BD MAX™ Enteric Bacterial Panel

REF **442963**

For *In Vitro* Diagnostic Use
For use with the BD MAX System

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English

25°C
2°C
IVD CE R_X Only

INTENDED 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 (*stx*1) / Shiga toxin 2 (*stx*2) 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 *stx*1 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 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.

SUMMARY AND EXPLANATION OF THE PROCEDURE

Organisms that cause enteric diseases represent a significant cause of morbidity and mortality worldwide. Enteric infections enter the body through the gastrointestinal tract and typically are spread via contaminated food and water or contact with vomit or feces. CDC estimates there are 48 million cases of foodborne illness in the United States each year resulting in 128,000 hospitalization and 3,000 deaths.[1] In the developing world, these illnesses cause approximately 2 million deaths annually in young children.[2] Each of the causative agents may result in slightly different symptomology, including abdominal cramps or pain, loss of appetite, nausea or vomiting; however, all result in diarrhea.[3] Repeated bouts of diarrhea and persistent diarrheal disease disrupt intestinal function and absorption, potentially leading to childhood malnutrition and growth retardation.[4] Although the most common gram-negative enteric bacterial agents are easily cultivated on standard selective and differential media with toxin detection by antibody mediated lateral flow, isolation and identification are time consuming. Diagnosis may take several days, which places patients at risk for an untreated infection as well as the spread of the infection to others. Alternatively, empirical antimicrobial therapy may have severe consequences for some enteric bacterial infections, such as those caused by Shiga toxin-producing *Escherichia coli* (STEC) potentially leading to fatal complications known as hemolytic uremic syndrome in children.[5] In persons with compromised immune systems, *Campylobacter* and *Salmonella* infections occasionally spread to the bloodstream and cause a serious life-threatening infection.[6,7]

The BD MAX Enteric Bacterial Panel procedure can be performed in approximately 3 hours, as compared to traditional culture methods which can take 48 to 96 hours. The BD MAX Enteric Bacterial Panel simultaneously detects the pathogens responsible for gastreoenteritis due to *Salmonella* spp., *Campylobacter* spp. (*jejuni* and *coli*), *Shigella* spp./ EIEC, and *stx*1/*stx*2 found in Shiga toxin-producing *E. coli*. The assay includes an internal Sample Processing Control. The BD MAX Enteric Bacterial Panel automates the testing process and minimizes operator intervention from the time the sample is placed onto the BD MAX System until results are available.

A soft to diarrheal stool specimen is collected and transported to the laboratory, homogenized and looped into a BD MAX Enteric Bacterial Panel Sample Buffer Tube. The Sample Buffer Tube is placed into the BD MAX System and the following automated procedures occur: The bacterial cells are lysed, DNA is extracted on magnetic beads and concentrated, and then an aliquot of the eluted DNA is added to PCR reagents which contain the target-specific primers used to amplify the genetic targets in the BD MAX PCR Cartridge, if present. The assay also includes a Sample Processing Control. The Sample Processing Control is present in the Extraction Tube and undergoes the extraction, concentration and amplification steps to monitor for inhibitory substances, instrument or reagent failure. No operator intervention is necessary once the clinical sample, the BD MAX Unitized Reagent Strip and the PCR Cartridge are loaded into the BD MAX System. The BD MAX System automates sample lysis, DNA extraction and concentration, reagent rehydration, nucleic acid amplification and detection of the target nucleic acid sequence using real-time polymerase chain reaction (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.

PRINCIPLES OF THE PROCEDURE

Stool specimens are collected from patients and transported to the laboratory unpreserved in a clean container or preserved in Cary-Blair transport media. A 10 µL loop is inserted to the depth of the loop into the specimen, and expressed via a swirling motion into a BD MAX Sample Buffer Tube. The Sample Buffer Tube is closed with a septum cap and vortexed. Once the work list is generated and the sample is loaded on the BD MAX instrument, along with a BD MAX Enteric Bacterial Panel Unitized Reagent Strip and PCR Cartridge, the run is started and no further operator intervention is required. The BD MAX System automates sample preparation, including target organism lysis, DNA extraction and concentration, reagent rehydration, target nucleic acid sequence amplification and detection using real-time PCR. The interpretation of the signal is performed automatically by the BD MAX System. The assay also includes a Sample Processing Control that is provided in the Extraction Tube and subjected to extraction, concentration and amplification steps. The Sample Processing Control monitors for the presence of potential inhibitory substances as well as system or reagent failures.

Following enzymatic cell lysis at an elevated temperature, the released nucleic acids are captured on magnetic affinity beads. The beads, with the bound nucleic acids, are washed and the nucleic acids are eluted. Eluted DNA is neutralized and transferred to the Master Mix Tube to rehydrate the PCR reagents. After rehydration, the BD MAX System dispenses a fixed volume of PCR-ready solution into the BD MAX PCR Cartridge. Microvalves in the BD MAX PCR Cartridge are sealed by the system prior to initiating PCR to contain the amplification mixture thus preventing 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 amplicons for enteric bacterial targets (*Campylobacter* specific *tuf*[17] gene sequence variants, the *SpaO*[16] gene for specific detection of *Salmonella* spp., the *ipaH*[9,10] gene for specific detection of *Shigella* spp. or Enteroinvasive *Escherichia coli* (EIEC), the *stx*1 & *stx*2 genes[8] associated with production of Shiga toxins in STEC and *Shigella dysenteriae)* and the Sample Processing Control in five different optical channels of the BD MAX 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 MAX System monitors these signals at each cycle and interprets the data at the end of the program to report the final results.

