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

I Background Information:

A 510(k) Number

K214122

B Applicant

Becton, Dickinson and Company

C Proprietary and Established Names

BD MAX Enteric Bacterial Panel, BD MAX Extended Enteric Bacterial Panel

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PCI	Class II	21 CFR 866.3990 - Gastrointestinal Microorganism Multiplex Nucleic Acid-Based Assay	MI - Microbiology
PCH	Class II	21 CFR 866.3990 - Gastrointestinal microorganism multiplex nucleic acid-based assay	MI - Microbiology
OOI	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 determine for the BD MAX Enteric Bacterial Panel and Extended Enteric Bacterial Panel on the BD MAX System with stool specimens collected using the Copan FecalSwab Collection, Transport and Preservation System (Copan FecalSwab) and BD FecalSwab Collection, Transport and Preservation System (BD FecalSwab). The Copan FecalSwab is also co-branded as the BD FecalSwab Collection, Transport and Preservation

System (BD FecalSwab) and has been FDA-cleared under K142094 (Copan Italia SpA, legal manufactutrer); the terms Copan FecalSwab, BD FecalSwab, and FecalSwab may be used interchangeably.

B Measurand:

Target DNA sequences with the BD MAX Enteric Bacterial Panel (EBP):

- *Salmonella* spp.
- *Campylobacter* spp. (*jejuni* and *coli*)
- *Shigella* spp. / Enteroinvasive E. coli (EIEC)
- Shiga toxin 1 (stx1) / Shiga toxin 2 (stx2) genes (found in Shiga toxin-producing *E. coli* [STEC]) as well as *Shigella dysenteriae*, which can possess a Shiga toxin gene (stx) that is identical to the stx1 gene of STEC.

Target DNA sequences with the BD MAX Extended Enteric Bacterial Panel (xEBP):

- *Plesiomonas shigelloides*
- *Vibrio* (*V. vulnificus*, *V. parahaemolyticus*, and *V. cholerae*)
- Enterotoxigenic *Escherichia coli* (ETEC) heat-labile enterotoxin (LT)/ heat-stable enterotoxin (ST) genes
- *Yersinia enterocolitica*

C Type of Test:

The BD MAX EBP is a qualitative real-time polymerase chain reaction (PCR) assay for the amplification and detection of DNA from *Salmonella* spp., *Shigella* spp., and *Campylobacter* spp., as well as the toxin genes stx1/and stx2 found in Shiga-toxin producing *Escherichia coli* (STEC).

The BD MAX xEBP is a qualitative real-time polymerase chain reaction (PCR) assay for the amplification and detection of DNA from *Plesiomonas shigelloides*, *Vibrio* (*V. vulnificus*, *V. parahaemolyticus*, and *V. cholerae*), and *Yersinia enterocolitica*, as well as toxin genes health-labile enterotoxin (LT)/and heat-stable enterotoxin (ST) genes from Enterotoxigenic *Escherichia coli* (ETEC).

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
<u>BD MAX Enteric Bacterial Panel</u>

The BD MAX Enteric Bacterial Panel performed on the BD MAX System is an automated in vitro diagnostic test for the direct qualitative detection and differentiation of enteric bacterial pathogens. The BD MAX Enteric Bacterial Panel detects nucleic acids from:

• Salmonella spp.

• Campylobacter spp. (jejuni and coli)

• Shigella spp. / Enteroinvasive E. coli (EIEC)

• Shiga toxin 1 (stx1) / Shiga toxin 2 (stx2) genes (found in Shiga toxin-producing E. coli [STEC]) as well as Shigella dysenteriae, which can possess a Shiga toxin gene (stx) that is identical to the stx1 gene of STEC.

Testing is performed on unpreserved soft to diarrheal stool specimens or Cary-Blair preserved stool specimens from symptomatic patients with suspected acute gastroenteritis, enteritis or colitis. The test is performed directly on the specimen, utilizing real-time polymerase chain reaction (PCR) for the amplification of SpaO, a Campylobacter specific tuf gene sequence, ipaH and stx1/stx2. The test utilizes fluorogenic sequence-specific hybridization probes for detection of the amplified DNA.

This test is intended for use, in conjunction with clinical presentation, laboratory findings, and epidemiological information, as an aid in the differential diagnosis of Salmonella, Shigella/EIEC, Campylobacter and Shiga toxin producing E. coli (STEC) infections. Results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out co-infection with other organisms that are not detected by this test and may not be the sole or definitive cause of patient illness. Negative results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.

<u>BD MAX Extended Enteric Bacterial Panel</u>

The BD MAX Extended Enteric Bacterial Panel performed on the BD MAX System, is an automated in vitro diagnostic test for the direct qualitative detection and differentiation of enteric bacterial pathogens. It is used in conjunction with the BD MAX Enteric Bacterial Panel as an optional Master Mix. The BD MAX Extended Enteric Bacterial Panel detects nucleic acids from:

• Plesiomonas shigelloides

• Vibrio (V. vulnificus, V. parahaemolyticus, and V. cholerae)

• Enterotoxigenic Escherichia coli (ETEC) heat-labile enterotoxin (LT)/ heat-stable enterotoxin (ST) genes

• Yersinia enterocolitica

Testing is performed on unpreserved soft to diarrheal or Cary-Blair preserved stool specimens from symptomatic patients with suspected acute gastroenteritis, enteritis or colitis. The test is performed directly on the specimen, utilizing real-time polymerase chain reaction (PCR) for the amplification of relevant gene target DNA. The test utilizes fluorogenic gene-specific hybridization probes for the detection of the amplified DNA.

