Analyte Levels | (Overall) BD COR/BDMAX Results by Level Percent Agreement [Bootstrap 95 % Confidence Interval] | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Bacterial Vaginosis Contrived | | Bacterial Vaginosis Natural | | *Candida group* | | *Candida glabrata* | | *Candida krusei* | | *Trichomonas vaginalis* | |
| | Positive | Negative | Positive | Negative | Positive | Negative | Positive | Negative | Positive | Negative | Positive | Negative |
| Negative | 0/0 | 306/308 99.4% [97.7-99.8] | 0/0 | 323/332 97.3% [94.9-98.6][1] | 0/0 | 364/368 98.9% [97.2-99.6] | 0/0 | 371/371 100% [99.0-100] | 0/0 | 371/371 100% [99-100] | 0/0 | 369/371 99.5% [98.1-99.9] |
| High Negative | 0/0 | 21/39 53.8% [38.6-68.4] | 0/0 | 19/29 65.5% [82.6-94.5] | 36/38 94.7% [82.7-92.5] | 0/0 | | | | | 16/18 88.9% [67.2-96.9] | 0/0 |
| Low Positive | 154/179 86% [80.2-90.4] | 0/0 | 90/100 90% [82.6-94.5] | 0/0 | 109/112 97.3% [92.4-99.1] | 0/0 | 62/62 100% [94.2-100] | 0/0 | 59/59 100% [93.9-100] | 0/0 | 88/89 98.9% [93.9-99.8] | 0/0 |
| Low Positive/Moderate Positive | | | 320/323 99.1% [97.3-99.7] | 0/0 | | | | | | | | |
| Moderate Positive | 138/139 99.3% [96.0-99.9] | 0/0 | 267/269 99.3% [97.3-99.8] | 0/0 | 120/120 100% [96.9-100] | 0/0 | 71/71 100% [94.9-100] | 0/0 | 59/59 100% [93.9/100] | 0/0 | 105/105 100% [96.5-100] | 0/0 |
| High Positive | | | | | 85/85 100% [95.7-100] | 0/0 | 39/39 100% [91-100] | 0/0 | 32/32 100% [89.3-100] | 0/0 | 117/117 100% [96.8-100] | 0/0 |

**Table 16: High Negative PPA for BD COR and BD MAX Systems**

| Target | Positivity Rate COR (95% CI) | Positive Rate MAX (95% CI) |
|---|---|---|
| BV High Negative | 65.1% (57.2% - 72.3%) | 68.7% (60.9% - 75.5%) |

The results for the method comparison studies shown above demonstrate equivalent performance for the BD Vaginal panel on both the BD MAX and the BD COR Systems.

Additional analyses of the clinical comparison study data were performed using Ct., SDPA and q-score values, when appropriate, as described in more detail below.

A paired t-test with 95% confidence interval to estimate the difference in Ct.score or SDPA between BD COR and BD MAX by target. The analysis was conducted by target for all COR sites combined for each test site. As seen in Table 17, the estimate of the difference in Ct.score of SDPA range from –0.6 to 0.8 (or -.0% to 5.1%) across all targets. Shifts in Ct.score or SDPA of up to 6% are expected to have little impact on the assay performance. Therefore, although some of the differences in Ct.score or SDPA were statistically significant (P-Value < 0.05), none of the identified differences are clinically significant.

**Table 17: Comparison Between BD COR and BD MAX Using Paired T-Test for Ct.score or SDPA**

| Score type | Target | N | BD COR Mean | BD MAX Mean | Estimate COR-MAX | Estimate % | 95% CI | *p*-value |
|---|---|---|---|---|---|---|---|---|
| Ct. Score | BV Contrived-*Atopobium* | **292** | **21.6** | **21.4** | **0.2** | **0.7%** | **0.1, 0.2** | **<0.001** |
| | BV Contrived-*Gardnerella* | **273** | **22.8** | **22.7** | **0** | **0.2%** | **0.0, 0.1** | **0.277** |
| | BV Contrived-Lactobacillus | **203** | **21** | **20.6** | **0.4** | **2.0%** | **0.3, 0.5** | **<0.001** |
| | BV Contrived-*Megasphera* | **190** | **22.7** | **22.7** | **0** | **0.1%** | **0.0, 0.1** | **0.611** |
| | BV Natural-*Atopobium* | **672** | **17.7** | **17.7** | **-0.1** | **-0.5%** | ***0.2, 0.0** | **0.092** |
| | BV Natural-*Gardnerella* | **639** | **17.1** | **17.3** | **-0.1** | **-0.8%** | **-0.3, 0.0** | **0.012** |
| | BV Natural-*Lactobacillus* | **291** | **16.6** | **15.9** | **0.7** | **4.2%** | **0.5, 0.8** | **<0.001** |
| | BV Natural-*Megasphera* | **644** | **18.1** | **18.6** | **-0.7** | **-3.6%** | **-0.8, -0.5** | **<0.001** |
| SDPA | *C. glabrata* | **172** | **29.3** | **29** | **0.4** | **1.2%** | **0.2,** | **<0.001** |
| | Cgroup | **314** | **27.1** | **27.3** | **-0.3** | **-0.9%** | **-0.4,-0.1** | **<0.001** |
| | *C. krusei* | **150** | **28.7** | **28.5** | **0.2** | **0.6%** | **0.0, 0.3** | **0.016** |
| | TV | **310** | **29.3** | **29.5** | **-0.2** | **-0.8%** | **-0.4, -0.1** | **0.001** |

Additional analyses using both Bland-Altman plots and Deming Regression by analyte was performed using the Ct., SDPA, or q-scores to estimate systematic bias. The Bland-Altman plots for each analyte did not show systematic bias. The Slope and Intercept points for the Deming Regression and their (bootstrap-calculated) 95% CI of each analyte are listed in Table 18).