REAGENTS AND MATERIALS

REF	Contents	Quantity
442963	**BD MAX™ Enteric Bacterial Panel Master Mix (B5)** *Oven-dried PCR Master Mix containing TaqMan specific molecular probe and primers along with Sample Processing Control-specific TaqMan probe and primers.*	24 tests (2 x 12 tubes)
	BD MAX™ Enteric Bacterial Panel Reagent Strips *Unitized Reagent Strip containing wash buffer (0.7 mL), elution buffer (0.7 mL) and neutralization buffer (0.7 mL) reagents and disposable pipette tips necessary for sample processing and DNA Extraction.*	24 tests
	BD MAX™ Enteric Bacterial Panel Extraction Tubes (B2) *Oven-dried pellet containing DNA magnetic affinity beads, protease reagents and Sample Processing Control.*	24 tests (2 x 12 tubes)
	BD MAX™ Enteric Bacterial Panel Sample Buffer Tubes	24 tests (2 x 12 tubes)
	Septum Caps	25

EQUIPMENT AND MATERIALS REQUIRED BUT NOT PROVIDED

- BD MAX™ PCR Cartridges (BD, Cat. No. 437519)
- VWR Multi-Tube Vortex Mixer (VWR, Cat. No. 58816-115)
- Vortex Genie 2 (VWR, Cat. No. 58815-234) or equivalent
- Nalgene™ Cryogenic Vial Holder (VWR, Cat. No. 66008-783)
- Rack compatible with a multi-tube vortex mixer (e.g., Cryogenic Vial Holder or equivalent)
- Disposable 10 µL inoculating loops (BD, Cat. No. 220216)
- Lab coat and powderless disposable gloves

For Unpreserved Stool Specimen types:

- Dry, clean containers for the collection of liquid or soft stool samples

For Preserved Stool Specimen types:

- Cary-Blair transport media (15 mL)

Suggested Media for Cultivation of Control Isolates (refer to the Quality Control section):

- BD Trypticase™ Soy Agar with 5% Sheep Blood (For *Salmonella*, *Shigella* and *Escherichia coli*) (e.g., BD BBL™ Trypticase Soy Agar with 5% Sheep Blood [TSA II], BD, Cat. No. 221292)
- Brucella Agar with 5% Sheep Blood, Hemin & Vitamin K_1 (For *Campylobacter jejuni*) (e.g., BD BBL™ Brucella Agar with 5% Sheep Blood, Hemin and Vitamin K_1, BD, Cat. No. 297848)

WARNINGS AND PRECAUTIONS

Danger

H319 Causes serious eye irritation.

H360 May damage fertility or the unborn child.

P280 Wear protective gloves/protective clothing/eye protection/face protection.

P264 Wash thoroughly after handling.

P201 Obtain special instructions before use.

P202 Do not handle until all safety precautions have been read and understood.

P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P308+P313 IF exposed or concerned: Get medical advice/attention.

P337+P313 If eye irritation persists: Get medical advice/attention.

P405 Store locked up.

P501 Dispose of contents/container in accordance with local/regional/national/international regulations.

- The BD MAX Enteric Bacterial Panel is for *in vitro* Diagnostic Use.
- State and local public health authorities have published guidelines for notification of reportable diseases in their jurisdictions including but not limited to *Salmonella, Shigella,* and Shiga toxin (*stx*1/*stx*2) producing *Escherichia coli* (STEC) to determine necessary measures for verification of results to identify and trace outbreaks. Laboratories are responsible for following their state or local regulations for submission of clinical material or isolates on positive specimens to their state public health laboratories.
- Do not use expired reagents and/or materials.
- Do not use the kit if the label that seals the outer box is broken upon arrival.
- Do not use reagents if the protective pouches are open or broken upon arrival.
- Do not use reagents if desiccant is not present or is broken inside reagent pouches.
- Do not remove desiccant from reagent pouches.
- Close protective pouches of reagents promptly with the zip seal after each use. Remove any excess air in the pouches prior to sealing.
- Protect reagents against heat and humidity. Prolonged exposure to humidity may affect product performance.
- Do not use reagents if the foil has been broken or damaged.
- Do not mix reagents from different pouches and/or kits and/or lots.
- Do not interchange or reuse caps, as contamination may occur and compromise test results.
- Check Unitized Reagent Strips for proper liquid fills (ensure that the liquids are at the bottom of the tubes) (refer to Figure 1).
- Check Unitized Reagent Strips to ensure that all pipette tips are present (refer to Figure 1).
- Proceed with caution when using chemical solutions as Master Mix and Extraction Tube barcode readability may be altered.
- Good laboratory technique is essential to the proper performance of this assay. Due to the high analytical sensitivity of this test, extreme care should be taken to preserve the purity of all materials and reagents.
- In cases where other PCR tests are conducted in the same general area of the laboratory, care must be taken to ensure that the BD MAX Enteric Bacterial Panel, any additional reagents required for testing, and the BD MAX System are not contaminated. Avoid microbial and deoxyribonuclease (DNase) contamination of reagents at all times. Gloves must be changed before manipulating reagents and cartridges.
- To avoid contamination of the environment by amplicons, do not break apart the BD MAX PCR Cartridges after use. The seals of the BD MAX PCR Cartridges are designed to prevent contamination.
- The laboratory should routinely perform environmental monitoring to minimize the risk of cross-contamination.
- Performing the BD MAX Enteric Bacterial Panel outside the recommended time and temperature ranges recommended for specimen transport and storage may produce invalid results. Assays not performed within the specified time ranges should be repeated.
- Additional controls may be tested according to guidelines or requirements of local, state, provincial and/or federal regulations or accrediting organizations.
- Always handle specimens as if they are infectious and in accordance with safe laboratory procedures such as those described in the CLSI Document M29[11] and in Biosafety in Microbiological and Biomedical Laboratories.[12]
- Wear protective clothing and disposable gloves while handling all reagents.
- Wash hands thoroughly after performing the test.
- Do not pipette by mouth.

- Do not smoke, drink, chew or eat in areas where specimens or kit reagents are being handled.
- Dispose of unused reagents and waste in accordance with local, state, provincial and/or federal regulations.
- Consult the BD MAX System User's Manual[13] for additional warnings, precautions and procedures.

STORAGE AND STABILITY

Collected specimens, either unpreserved stool or stool stored in 15 mL Cary-Blair transport media, should be kept between 2 °C and 25 °C during transport. Protect against freezing or exposure to excessive heat.

Specimens can be stored for up to 120 hours (5 days) at 2–8 °C or for up to 24 hours at 2–25 °C before testing.

BD MAX Enteric Bacterial Panel components are stable at 2–25 °C through the stated expiration date. Do not use expired components.