This test is intended for use, in conjunction with clinical presentation, laboratory findings, and epidemiological information, as an aid in the differential diagnosis of Plesiomonas shigelloides, Vibrio (V. vulnificus, V. parahaemolyticus, and V. cholerae) Enterotoxigenic Escherichia coli

(ETEC) LT/ST and Yersinia enterocolitica infections. Results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out co-infection with other organisms that are not detected by this test and may not be the sole or definitive cause of patient illness. Negative results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Both assays are performed on the BD MAX System.

IV Device/System Characteristics:

A Device Description:

The BD MAX System with the BD MAX Enteric Bacterial Panel (EBP) and BD MAX Extended Enteric Bacterial Panel (xEBP) are gastrointestinal bacterial panel multiplex nucleic acid-based assay system comprised of an instrument with associated hardware and accessories, disposable microfluidic cartridges, real-time PCR master mixes, unitized reagent strips, extraction reagents, and sample buffer tubes (SBT). The instrument automates sample preparation including target lysis, DNA extraction and concentration, reagent rehydration, and target nucleic acid amplification and detection using real-time PCR. The assays include a Sample Processing Control (SPC) that is present in the Extraction Tube. The SPC monitors DNA extraction steps, thermal cycling steps, reagent integrity and the presence of inhibitory substances. The BD MAX System software automatically interprets test results. The BD MAX EBP and xEBP are FDA-cleared under K140111 and K170308, respectively.

The BD MAX EBP and BD MAX xEBP instructions for use include testing of unpreserved stool specimens collected and transported to the laboratory in a dry, clean container, Cary-Blair preserved stool specimens collected using a plastic paddle (scoop) to place a stool sample into 15 mL of Cary-Blair media for transport, or stool specimens collected and transported using the Copan FecalSwab Collection, Transport, and Preservation System (Copan FecalSwab). Stool specimens from rectal swabs or fixed stools have not been validated with the BD MAX EBP or xEBP.

The Copan FecalSwab is comprised of a nylon flocked specimen collection swab co-packaged with a tube filled pre-filled with 2 mL of a modified Cary-Blair preservative. The Copan FecalSwab is also co-branded as the BD FecalSwab Collection, Transport and Preservation System (BD FecalSwab); the terms Copan FecalSwab, BD FecalSwab, and FecalSwab are used interchangeably below.

B Principle of Operation:

A stool specimen is collected and transported to the laboratory in a dry, clean container (for unpreserved specimens), in Cary-Blair transport media, or using the Copan FecalSwab Collection, Transport, and Preservation System. Unpreserved stool samples and Cary-Blair preserved stool samples are placed in a BD MAX SBT using a 10 µL transfer loop for analysis on the BD Max System.

To use the Copan FecalSwab stool specimens, the operator transfers fecal material from an unpreserved stool specimen to the vial of FecalSwab transport medium using the nylon flocked specimen collection swab. The operator unscrews the cap of the FecalSwab transport medium tube and transfers the swab with sample into the tube. The operator breaks the swab shaft at the break point line molded into the shaft, discards the handle part of the swab shaft, and screws the cap onto the FecalSwab tube to close. Before analysis on the BD MAX system, FecalSwab stool samples are vortexed and then 50 µL of sample is pipetted into a BD MAX SBT.

The SBT is closed with a septum cap and vortexed. A worklist is created and the SBT, unitized reagent strips, master mix, extraction tubes, and PCR cartridges are loaded onto the BD MAX System. The BD MAX System automates sample preparation including cell lysis, DNA extraction and concentration, reagent rehydration, and target nucleic acid amplification and detection using real-time PCR. Amplified targets are detected with hydrolysis probes labeled with quenched fluorophores. The amplification, detection and interpretation of the signals are done automatically by the BD MAX System.

C Instrument Description Information:

1. Instrument Name:
   BD MAX System

2. Specimen Identification:
   The BD MAX System fully automates cell lysis, nucleic acid extraction, PCR set-up, target amplification and detection. The system can process and analyze up to 24 specimens in one cartridge with two cartridges running simultaneously on the instrument. The system includes external and internal barcode reading, ensuring traceability throughout extraction and PCR process. The system includes a heater module, temperature sensors, and a fluorescence detection system with six optical channels. Detection of the target analyte from real-time PCR is by flurogenic target-specific hybridization (TaqMan Probes).

3. Specimen Sampling and Handling:
   A trained operator uses a disposable inoculating loop to place 10 µL of unpreserved or Cary-Blair stool specimen into a SBT which is then vortexed and placed onto the system. Alternatively, a trained operator can manually pipette 50 µL of preserved stool specimen from the FecalSwab collection tube into a SBT which is then vortexed and placed onto the system.