**Table 18: Coefficients of Deming Regression of BD COR vs BD MAX for Q Score (MM1) or SDPA (MM2)**

| Score type | Target | Intercept (95% CI) | Slope (95% CI) |
|---|---|---|---|
| Q. Score | BV Contrived-*Lactobacillus* Negative | -0.02 (-0.07, 0.07) | 1.00 (0.93, 1.07) |
| | BV Contrived-*Lactobacillus* Positive | -0.02 (-0.04, -0.01) | 1.06 (1.04, 1.08) |
| | BV Natural-*Lactobacillus* Negative | -0.05 (-0.21, 0.11) | 1.05 (0.89, 1.21) |
| | BV Natural-*Lactobacillus* Positive | 0.01 (-0.04, 0.06) | 1.03 (0.97, 1.09) |
| SDPA | *C. glabrata* | 1.00 (-4.13, 6.12) | 0.98 (0.8, 1.16) |
| | Cgroup | -5.44 (-8.29, -2.59 | 1.19 (1.09, 1.30) |
| | *C. krusei* | 3.08 (-1.53, 7.68) | 0.9 (0.73, 1.06) |
| | TV | -2.77 (-4.63, -0.91) | 1.09 (1.02, 1.15) |

Deming Regression analysis was also performed using Ct. values measured for each BV analyte. The intercepts and slopes coefficients fell within acceptable bias limits. However, the coefficients calculated for BV – Contrived *Lactobacillus* using Ct. values were above acceptance bias levels (Slope =1.30 [95% CI:1.17, 1.43]). The q-score is a more appropriate method to evaluate BV due to its dependence on *Lactobacillus* concentrations and its clinical significance. Therefore, the apparent bias observed in the Ct values is acceptable for this

analyte. Additionally, when bias estimates were calculated for each BV analyte by panel member concentration using Ct. scores, negative samples accounted for the highest bias estimate among the *Lactobacillus* analyte (Table 19).

**Table 19: Deming Regression Bias Estimate of BD COR vs BD MAX for Ct Score (BV-MM1 Analytes)**

| Target | Analyte Level | Ct.score/SDPA of BD MAX | Bias Estimate | 95% CI |
|---|---|---|---|---|
| BV Contrived *Atopobium* | Moderate Positive | 19.38 | 0.13 | 0.05, 0.20 |
| | Low Positive | 23.31 | 0.18 | 0.13, 0.24 |
| | Negative | 35.00 | 0.35 | 0.16, 0.53 |
| BV Contrived – *Gardnerella* | Moderate Positive | 21.59 | 0.00 | -0.10, 0.11 |
| | Low Positive | 23.84 | 0.07 | 0.02, 0.13 |
| | Negative | 35.00 | 0.43 | -0.06, 0.92 |
| BV Contrived *Lactobacillus* | Moderate Positive | 20.47 | 0.38 | 0.26, 0.50 |
| | Low Positive | 20.68 | 0.45 | 0.30, 0.59 |
| | Negative | 35.00 | 4.72 | 2.71, 6.72 |
| BV Contrived *Megasphera-1* | Moderate Positive | 22.00 | 0.01 | -0.04, 0.06 |
| | Low Positive | 23.34 | 0.00 | -0.05, 0.06 |
| | Negative | 35.00 | -0.05 | -0.28, 0.18 |
| BV Natural *Atopobium* | Moderate Positive | 17.16 | -0.09 | -0.20, 0.03 |
| | Moderate Positive/Low Positive | 17.45 | -0.08 | 0.20, 0.03 |
| | Low Positive | 20.39 | -0.06 | 0.20, 0.08 |
| | Negative | 35.00 | 0.05 | -0.50, 0.61 |
| BV Natural – *Gardnerella* | Moderate Positive | 16.97 | -0.16 | -0.29, -0.03 |
| | Moderate Positive/Low Positive | 16.78 | -0.17 | -0.30, -0.04 |
| | Low Positive | 20.38 | 0.11 | -0.09, 0.31 |
| | Negative | 35.00 | 1.24 | 0.42, 2.06 |
| BV Natural *Lactobacillus* | Moderate Positive | 15.61 | 0.63 | 0.41, 0.085 |
| | Low Positive | 16.79 | 0.73 | 0.47, 0.99 |
| | Negative | 35.00 | 2.27 | 0.61, 3.93 |
| BV Natural *Megasphera-1* | Moderate Positive | 18.03 | -0.47 | -0.60, -0.34 |
| | Moderate Positive/Low Positive | 18.35 | -0.45 | -0.58, -0.31 |
| | Low Positive | 21.53 | -0.19 | -0.44, 0.06 |
| | Negative | 35.00 | 0.89 | -0.12, 1.91 |

2. Matrix Comparison:

Not applicable

## C Clinical Studies:

Clinical validation of the BD Vaginal Panel was evaluated as part of DEN160001. Please refer to the published decision summary for additional information.

1. Clinical Sensitivity and Specificity:
   Not applicable

2. Clinical Specificity:
   Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):
   Not applicable

**D Clinical Cut-Off:**

Not applicable

**E Expected Values/Reference Range:**
Please refer to the published decision summary for DEN160001.

**F Other Supportive Instrument Performance Characteristics Data:**

Not applicable.

## VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

## IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.