BD MAX Enteric Bacterial Panel Master Mix and Extraction Tubes are provided in sealed pouches. To protect product from humidity, immediately re-seal after opening. Reagent tubes are stable for up to 14 days at 2–25 °C after initial opening and re-sealing of the pouch.

INSTRUCTIONS FOR USE

Specimen Collection/Transport

In order to obtain an adequate specimen, the procedure for specimen collection must be followed closely. Using a dry, clean container, liquid or soft stool specimens are collected according to the following procedure:

1. Unpreserved specimens: Transfer the liquid or soft stool specimen to a dry, clean container. Avoid contamination with water or urine. Label the container and transport to the laboratory according to institutional standard operating procedures (refer to the Storage and Stability section). Avoid mixing toilet paper, water or soap with the specimen.
2. Cary-Blair preserved specimens: Transfer the liquid or soft stool specimen to a 15 mL transport device according to the manufacturer's instructions. Avoid contamination with water or urine and avoid mixing toilet paper or soap with the specimen. Label the container and transport to the laboratory according to institutional standard operating procedures (refer to the Storage and Stability section).

Specimen Preparation

NOTE: One (1) Sample Buffer Tube, one (1) Septum Cap, one (1) Master Mix (B5), one (1) Extraction Tube (B2) and one (1) Unitized Reagent Strip are required for each specimen and each External Control to be tested. Set aside the required number of materials from their protective pouches or boxes. To store opened Master Mix or Extraction Tube pouches, remove excess air and close using the zip seal.

1. Label a bar-coded BD MAX Sample Buffer Tube (clear cap) with the appropriate specimen identification. Do not obscure, write or label over the 2D-barcode.
2. Vortex unpreserved or Cary-Blair preserved specimens at high speed for 15 seconds.
3. Remove the clear cap from the Sample Buffer Tube and inoculate as follows:
   a. Insert a 10 µL disposable inoculation loop until the entire loop portion is submerged in the specimen. Do not insert beyond the loop as any additional stool on the shaft can overload the PCR reaction;
   b. Insert the loaded loop into the Sample Buffer Tube and express the specimen using a swirling motion.

   NOTE: Removal of the entire specimen from the loop is not necessary. The resultant Sample Buffer Tube solution should be "tea-stained" in color.
4. Recap the inoculated Sample Buffer Tube using a Septum Cap.
5. Place the Sample Buffer Tube in a rack compatible with a multi-tube vortex mixer, if available (e.g., cryogenic vial holder or equivalent).
6. Prepare any additional specimens for testing by repeating Steps 1 through 5, ensuring gloves are clean prior to handling additional specimens.
7. Vortex all prepared samples simultaneously at maximum speed for one (1) min with the multi-tube vortex mixer.
8. Proceed to the BD MAX System Operation section to perform testing of the BD MAX Enteric Bacterial Panel on the BD MAX System.

BD MAX System Operation

NOTE: Refer to the BD MAX System User's Manual[13] for detailed instructions (refer to the Operation section).

NOTE: Testing of the BD MAX Enteric Bacterial Panel must be performed immediately after the vortexing step above (Specimen Preparation, Step 7). If retesting is necessary, re-vortex sample(s).

1. Power on the BD MAX System (if not already done) and log in by entering **<user name>** and **<password>**.
2. Gloves must be changed before manipulating reagents and cartridges.
3. Remove the required number of Unitized Reagent Strips from the BD MAX Enteric Bacterial Panel kit. Gently tap each Unitized Reagent Strip onto a hard surface to ensure that all liquids are at the bottom of the tubes.
4. Remove the required number of Extraction Tube(s) and Master Mix Tube(s) from their protective pouches. Remove excess air, and close pouches with the zip seal.
5. For each sample to be tested, place one (1) Unitized Reagent Strip on the BD MAX System Rack, starting with Position 1 of Rack A.

6. Snap one (1) Extraction Tube (white foil) into each Unitized Reagent Strip in Position 1 as shown in Figure 1.
7. Snap one (1) Master Mix Tube (green foil) into each Unitized Reagent Strip in Position 2 as shown in Figure 1.

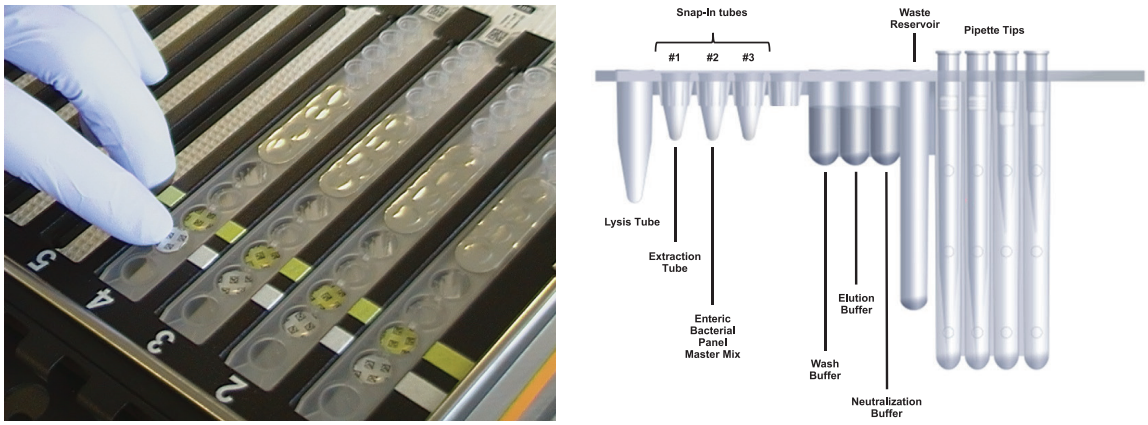

Figure 1: Snap BD MAX Enteric Bacterial Panel Extraction Tubes and Master Mix Tubes into Unitized Reagent Strips.