4. Calibration:
   The system is calibrated by the manufacturer on-site as part of the installation procedure as well as during biannual preventive maintenance.

5. Quality Control:
External controls are not provided with the BD MAX EBP or xEBP; however recommendations for control preparation and testing are provide in the package inserts. Both panels include an individual Sample Processing Control (SPC) as part of every test that undergoes the extraction, concentration and amplification steps to monitor for potential inhibitory substances which may be present. Additionally, the SPC monitors for potential process inefficiency due to instrument or reagent failure. External quality control and SPC have not changed since the clearance of K140111 and K170308.

V Substantial Equivalence Information:

A Predicate Device Name(s):
BD MAX Extended Enteric Bacterial Panel, BD MAX System, BD Max Enteric Bacterial Panel; BD MAX System Instrument

B Predicate 510(k) Number(s):
K170308, K140111

C Comparison with Predicate(s):

Device & Predicate Device(s):	K214122	K140111
Device Trade Name	BD MAX Enteric Bacterial Panel	Same
General Device Characteristic Similarities		
Intended Use/Indications For Use	The BD MAX Enteric Bacterial Panel performed on the BD MAX System is an automated *in vitro* diagnostic test for the direct qualitative detection and differentiation of enteric bacterial pathogens. The BD MAX Enteric Bacterial Panel detects nucleic acids from: • *Salmonella* spp. • *Campylobacter* spp. (*jejuni* and *coli*) • *Shigella* spp. / Enteroinvasive *E. coli* (EIEC) • Shiga toxin 1 (*stx1*) / Shiga toxin 2 (*stx2*) genes (found in Shiga toxin-producing *E.*	Same

	coli [STEC]) as well as *Shigella dysenteriae*, which can possess a Shiga toxin gene (*stx*) that is identical to the *stx1* gene of STEC. Testing is performed on unpreserved soft to diarrheal stool specimens or Cary-Blair preserved stool specimens from symptomatic patients with suspected acute gastroenteritis, enteritis or colitis. The test is performed directly on the specimen, utilizing real-time polymerase chain reaction (PCR) for the amplification of *SpaO*, a *Campylobacter* specific *tuf* gene sequence, *ipaH* and *stx*1/*stx*2. The test utilizes fluorogenic sequence-specific hybridization probes for detection of the amplified DNA. This test is intended for use, in conjunction with clinical presentation, laboratory findings, and epidemiological information, as an aid in the differential diagnosis of *Salmonella*, *Shigella*/EIEC, *Campylobacter* and Shiga toxin-producing *E. coli* (STEC) infections. Results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out coinfection with other organisms that are not detected by this	

	test, and may not be the sole or definitive cause of patient illness. Negative results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.	
Organisms Detected	• *Salmonella* spp. • *Campylobacter* spp. (*jejuni* and *coli*) • *Shigella* spp. / Enteroinvasive *E. coli* (EIEC) • Shiga toxin 1 (*stx1*) / Shiga toxin 2 (*stx2*) genes (found in Shiga toxin-producing *E. coli* [STEC]) as well as *Shigella dysenteriae*, which can possess a Shiga toxin gene (*stx*) that is identical to the *stx1* gene of STEC.	Same
Assay Format	Amplification: PCR Detection: Fluorogenic target-specific hybridization	Same
Assay Targets	Presence of • *tuf* gene specific for *Campylobacter* • *SpaO* gene specific for *Salmonella* • *ipaH* gene specific for *Shigella* • *stx1a* and *stx2a* genes specific to Shiga-toxin producing organisms	Same
Interpretation of Test Results	Automated (BD MAX System diagnostic software)	Same
Analysis Platform	BD MAX System	Same

PCR Sample Preparation	Automated by the BD MAX System	Same
Detection probes	TaqMan Probe	Same
Assay Controls	Sample Processing Control (SPC)	Same
General Device Characteristic Differences		
Specimen Type	• Unpreserved stool • Cary-Blair preserved stool • FecalSwab (modified Cary-Blair) preserved stool	• Unpreserved stool • Cary-Blair preserved stool
Sample Volume Tested	• 50 µL via Pipette from the FecalSwab collection tube • 10 µL via Transport Loop from the unpreserved or Cary-Blair preserved stool	• 10 µL via Transport Loop from the unpreserved or Cary-Blair preserved stool

Device & Predicate Device(s):	K214122	K170308
Device Trade Name	BD MAX Extended Enteric Bacterial Panel	Same
General Device Characteristic Similarities		
Intended Use/Indications For Use	The BD MAX Extended Enteric Bacterial Panel performed on the BD MAX System, is an automated *in vitro* diagnostic test for the direct qualitative detection and differentiation of enteric bacterial pathogens. It is used in conjunction with the BD MAX Enteric Bacterial Panel as an optional Master Mix. The BD MAX Extended Enteric Bacterial Panel detects nucleic acids from: • *Plesiomonas shigelloides* • *Vibrio* (*V. vulnificus, V.*	Same

	parahaemolyticus, and *V. cholerae*) • Enterotoxigenic *Escherichia coli* (ETEC) heat-labile enterotoxin (LT)/ heat-stable enterotoxin (ST) genes • *Yersinia enterocolitica* Testing is performed on unpreserved soft to diarrheal or Cary-Blair preserved stool specimens from symptomatic patients with suspected acute gastroenteritis, enteritis or colitis. The test is performed directly on the specimen, utilizing real-time polymerase chain reaction (PCR) for the amplification of relevant gene target DNA. The test utilizes fluorogenic gene-specific hybridization probes for the detection of the amplified DNA. This test is intended for use, in conjunction with clinical presentation, laboratory findings, and epidemiological information, as an aid in the differential diagnosis of *Plesiomonas shigelloides*, *Vibrio (V. vulnificus, V. parahaemolyticus,* and *V. cholerae)* Enterotoxigenic *Escherichia coli* (ETEC) LT/ST and *Yersinia enterocolitica* infections. Results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule	

	out co-infection with other organisms that are not detected by this test and may not be the sole or definitive cause of patient illness. Negative results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.	
Organisms Detected	• *Plesiomonas shigelloides* • *Vibrio* (*V. vulnificus, V. parahaemolyticus,* and *V. cholerae*) • Enterotoxigenic *Escherichia coli* (ETEC) heat-labile enterotoxin (LT)/ heat-stable enterotoxin (ST) genes • *Yersinia enterocolitica*	Same
Assay Format	Amplification: PCR Detection: Fluorogenic target-specific hybridization	Same
Assay Targets	Presence of: • Undefined gene suspected to be implicated in Fe3+ transport for *Plesiomonas shigelloides* • *atpA* gene specific for *Vibrio* • *eltA* gene specific for *Enterotoxigenic Escherichia coli* • *invA* gene for *Yersinia enterocolitica*	Same
Interpretation of Test Results	Automated (BD MAX System diagnostic software)	Same
Analysis Platform	BD MAX System	Same

PCR Sample Preparation	Automated by the BD MAX System	Same
Detection probes	TaqMan Probe	Same
Assay Controls	Sample Processing Control (SPC)	Same
General Device Characteristic Differences		
Specimen Type	• Unpreserved stool • Cary-Blair preserved stool • FecalSwab (modified Cary-Blair) preserved stool	• Unpreserved stool • Cary-Blair preserved stool
Sample Volume Tested	• 50 µL via Pipette from the FecalSwab collection tube • 10 µL via Transport Loop from the unpreserved or Cary-Blair preserved stool	• 10 µL via Transport Loop from the unpreserved or Cary-Blair preserved stool

VI Standards/Guidance Documents Referenced:

Class II Special Controls Guideline: Gastrointestinal Microorganism Multiplex Nucleic Acid-Based Assays for Detection and Identification of Microorganisms and Toxin Genes from Human Stool Specimens, November 2, 2015.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Within-lab precision and reproducibility studies were evaluated previously using unpreserved stool specimens. This represents the most challenging specimen type and therefore additional studies were not conducted. See K140111 and K170308 for the BD MAX Enteric Bacterial Panel and the BD MAX Extended Bacterial Panel, respectively.

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Analytical Specificity/Cross-Reactivity: Analytical specificity/cross-reactivity was evaluated previously in the presence of unpreserved stool which represents the most challenging specimen type. Please refer to K140111 and K170308. No specificity issues were identified from additional studies conducted to support testing FecalSwab stool specimens.

Interference Substances (exogenous/endogenous): Interfering substances were previously evaluated in the presence of unpreserved stool which contains the highest concentration of potential inhibitors. Please refer to K140111 and K170308.

4. Assay Reportable Range:
   Not applicable.

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

   Please refer to K140111 and K170308.

   An additional specimen stability study was conducted to evaluate specimen stability in FecalSwab collection tube and corresponding SBT meet the following BD MAX EBP and BD MAX xEBP assay specimen stability claims:
   1. FecalSwab stool specimens before testing: 25 ± 2˚C up to 24 hours (1 day) or 2-8˚C up to 120 hours (5 days)
   2. Specimen added to the BD MAX SBT: 25 ± 2˚C up to 48 hours (2 days) or 2-8˚C up to 120 hours (5 days)

   Three stool pool matrices were contrived from asymptomatic volunteers. All stools were confirmed negative for target analytes in both panels. Each stool pool was split into two portions that were used to generate the inoculated positive fecal matrix and un-inoculated negative fecal matrix. Bacterial mixes were prepared in PBS. For BD MAX EBP targets, two mixes comprised of *Campylobacter*/*Shigella* (BD MAX EBP multiplex mix #1) and STX/*Salmonella* (BD MAX EBP multiplex mix #2) were prepared. For BD MAX xEBP targets, two mixes comprised of *Yersinia*/ETEC (BD MAX xEBP multiplex mix #1) and *Plesiomonas*/*Vibrio* (BD MAX xEBP multiplex mix #2) were prepared. All positive fecal matrices were inoculated with bacterial mixes at approximately two times the limit of detection for each assay. A FecalSwab flocked swab was used to collect sample from the positive and negative fecal matrices to add to the FecalSwab collection tubes and tested independently.