8. Click on the Run icon, then Inventory. Enter the kit lot number for the BD MAX Enteric Bacterial Panel (for lot traceability) by either scanning the barcode with the scanner or by manual entry.
   NOTE: Repeat step 8 each time a new kit lot is used.
9. Navigate to the Worklist. Using the pull down menu select **<BD MAX ENT BAC 52>**.
10. Enter the Sample Buffer Tube ID, Patient ID and Accession Number (if applicable) into the Worklist, either by scanning the barcode with the scanner or by manual entry.
11. Select the appropriate kit lot number (found on the outer box) from the pull down menu.
12. Repeat steps 9 to 11 for all remaining Sample Buffer Tubes.
13. Place the Sample Buffer Tubes in the BD MAX System Rack(s) corresponding to the Unitized Reagent Strips assembled in steps 5 to 7.
    NOTE: Place the Sample Buffer Tubes in the sample rack(s) with the 1D barcode labels facing outward (this makes scanning Sample Buffer Tubes easier during sample login).
14. Place the required number of BD MAX PCR Cartridge(s) into the BD MAX System (refer to Figure 2).
    - Each BD MAX PCR Cartridge accommodates up to 24 samples.
    - The BD MAX System will automatically select the position and row on the BD MAX PCR Cartridge for each run. BD MAX PCR Cartridges may be used multiple times until all lanes have been utilized.
    - To maximize use of BD MAX PCR Cartridges, using 2000 Sample Mode, select Run Wizard under the Worklist tab for lane assignments.
    - Consult the BD MAX System User's Manual[13] for more details.

Figure 2: Load BD MAX PCR Cartridges.

15. Load rack(s) onto the BD MAX System (refer to Figure 3).

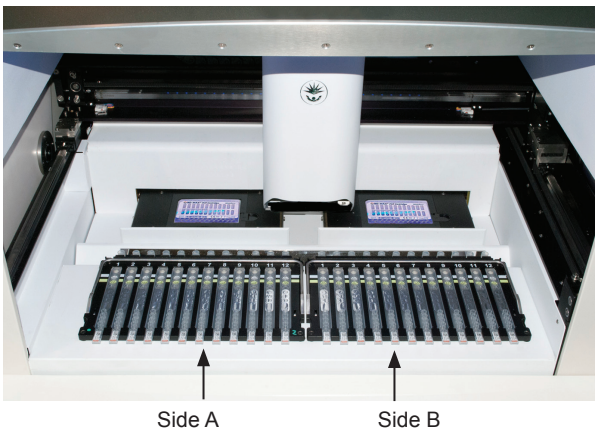

Figure 3: Load Rack(s) onto the BD MAX System.

16. Close the BD MAX System lid and click **<Start>** to begin processing.
17. **At the end of the run, check results immediately or store Sample Buffer Tubes at 2–8 °C for up to 120 hours (5 days) OR at 25 ± 2 °C for a maximum of 48 hours until the results are checked.**

NOTE: If a septum cap was damaged during the run, replace it with a new one before storing the sample.

NOTE: Prepared BD MAX Enteric Bacterial Panel Sample Buffer Tubes can be stored at 2–8 °C for a maximum of 120 hours (5 days) OR at 25 ± 2 °C for a maximum of 48 hours after the sample has been added to the Sample Buffer Tube. When an Indeterminate (IND), Unresolved (UNR), or Incomplete (INC) result is obtained, or when an External Control failure occurs, a repeat test from the prepared Sample Buffer Tube must be performed within this timeframe (refer to the Repeat Test Procedure section).

QUALITY CONTROL

Quality control procedures monitor the performance of the assay. Laboratories must establish the number, type and frequency of testing control materials according to guidelines or requirements of local, provincial, state, federal and/or country regulations or accreditation organizations in order to monitor the effectiveness of the entire analytical process. For general Quality Control guidance, the user may wish to refer to CLSI MM3 and EP12.[14,15]

1. External Control materials are not provided by BD. External Positive and Negative Controls are not used by the BD MAX System software for the purpose of sample test result interpretation. External Controls are treated as if they were patient samples. (Refer to Table 1 for the interpretation of External Control assay results.)
2. One (1) External Positive Control and one (1) External Negative Control should be run at least daily until adequate process validation is achieved on the BD MAX System in each laboratory setting. Reduced frequency of control testing should be in accordance with applicable regulations.
3. The External Positive Control is intended to monitor for substantial reagent failure. The External Negative Control is intended to detect reagent or environmental contamination (or carry-over) by target nucleic acids.
4. Various types of External Controls are recommended to allow the user to select the most appropriate for their laboratory quality control program.
   a. External Negative Control: Commercially available control material or a previously characterized sample known to be negative. BD recommends that the External Negative Control be prepared prior to the External Positive Control in order to reduce the potential for contamination as a result of control preparation.
   b. External Positive Control: Commercially available controlled materials, such as the ATCC® strains listed below, or previously characterized samples known to be positive.

Table 1: Commercially Available Strains for External Positive Control

External Positive Control Strain	Target	Culture Condition	Final Dilution from 0.5 McFarland (1 x 10^8 CFU/mL)
***Salmonella enterica* ssp. *enterica* serovar Typhimurium (ATCC 14028)**	*spaO* gene	BD Trypticase Soy Agar with 5% Sheep Blood 18–24 h ambient air	1.0 x 10^6 CFU/mL
***Shigella sonnei* (ATCC 9290)**	*ipaH* gene		
***Escherichia coli*, *stx 1* (ATCC 43890)**	*stx 1* gene		
***Campylobacter jejuni* ssp. *jejuni* (ATCC 33291)**	*tuf* gene sequence variants	Brucella Agar with 5% Sheep Blood, Hemin, and Vitamin K_1 2–3 d microaerophilic environment, or until sufficient growth	1.0 x 10^5 CFU/mL

NOTE: All plates must be prepared fresh daily. Alternate culture storage conditions should be validated by individual laboratories as appropriate.

For the preparation of External Control suspensions, it is recommended that isolates be re-suspended in a saline solution to a turbidity of 0.5 McFarland (~1 x 10^8 CFU/mL). Perform serial dilutions with saline to obtain a suspension of ~1.0 x 10^6 CFU/mL (for *Salmonella* spp., *Shigella* spp., or *E. coli* organisms) or ~1.0 x 10^5 CFU/mL (for *Campylobacter* spp.) and inoculate the corresponding Sample Buffer Tube with a 10 µL loop of the bacterial suspension. Process and test as a sample (refer to the Specimen Preparation and BD MAX System Operation sections).