   On Day 0, FecalSwab collection tubes were prepared with the positive and negative matrices for testing. Two replicates for each of three FecalSwab collection tube lots were prepared for each of the three stool pools for a total of 18 positive FecalSwab collection tubes. One replicate for each of three FecalSwab collection tube lots were prepared for each of the three stool pools for a total of nine negative FecalSwab collection tubes. For subsequent positive time points, two positive FecalSwab collection tubes per stool pool were used to prepare four SBTs for a total of 24 positive replicates. For subsequent negative time points, one positive FecalSwab collection tube per stool tool was used to prepare two (2) SBTs for a total of six negative replicates. Table 1 below describes the stability conditions and timepoints.

Table 1: Nested FecalSwab Specimen Stability Conditions and Timepoints

FecalSwab		*SBT*		*Minimum Total Days*
Storage Condition 1		***Storage Condition 2***		
N/A				0
25 °C ± 2 °C	1 day	N/A		1
		25 °C ± 2 °C	2 days	3
			3 days	4
		2 - 8 °C	5 days	6
			6 days	7
	2 days	N/A		2
2 - 8 °C	5 days	N/A		5
		25 °C ± 2 °C	2 days	7
			3 days	8
		2 - 8 °C	5 days	10
			6 days	11
	6 days	N/A		6

The acceptance criteria for the study were 100% of spiked positive samples at baseline should report "POS" as the result and 100% of un-inoculated negative samples at baseline should report "NEG" as the result. For all subsequent time points, ≥95% of spiked positive samples should report "POS" as the result and 100% of un-inoculated negative samples should report "NEG" as the result. To establish specimen stability under any given condition, the mean Ct value for each organism must be within + 2 Ct of the mean baseline value. Growth may occur with some bacterial species in the FecalSwab collection tube or SBT under the storage conditions resulting in lower Ct values.

All target organisms passed the prespecified acceptance criteria except for *Campylobacter* at the day six timepoint with <95% of positive samples yielding "POS" results (22/24 replicates). However, all other timepoints with positive *Campylobacter* samples exhibited 100% "POS" results, therefore the data were considered acceptable for the proposed stability claim. Stool preserved in FecalSwab collection tubes can be stored for 48 hours (2 days) at 25 ± 2 °C and 120 hours (5 days) at 2 - 8 °C and SBTs inoculated with FecalSwab specimen can be stored for 48 hours (2 days) at 25 ± 2 °C and 120 hours (5 days) at 2 - 8 °C.

6. Limit of Detection – Equivalency Study

The LoD for each target on the BD MAX EBP and xEBP panels was previously determined in unpreserved stool specimens and Cary-Blair preserved stool specimens (see K140111 and K170308). A LoD equivalency study was performed to demonstrate comparable analytical sensitivity for the BD MAX EBP and xEBP panels testing Cary-Blair preserved stool samples and FecalSwab preserved stool samples.

Two independent stool pools were prepared consisting of 70% stool and 30% PBS. All stool samples used to generate stool pools were confirmed negative for all targets. Each stool pool was divided into six aliquots to which serially diluted target organisms were added. Multiplex mixes of BD MAX EBP targets (*Salmonella*, STX, *Campylobacter*, and *Shigella*) and BD MAX xEBP targets (*Plesiomonas*, *Yersinia*, *Vibrio*,and ETEC) prepared in PBS were used to incoulate stool pool #1 and stool pool #2, respectively. Briefly, each organism

was prepared at 0.5 McFarland turbidity in a single suspension and diluted 1:10 in PBS to create Concentration #1. Five additional concentrations (Concentrations #2-6) were prepared by 5-fold serial dilutions from Concentration #1. Concentrations #1-6 were diluted 1:10 into stool pool mixes #1 and #2. The multiplex mix/stool pool used to inoculate 12 FecalSwab tubes and 12 Cary-Blair vials. Two SBTs were prepared for each FecalSwab tube or Cary-Blair tube for a total of 24 SBTs.

Equivalence between the specimen collection methods was confirmed when LoDs for each target were within one five-fold dilution of each other. LoD is defined as when positivity is greater than 95% (23/24 or more POS or NEG results).

The LoDs using Cary-Blair preserved stool specimens and FecalSwab stool specimens were within one five-fold dilution of each other for all EBP and xEBP targets. All analytes met the acceptance criteria and the results demonstrated comparable analytical sensitivity when FecalSwab preserved stool specimens and Cary-Blair preserved stool specimens were tested with BD MAX EBP and xEBP targets on the BD MAX System.

7. Assay Cut-Off:

   Assay cut-offs remain unchanged from previously cleared versions of the BD MAX EBP (K40111) and xEBP (K170308).

8. Accuracy (Instrument):

   Not applicable.

9. Carry-Over:

   Carry-over was established previously using unpreserved stool in EBP sample buffer which represents the worst-case scenario for carry-over contamination; therefore, additional studies were not necessary. Please refer to K140111 and K170308.

10. Detection Limit

    Not applicable.

Lead Reviewer or Consulting Reviewer Comments for Internal Discussion Only

The Detection Limit study results are acceptable.