5. All External Controls should yield the expected results (positive for External Positive Control, negative for External Negative Control) and no failed external controls (Unresolved or Indeterminate results).
6. An External Negative Control that yields a positive test result is indicative of a specimen handling and/or contamination event. Review the specimen handling technique to avoid mix-up and/or contamination. An External Positive Control that yields a negative result is indicative of a specimen handling/ preparation problem. Review the specimen handling/preparation technique.
7. An External Control that yields an Unresolved, Indeterminate or Incomplete test result is indicative of a reagent or a BD MAX System failure. Check the BD MAX System monitor for any error messages. Refer to the System Error Summary section of the BD MAX System User's Manual[13] for interpretation of warning and error codes. If the problem persists, use reagents from an unopened pouch or use a new assay kit.
8. Each Extraction Tube contains a Sample Processing Control which is a plasmid containing a synthetic target DNA sequence. The Sample Processing Control is extracted, eluted, and amplified along with any DNA present in the processed specimen, ensuring the predictivity of the assay The Sample Processing Control 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 Sample Processing Control result fails to meet the acceptance criteria, the result of the specimen will be reported as Unresolved; however, any positive (POS) assay results will be reported and no targets will be called NEG. An Unresolved result is indicative of specimen-associated inhibition or reagent failure. Repeat any specimen reported as Unresolved according to the Repeat Test Procedure section below.

RESULTS INTERPRETATION

Results are available on the **<Results>** tab in the **<Results>** window on the BD MAX System monitor. The BD MAX System software automatically interprets test results. Results are reported for each of the analytes and for the Sample Processing Control. A test result may be called NEG (Negative), POS (Positive) or UNR (Unresolved) based on the amplification status of the target and of the Sample Processing Control. IND (Indeterminate) or INC (Incomplete) results are due to BD MAX System failure. In the case of a partial UNR, where one or more targets have a POS result and all other targets have a UNR result, no targets will be called NEG.

Table 2: BD MAX Enteric Bacterial Panel Result Interpretation

Assay Result Reported	Interpretation of Result[a]
Shig POS	*Shigella* spp. / EIEC DNA Detected[b,c]
Shig NEG	No *Shigella* spp. / EIEC DNA Detected
Shig UNR	Unresolved – inhibitory sample or reagent failure; no target or Sample Processing Control amplification
STX POS	Shiga toxin-producing gene(s) Detected[b,d]
STX NEG	No Shiga toxin-producing gene(s) Detected
STX UNR	Unresolved – inhibitory sample or reagent failure; no target or Sample Processing Control amplification
Campy POS	*Campylobacter* spp. (*jejuni* or *coli*) DNA Detected
Campy NEG	No *Campylobacter* spp. (*jejuni* and *coli*) DNA Detected
Campy UNR	Unresolved – inhibitory sample or reagent failure; no target or Sample Processing Control amplification
Salm POS	*Salmonella* spp. DNA Detected
Salm NEG	No *Salmonella* spp. DNA Detected
Salm UNR	Unresolved – inhibitory sample or reagent failure; no target or Sample Processing Control amplification
IND	Indeterminate result due to BD MAX System failure (with Warning or Error Codes[e])
INC	Incomplete run (with Warning or Error Codes[e])

[a] BD MAX Enteric Bacterial Panel results may be used to guide the level of precautions in accordance with institutional programs and practices.

[b] Analytical studies have demonstrated that certain strains of *Shigella dysenteriae* may harbor both the *ipaH* and *stx* BD MAX Enteric Bacterial Panel targets. Additionally, there have been literature reports of *Shigella boydii* strains presenting with both *ipaH* and *stx*. On rare occasions it may be possible that more than one BD MAX Enteric Bacterial Panel target is positive from a single organism that harbors two or more genes detected by the assay. The presence of more than one positive BD MAX Enteric Bacterial Panel target may also be indicative of a dual-infection.

[c] A positive BD MAX Enteric Bacterial Panel result for *Shigella* spp. may be indicative of the presence of *Shigella* spp. or Enteroinvasive *Escherichia coli* DNA.

[d] A positive BD MAX Enteric Bacterial Panel result for Shiga toxin (*stx*1 or 2) may be indicative of the presence of Shiga toxin-producing *Escherichia coli*, *Shigella dysenteriae* or other *Enterobacteriaceae* that rarely carry Shiga toxin genes.

[e] Refer to the Troubleshooting section of the BD MAX System User's Manual[13] for interpretation of warning and error codes.

REPEAT TEST PROCEDURE

NOTE: Suficient volume is available for one repeat test from the Sample Buffer Tube. For Sample Buffer Tubes stored at room temperature, retesting must be performed within 48 hours following the initial Sample Buffer Tube inoculation with the sample. Alternatively, for Sample Buffer Tubes stored at 2–8 °C, retesting must be performed within 120 hours (5 days). The remaining stool specimen may also be used for repeat testing within 5 days of collection if stored at 2–8 °C or within 24 hours if stored at 2–25 °C.

NOTE: New samples may be tested in the same run with repeat samples.

Unresolved Result

Unresolved results may be obtained in the event that specimen-associated inhibition or reagent failure prevents proper target or Sample Processing Control amplification. If the Sample Processing Control does not amplify, the sample will be reported as UNR; however, any positive (POS) assay results will be reported and no targets will be called NEG.

The BD MAX System reports results for each target individually and a UNR result may be obtained for one or more BD MAX Enteric Bacterial Panel targets. In the case of a complete UNR, where all targets have a UNR result, it is necessary to repeat the test. In the case of a partial UNR, when one or more targets have a POS result and all other targets have a UNR result, it is recommended that the test be repeated as described above. In rare cases, discrepant results may be observed when a repeat test is run for those targets that were initially reported as POS. Follow appropriate procedures in accordance with current laboratory procedures.

Sample(s) can be repeated from their corresponding Sample Buffer Tubes within the timeframes defined above. Vortex the sample(s) for one (1) min and restart from the BD MAX System Operation section. The remaining stool specimen may also be used for repeat testing with a new Sample Buffer Tube within the timeframes defined above. Restart from the Sample Preparation section.

Indeterminate Result

Indeterminate results may be obtained in the event that a System failure occurs. Sample(s) can be repeated from their corresponding Sample Buffer Tubes within the timeframe defined above. Vortex the sample(s) for one (1) min and restart from the BD MAX Operation section. The remaining stool specimen, with a new Sample Buffer Tube, may also be used for repeat testing within the timeframes defined above. Restart from the Specimen Preparation section. For the interpretation of warning or error code messages, refer to the BD MAX System User's Manual[13] (Troubleshooting section).

Incomplete Result

Incomplete results may be obtained in the event that the Specimen Preparation or the PCR failed to complete. Sample(s) can be repeated from their corresponding Sample Buffer Tubes within the allowed timeframes defined above. Vortex the sample(s) for one (1) min and restart from the BD MAX System Operation section. The remaining stool specimen may also be used for repeat testing with a new Sample Buffer Tube within the timeframes defined above. Restart from the Specimen Preparation section. For the interpretation of warning or error code messages, refer to the BD MAX System User's Manual[13] (Troubleshooting section).

External Control Failure

External Controls should yield expected results when tested. If samples have to be repeated due to an incorrect External Control result, they should be repeated from their Sample Buffer Tube along with freshly prepared External Controls within the allowed timeframes defined above. Vortex the sample(s) for one (1) min and restart from the BD MAX System Operation section.

CULTURING OF SPECIMENS

Culture and identification of organisms from positive specimens should be performed per laboratory procedures.

LIMITATIONS OF THE PROCEDURE

- This product can only be used on the BD MAX System by trained laboratory personnel.
- This product is intended for use only with unpreserved and Cary-Blair preserved human stool specimens. Stool specimens from rectal swabs or fixed stools have not been validated with the BD MAX Enteric Bacterial Panel.
- Erroneous results may occur from improper specimen collection, handling, storage, technical error, sample mix-up, or because the number of organisms in the specimen is below the analytical sensitivity of the test.
- If the BD MAX Enteric Bacterial Panel result is IND, INC, or UNR (for one or more targets) then the test should be repeated.
- A BD MAX Enteric Bacterial Panel positive result does not necessarily indicate the presence of viable organisms. It does however, indicate the presence of the *Campylobacter* specific *tuf* gene sequence variants, *SpaO*, *ipaH* and *stx*1/*stx*2 genes and allows for identification of the Enteric Bacterial Panel organisms.
- Mutations or polymorphisms in primer- or probe-binding regions may affect detection of the genera *Salmonella* and *Campylobacter* (*jejuni* and *coli*), *Shigella* spp., Enteroinvasive *Escherichia coli* (EIEC] as well as Shiga toxin-producing *E. coli* variants, resulting in a false negative result with the BD MAX Enteric Bacterial Panel.
- The BD MAX Enteric Bacterial Panel does not distinguish which Shiga toxin gene (*stx*1/*stx*2) is present in a specimen.
- In rare instances, Shiga toxin genes can be found in *Enterobacteriaceae* other than STEC or *Shigella dysenterieae.*
- The BD MAX Enteric Bacterial Panel detects only *Campylobacter jejuni* and *Campylobacter coli* and does not differentiate between the species. Other *Campylobacter* species are not detected by the assay.
- *In silico* analysis predicts that variant *stx*2f will not be detected by the BD MAX Enteric Bacterial Panel.
- The BD MAX Enteric Bacterial Panel does not differentiate between *Shigella* spp. and Enteroinvasive *Escherichia coli* (EIEC).
- Not all serotypes of *Salmonella* were evaluated in analytical studies; however all but one (*Salmonella enterica* serotype Mississippi) of the most prevalent serotypes recently circulating in the U.S. were evaluated.[18] As with all PCR-based *in vitro* diagnostic tests, extremely low levels of target below the analytical sensitivity of the assay may be detected, but results may not be reproducible.

- False negative results may occur due to loss of nucleic acid from inadequate collection, transport or storage of specimens, or due to inadequate bacterial cell lysis. The Sample Processing Control has been added to the test to aid in the identification of specimens that contain inhibitors to PCR amplification. The Sample Processing Control does not indicate if nucleic acid has been lost due to inadequate collection, transport or storage of specimens, or whether bacterial cells have been inadequately lysed.
- Results from the BD MAX Enteric Bacterial Panel should be used as an adjunct to clinical observations and other information available to the physician.
- As with all *in vitro* diagnostic tests, positive and negative predictive values are highly dependent on prevalence. The BD MAX Enteric Bacterial Panel performance may vary depending on the prevalence and population tested.
- BD MAX Enteric Bacterial Panel results may or may not be affected by concurrent antimicrobial therapy, which may reduce the amount of target present.
- The Sample Buffer Tube has not been designed to support organism viability. If culture is necessary it must be performed from the original specimen.
- The performance of this test has not been established for monitoring treatment of *Salmonella* spp., *Shigella* spp., *Campylobacter jejuni*, *Campylobacter coli* or STEC infections.
- This test is a qualitative test and does not provide quantitative values nor indicate the quantity of organisms present.
- The performance of this test has not been evaluated for immunocompromised individuals or for patients without symptoms of gastrointestinal infection.
- The effect of interfering substances has only been evaluated for those listed in this labeling. Potential interference has not been evaluated for substances other than those described in the Interference section below.
- Cross-reactivity with organisms other than those listed in the Analytical Specificity section below have not been evaluated.

PERFORMANCE CHARACTERISTICS

Performance characteristics of the BD MAX Enteric Bacterial Panel were determined in a multi-site investigational study. The study involved a total of eight (8) geographically diverse clinical centers where specimens were collected as part of routine patient care, enrolled into the trial, and tested with the BD MAX Enteric Bacterial Panel. An additional four (4) collection centers enrolled specimens to be evaluated at a central location. Specimens were obtained from pediatric or adult patients suspected of acute bacterial gastroenteritis, enteritis or colitis, for which stool culture had been ordered by a healthcare provider. For prospective (fresh) specimens, clinical centers performed their standard culture and identification method for *Salmonella*, *Shigella*, *Campylobacter* and *Escherichia coli* O157, with a reference center performing culture and identification for three (3) sites. The reference method for Shiga toxin 1 and 2 detection was via broth enriched enzyme immunoassay. Reference method testing was performed in accordance with each product's respective package insert. For retrospective (frozen) specimens, the historical culture results were recorded at the collection site and the specimens were not re-cultured. The historical culture results were confirmed using an alternate PCR assay and bi-directional sequencing as part of the composite reference method in order to confirm the presence of target DNA.