11. User Variability

    The objective of this study was to determine whether the preparation of the FecalSwab collection tube by different users introduces variability in the expected results for the BD MAX EBP and BD MAX xEBP assays on the BD MAX System.

    Two different FecalSwab collection tubes were prepared by six different operators for each of the five panel member stools: one negative panel, three panel members at two times the limit of detection, and one panel member at four times the limit of detection. LOD panel

members consisted of duplex mixes of *Campylobacter* for the BD MAX EBP and ETEC for the BD MAX xEBP because both are the most prevalent organisms for their respective panels and have low LODs. A different and single operator prepared one SBT for each of the six operators FecalSwab collection tubes. The panels were designed to yield a total of 12 results for the negative panel, 36 results for the 2X LOD panel, and 12 results for the 4X LOD panel.

For acceptance criteria, 100% negative results for the 12 negative samples, ≥95% positive results for the 36 samples tested at 2X LoD, and 100% positive for the 12 samples tested at 4X LoD.

Tables 2 and 3 present results for user variability testing with Campylobacter and ETEC, respectively.

Table 2: User Variability of the FecalSwab Collection Tube with *Campylobacter*

EBP Target: *Campylobacter*							
Panel	**2X LOD**		**4X LOD**		**Negative**		**Grand Total**
Result	**NEG**	**POS**	**NEG**	**POS**	**NEG**	**POS**	
User 1	0	6	0	2	2	0	10
User 2	0	6	0	2	2	0	10
User 3	0	6	0	2	2	0	10
User 4	0	6	0	2	2	0	10
User 5	0	6	0	2	2	0	10
User 6	0	6	0	2	2	0	10
Grand Total	0	36	0	12	12	0	60

Table 3: User Variability of the FecalSwab Collection Tube with ETEC

xEBP Target: ETEC							
Panel	**2X LOD**		**4X LOD**		**Negative**		**Grand Total**
Result	**NEG**	**POS**	**NEG**	**POS**	**NEG**	**POS**	
User 1	0	6	0	2	2	0	10
User 2	0	6	0	2	2	0	10
User 3	0	6	0	2	2	0	10
User 4	0	6	0	2	2	0	10
User 5	0	6	0	2	2	0	10
User 6	0	6	0	2	2	0	10
Grand Total	0	36	0	12	12	0	60

Results for both targets met the acceptance criteria. Differences in specimen workflow between the FecalSwab and Cary-Blair collection procedures did not demonstrate an observable effect on expected results with the BD MAX EBP and xEBP on the BD MAX System.

Lead Reviewer or Consulting Reviewer Comments for Internal Discussion Only

The User Variability information is acceptable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was performed to demonstrate equivalent performance between testing FecalSwab stool specimens and Cary-Blair preserved stool specimens with the BD MAX EBP and xEBP on the BD MAX System.

The study protocol was reviewed and approved by Institutional Review Boards or Ethics Committees. The study was conducted according to the Declaration of Helsinki and in compliance with ICH Good Clinical Practice. Informed consent was not needed because only de-identified remnant specimens were enrolled and tested. Fresh prospective specimen were collected at six external sites. Previously characterized retrospective specimen were collected at two external sites and one internal site at BD. Samples were also contrived, where applicable, at an internal BD site. The following inclusion and exclusion criteria were used for prospective and retrospective specimen collection:

- *Prospective inclusion criteria*: unpreserved soft to diarrheal stool specimen from a pediatric or adult patient admitted to a healthcare facility (e.g., hospital, outpatient clinica, or long-term care facility) and suspected of having acute hasteroenteritis, enteritis, or colitis for which diagnostic tests were indicated and/or ordered
- *Prospective exclusion criteria*: unlabeled or mislabeled solid/formed stools or rectal swabs and specimen from patients suspected and/or confirmed *Clostridioides* (*Clostridium*) *difficile* diarrheal disease
- *Retrospective inclusion criteria*: unpreserved stool specimen confirmed positive for one of the EBP or xEBP targets
- *Retrospective exclusion criteria*: unlabeled or mislabeled specimens

At clinical sites for prospective specimen, paired FecalSwab and Cary-Blair specimens were collected from individual unpreserved stool specimens according to the manufacturer's instructions. Retrospective specimen and contrived samples prepared at the internal BD site followed the same workflow. Contrived samples were prepared for low prevalence targets, specifically all of the analytes on the xEBP panel and the Shiga toxin (STX) target on the EBP panel, to reach the goal of 100 positive test results for each target analyte. A total of 53 positive and 53 negative samples were prepared using 53 unique negative stool specimen matrices that had been previously determined to be negative for all targeted analytes. Table 4 describes the number of samples at each target level based on the limit of detection for each analyte.

Table 4: Contrived Samples Panel Target Level Description

xLOD	*Vibrio*	*Plesiomonas*	*Yersinia*	ETEC	STX
1.99	27	27	27	27	27
4	7	7	7	7	10
10	7	7	7	7	10
25	6	6	6	6	6
75	6	6	6	6	-
Negative	53	53	53	53	53
Total	106	106	106	106	106

A total of 916 prospective and retrospective samples were collected and 897/917 samples were used in the analysis to compare the performance of testing FecalSwab stool specimens to the performance of testing Cary-Blair stool specimens with the BD MAX EBP and xEBP assays on the BD MAX System. Tables 5 and 6 summarize specimen accessioning and patient demographics for complaint subjects, respectively.

Table 5: Tabular Listing of Specimen Accessioning

	Investigational Product N = n (%)
Total Number of Specimens Collected	916 (100%)
Number of Specimen Rejected	-
Did not meet inclusion/exclusion criteria	3
Labeling Issue	3
Shipment issue	10
Expired testing material	3
Total number of specimens rejected	19 (2%)
Number of Specimen Included	897 (98%)

Table 6: Clinical Trial Enrollment Summary by Age, Sex, and Specimen Type

Specimen Type	**Mean Age in Years (SD)**	**Median Age in Years**	**Min Age in Years**	**Max Age in Years**	**Sex of Total N**
Prospective Total N = 618	47.1 (22.4)	49.0	<1	95	Male: 44.8%
Unknown Age: 0					Female: 55.2%
Known Age: 618					Unknown 0%
Retrospective Total N = 295	37.2 (20.8)	33.5	<1	86	Male: 30.5%
Unknown Age: 149					Female: 24.1%
Known Age: 146					Unknown: 45.4%
Overall Total N = 913	45.2 (22.4)	47.0	<1	95	Male: 40.2%
Unknown Age: 149					Female: 45.1%
Known Age: 764					Unknown: 14.7%

The primary study endpoint was to demonstrate equivalent performance of testing FecalSwab stool specimens to the performance of testing Cary-Blair stool specimen with the BD MAX EBP and xEBP on the BD MAX System using the following for percent agreement acceptance criteria:

- PPA ≥ 95% for each target
- NPA ≥ 90% for each target
- Lower bound of the 95% confidence interval for PPA and NPA ≥ 90% for each target

Percent agreement comparing the FecalSwab specimen performance to the Cary-Blair specimen performance with the BD MAX EBP targets is presented in Tables 7-10 and xEBP targets presented in Tables 11-14.

Table 7: Percent Agreement with BD MAX EBP target *Campylobacter*

Prospective Samples Only					
Campylobacter	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	9	1[a]	10	100% [70.1-100%]	99.8% [99.0-100%]
Negative	0	585	585		
Total	9	586	595		
Retrospective Samples Only					
Campylobacter	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	88	6[b]	94	100% [95.8-100%]	97.1% [93.8-98.7%]
Negative	0	200	200		
Total	88	206	294		

a. One prospective specimen with a false positive result. Sample had a Ct value near the mean LOD Ct value with the Cary-Blair specimen collection type for *Campylobacter* at 34.05 ± 0.82.
b. Six retrospective specimens with false positive results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for *Campylobacter* at 34.05 ± 0.82.

Table 8: Percent Agreement with BD MAX EBP target *Shigella*

Prospective Samples Only					
Shigella	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	7	0	7	100% [64.6-100%]	99.8% [99.4-100%]
Negative	0	588	588		
Total	7	588	595		
Retrospective Samples Only					
Shigella	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	52	1[c]	53	98.1% [90.1-99.7%]	99.6% [97.7-99.9%]
Negative	1[d]	240	241		
Total	53	241	294		

c. One retrospective specimen with a false positive result. Sample had a Ct value near the mean LOD Ct value with the Cary-Blair specimen collection type for *Shigella* at 31.42 ± 0.72.
d. One retrospective specimen with a false negative result. Sample had a Ct value near the mean LOD Ct value with the Cary-Blair specimen collection type for *Shigella* at 31.42 ± 0.72.

Table 9: Percent Agreement with BD MAX EBP target *Salmonella*

Prospective Samples Only					
Salmonella	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	4	0	4	100% [51.0-100%]	99.8% [99.4-100%]
Negative	0	591	591		
Total	4	591	595		
Retrospective Samples Only					
Salmonella	Cary-Blair		Total	PPA	NPA

FecalSwab	Positive	Negative			
Positive	70	9[e]	79	93.3% [85.3-97.1%]	95.9% [92.4-97.8%]
Negative	5[f]	210	215		
Total	75	219	294		

e. Nine retrospective specimens with false positive results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for *Salmonella* at 33.05 ± 0.72.
f. Five retrospective specimens with false negative results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for *Salmonella* at 33.05 ± 0.72.

Table 10: Percent Agreement with BD MAX EBP target STX

Prospective Samples Only					
STX	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	1	3[g]	4	100% [20.7-100%]	99.5% [98.5-99.8%]
Negative	0	591	591		
Total	1	594	595		
Retrospective Samples Only					
STX	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	13	0	13	92.9% [68.5-98.7%]	100% [98.7-100%]
Negative	1[h]	281	282		
Total	14	281	295		
Contrived Samples Only					
STX	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	50	3[i]	53	100% [92.9-100%]	94.6% [85.4-98.2%]
Negative	0	53	53		
Total	50	56	106		

g. Three prospective specimens with false positive results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for STX at 33.83 ± 0.85.
h. One retrospective specimen with a false negative result. Sample had a Ct value near the mean LOD Ct value with the Cary-Blair specimen collection type for STX at 33.83 ± 0.85.
i. Three contrived samples expected to be positive, but tested negative with the predicate.