A total of 3,457 prospective specimens (2,112 Cary-Blair preserved and 1,345 unpreserved) and 785 retrospective specimens (464 Cary-Blair preserved and 321 unpreserved) were enrolled in the clinical evaluation. Table 3 describes the number of compliant specimens enrolled by patient age and specimen type. A total of 104 retrospective specimens were not included in the performance calculations below as the historical results were not confirmed by an alternate PCR and bi-directional sequencing. Tables 4 through 7 describe the performance characteristics of the BD MAX Enteric Bacterial Panel that were observed during the clinical trial.

Table 3: Compliant Clinical Trial Enrollment Summary by Age Group and Specimen Type

Age Group	Cary-Blair Preserved	Unpreserved	Combined
<1	110	43	153
1–4	302	128	430
5–12	270	209	479
13–18	271	168	439
19–65	1,222	799	2,021
Over 65	388	249	637
Unknown	3	2	5
Total	2,566	1,598	4,164

For the Cary-Blair preserved specimen type, the BD MAX Enteric Bacterial Panel identified 96.2% and 98.7% of the *Campylobacter* spp. prospective positive and negative specimens, respectively, and 97% and 100% of the retrospective positive and negative specimens, respectively. For the unpreserved specimen type, the BD MAX Enteric Bacterial Panel identified 100% and 97.5% of the *Campylobacter* spp. prospective positive and negative specimens, respectively, and 97% and 99.1% of the retrospective positive and negative specimens, respectively (refer to Table 4).

Table 4: *Campylobacter* spp. - Overall Performance

Specimen Type	Specimen Origin	BD MAX	RM		Total
			P	N	
Cary-Blair	Prospective (Fresh)	P	25	23[b]	48
		N	1[a]	1,751	1,752
		Total	26	1,774	1,800
PPA (95% CI): 96.2% (81.1%, 99.3%) NPA (95% CI): 98.7% (98.1%, 99.1%)					
Cary-Blair	Retrospective (Frozen)	P	64	0	64
		N	2	151	153
		Total	66	151	217
PPA (95% CI): 97% (89.6%, 99.2%) NPA (95% CI): 100% (97.5%, 100%)					
Unpreserved	Prospective (Fresh)	P	22	31[c]	53
		N	0	1,185	1,185
		Total	22	1,216	1,238
PPA (95% CI): 100% (85.1%, 100%) NPA (95% CI): 97.5% (96.4%, 98.2%)					
Unpreserved	Retrospective (Frozen)	P	65	2	67
		N	2	221	223
		Total	67	223	290
PPA (95% CI): 97% (89.8%, 99.2%) NPA (95% CI): 99.1% (96.8%, 99.8%)					

[a] This specimen was also tested using an alternate PCR assay followed by bi-directional sequencing and gave a negative result.

[b] These twenty-three (23) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; ten (10) of twenty-three (23) gave a positive result.

[c] These thirty-one (31) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; fourteen (14) of thirty-one (31) gave a positive result.

For the Cary-Blair preserved specimen type, the BD MAX Enteric Bacterial Panel identified 85% and 99.1% of the *Salmonella* spp. prospective positive and negative specimens, respectively, and 99.1% and 100% of the retrospective positive and negative specimens, respectively. For the unpreserved specimen type, the BD MAX Enteric Bacterial Panel identified 91.7% and 98.9% of the *Salmonella* spp. prospective positive and negative specimens, respectively, and 100% and 99.6% of the retrospective positive and negative specimens, respectively (refer to Table 5).

Table 5: *Salmonella* spp. – Overall Performance

Specimen Type	Specimen Origin	BD MAX	RM		Total
			P	N	
Cary-Blair	**Prospective (Fresh)**	**P**	17	17[b]	34
		N	3[a]	1,791	1,794
		Total	20	1,808	1,828
PPA (95% CI): 85% (64%, 94.8%) NPA (95% CI): 99.1% (98.5%, 99.4%)					
Cary-Blair	**Retrospective (Frozen)**	**P**	105	0	105
		N	1	213	214
		Total	106	213	319
PPA (95% CI): 99.1% (94.8%, 99.8%) NPA (95% CI): 100% (98.2%, 100%)					
Unpreserved	**Prospective (Fresh)**	**P**	22	13[c]	35
		N	2[a]	1,202	1,204
		Total	24	1,215	1,239
PPA (95% CI): 91.7% (74.2%, 97.7%) NPA (95% CI): 98.9% (98.2%, 99.4%)					
Unpreserved	**Retrospective (Frozen)**	**P**	61	1	62
		N	0	237	237
		Total	61	238	299
PPA (95% CI): 100% (94.1%, 100%) NPA (95% CI): 99.6% (97.7%, 99.9%)					

[a] These three (3) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing and gave a negative result.

[b] These seventeen (17) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; eleven (11) of seventeen (17) gave a positive result.

[c] These thirteen (13) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; eleven (11) of thirteen (13) gave a positive result.

For the Cary-Blair preserved specimen type, the BD MAX Enteric Bacterial Panel identified 100% and 99.7% of the *Shigella* spp. / EIEC organisms prospective positive and negative specimens, respectively, and 98% and 100% of the retrospective positive and negative specimens, respectively. For the unpreserved specimen type, the BD MAX Enteric Bacterial Panel identified 100% and 99.4% of the *Shigella* spp. / EIEC organisms prospective positive and negative specimens, respectively, and 100% and 100% of the retrospective positive and negative specimens, respectively (refer to Table 6).