Table 11: Percent Agreement with BD MAX xEBP target *Yersinia*

Prospective Samples Only					
Yersinia	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	0	0	0	0% [0-79.4%]	100% [99.4-100%]
Negative	1[j]	593	594		
Total	1	593	594		
Retrospective Samples Only					
Yersinia	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	4	3[k]	7	100% [51.0-100%]	99% [97.0-99.7%]
Negative	0	287	287		

Total	4	290	294		

Contrived Samples Only					
Yersinia	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	49	3[l]	52	100% [92.7-100%]	94.7% [85.6-98.2%]
Negative	0	54	54		
Total	49	57	106		

j. One prospective specimen with a false negative result. Sample had a Ct value near the mean LOD Ct value with the Cary-Blair specimen collection type for *Yersinia* at 34.98 ± 1.58.
k. Three retrospective specimens with false positive results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for *Yersinia* at 34.98 ± 1.58.
l. Three contrived samples expected to be positive, but tested negative with the predicate.

Table 12: Percent Agreement with BD MAX xEBP target *Plesiomonas*

Prospective Samples Only					
Plesiomonas	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	2	6[m]	8	100% [34.2-100%]	99.0% [97.8-99.5%]
Negative	0	586	586		
Total	2	592	594		

Retrospective Samples Only					
Plesiomonas	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	1	0	1	33.3% [6.1-79.2%]	100% [98.7-100%]
Negative	2[n]	291	293		
Total	3	291	294		

Contrived Samples Only					
Plesiomonas	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	50	3[o]	53	100% [92.9-100%]	94.6% [85.4-98.2%]
Negative	0	53	53		
Total	50	56	106		

m. Six prospective specimens with false positive results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for *Plesiomonas* at 36.28 ± 2.38.
n. Two retrospective specimens with false negative results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for *Plesiomonas* at 36.28 ± 2.38.
o. Three contrived samples expected to be positive, but tested negative with the predicate.

Table 13: Percent Agreement with BD MAX xEBP target *Vibrio*

Prospective Samples Only					
Vibrio	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	0	2[p]	2	N/A	99.7% [98.8-99.9%]
Negative	0	592	592		
Total	0	594	594		

Retrospective Samples Only					
Vibrio	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	4	0	4	100% [51.0-100%]	100% [98.7-100%]
Negative	0	290	290		
Total	4	290	294		
Contrived Samples Only					
Vibrio	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	46	6[q]	52	100% [92.7-100%]	90.0% [79.9-95.3%]
Negative	0	54	54		
Total	46	60	106		

p. Two prospective specimens with false positive results. Samples had Ct values near the mean LOD Ct value with the Cary-Blair specimen collection type for *Vibrio* at 34.25 ± 1.32.
q. Six contrived samples expected to be positive, but tested negative with the predicate.

Table 14: Percent Agreement with BD MAX xEBP target ETEC

Prospective Samples Only					
ETEC	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	2	0	2	100% [34.2-100%]	100% [99.4-100%]
Negative	0	592	592		
Total	2	592	594		
Retrospective Samples Only					
ETEC	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	14	1[r]	15	100% [78.5-100%]	99.6% [98.0-99.9%]
Negative	0	279	279		
Total	14	280	294		
Contrived Samples Only					
ETEC	Cary-Blair		Total	PPA	NPA
FecalSwab	Positive	Negative			
Positive	51	2[s]	53	100% [93.0-100%]	96.4% [87.7-99.0%]
Negative	0	53	53		
Total	51	55	106		

r. One retrospective specimen with a false positive result. Sample had a Ct value near the mean LOD Ct value with the Cary-Blair specimen collection type for ETEC at 34.98 ± 1.58.
s. Two contrived samples expected to be positive, but tested negative with the predicate.

These results demonstrate the FecalSwab specimen collection type has comparable and acceptable performance when compared to the predicate Cary-Blair specimen type with all targets in the BD MAX EBP and xEBP on the BD MAX System.

Non-Reportable Results:
The rates of unresolved (UNR) results due to sample processing control (SPC) failure and the rates of indeterminate (IND) results due to a BD MAX System failure were also estimated

for FecalSwab stool specimens and Cary-Blair stool specimens tested with the EBP and xEBP assays. The total non-reportable rates (NRR) observed in the clincal study were 1% (6/602) and 0% (0/602) for FecalSwab and Cary-Blair stool specimens, respectively.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Performance Studies

Clinical performance of the BD MAX EBP and xEBP was established previously with prospective clinical studies. See K140111 and K170308 for additional details.

2. Clinical Specificity:

Clinical performance of the BD MAX EBP and xEBP was established previously with prospective clinical studies. See K140111 and K170308 for additional details.

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:

The expected values/reference range for analytes on the BD MAX EBP and xEBP panels were established previously. See K140111 and K170308.

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.