Table 6: *Shigella* spp. / EIEC – Overall Performance

Specimen Type	Specimen Origin	BD MAX	RM		Total
			P	N	
Cary-Blair	Prospective (Fresh)	P	19	5[a]	24
		N	0	1,804	1,804
		Total	19	1,809	1,828
PPA (95% CI): 100% (83.2%, 100%) NPA (95% CI): 99.7% (99.4%, 99.9%)					
Cary-Blair	Retrospective (Frozen)	P	50	0	50
		N	1	187	188
		Total	51	187	238
PPA (95% CI): 98% (89.7%, 99.7%) NPA (95% CI): 100% (98%, 100%)					
Unpreserved	Prospective (Fresh)	P	22	7[b]	29
		N	0	1,212	1,212
		Total	22	1,219	1,241
PPA (95% CI): 100% (85.1%, 100%) NPA (95% CI): 99.4% (98.8%, 99.7%)					
Unpreserved	Retrospective (Frozen)	P	41	0	41
		N	0	264	264
		Total	41	264	305
PPA (95% CI): 100% (91.4%, 100%) NPA (95% CI): 100% (98.6%, 100%)					

[a] These five (5) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; all five (5) specimens gave a positive result.
[b] These seven (7) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; six (6) of seven (7) gave a positive result.

For the Cary-Blair preserved specimen type, the BD MAX Enteric Bacterial Panel identified 75% and 99.3% of the Shiga toxins (*stx*1/*stx*2) prospective positive and negative specimens, respectively, and 100% and 100% of the retrospective positive and negative specimens, respectively. For the unpreserved specimen type, the BD MAX Enteric Bacterial Panel identified 100% and 99% of the Shiga toxins (*stx*1 and/or *stx*2) prospective positive and negative specimens, respectively, and 100% and 100% of the retrospective positive and negative specimens, respectively (refer to Table 7).

Table 7: Shiga toxins (*stx*1/*stx*2) – Overall Performance

Specimen Type	Specimen Origin	BD MAX	RM		Total
			P	N	
Cary-Blair	Prospective (Fresh)	P	6	13[b]	19
		N	2[a]	1,768	1,770
		Total	8	1,781	1,789
PPA (95% CI): 75% (40.9%, 92.9%) NPA (95% CI): 99.3% (98.8%, 99.6%)					
Cary-Blair	Retrospective (Frozen)	P	41	0	41
		N	0	79	79
		Total	41	79	120
PPA (95% CI): 100% (91.4%, 100%) NPA (95% CI): 100% (95.4%, 100%)					
Unpreserved	Prospective (Fresh)	P	2	7[c]	9
		N	0	704	704
		Total	2	711	713
PPA (95% CI): 100% (34.2%, 100%) NPA (95% CI): 99% (98%, 99.5%)					
Unpreserved	Retrospective (Frozen)	P	25	0	25
		N	0	11	11
		Total	25	11	36
PPA (95% CI): 100% (86.7%, 100%) NPA (95% CI): 100% (74.1%, 100%)					

[a] These two (2) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing and gave a negative result.
[b] These thirteen (13) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; seven (7) of thirteen (13) gave a positive result.
[c] These seven (7) specimens were also tested using an alternate PCR assay followed by bi-directional sequencing; three (3) of seven (7) gave a positive result.

Performance of the BD MAX Enteric Bacterial Panel by species/toxin type as observed during the clinical trial is presented below in Tables 8 through 10. The species identification was obtained either from the culture and identification portion of the reference method testing or from sequencing performed for the confirmation of retrospective specimen historical results and on discrepant prospective specimens. While the BD MAX Enteric Bacterial Panel is designed to detect the species and toxin types described below, the panel does not report results to the species or toxin level.

Table 8: *Campylobacter* Performance per Species Observed During the Clinical Trial

Campylobacter			**PPA**	
Specimen Type	**Specimen Origin**	**Species**	**Estimate**	**95% CI**
Cary-Blair Preserved	Prospective (Fresh)	*jejuni*[a]	95.8% (23/24)	(79.8%, 99.3%)
		Untyped	100.0% (2/2)	(34.2%, 100.0%)
	Retrospective (Frozen)	*coli*	100.0% (2/2)	(34.2%, 100.0%)
		jejuni	96.9% (62/64)	(89.3%, 99.1%)
Unpreserved	Prospective (Fresh)	*jejuni*	100.0% (19/19)	(83.2%, 100.0%)
		jejuni or *coli*	100.0% (1/1)	(20.7%, 100.0%)
		Untyped	100.0% (2/2)	(34.2%, 100.0%)
	Retrospective (Frozen)	*coli*	100.0% (5/5)	(56.6%, 100.0%)
		jejuni	96.8% (60/62)	(89.0%, 99.1%)

[a] Of these specimens, one (1) prospective specimen was also tested using a validated PCR assay followed by bi-directional sequencing and gave a negative result.

Table 9: *Shigella* Performance per Species Observed During the Clinical Trial

Shigella			**PPA**	
Specimen Type	**Specimen Origin**	**Species**	**Estimate**	**95% CI**
Cary-Blair Preserved	Prospective (Fresh)	*flexneri*	100.0% (1/1)	(20.7%, 100.0%)
		sonnei	100.0% (18/18)	(82.4%, 100.0%)
	Retrospective (Frozen)	*sonnei*	98.0% (50/51)	(89.7%, 99.7%)
Unpreserved	Prospective (Fresh)	*flexneri*	100.0% (2/2)	(34.2%, 100.0%)
		sonnei	100.0% (20/20)	(83.9%, 100.0%)
	Retrospective (Frozen)	*flexneri*	100.0% (1/1)	(20.7%, 100.0%)
		sonnei	100.0% (40/40)	(91.2%, 100.0%)

Table 10: Shiga toxins Performance per Species Observed During the Clinical Trial

Shiga toxins			**PPA**	
Specimen Type	**Specimen Origin**	**Toxin Type**	**Estimate**	**95% CI**
Cary-Blair Preserved	Prospective (Fresh)	*stx*1	100.0% (4/4)	(51.0%, 100.0%)
		*stx*2	100.0% (1/1)	(20.7%, 100.0%)
		*stx*1 and *stx*2[a]	33.3% (1/3)	(6.1%, 79.2%)
	Retrospective (Frozen)	*stx*1	100.0% (28/28)	(87.9%, 100.0%)
		*stx*2	100.0% (6/6)	(61.0%, 100.0%)
		*stx*1 and *stx*2	100.0% (7/7)	(64.6%, 100.0%)
Unpreserved	Prospective (Fresh)	*stx*1	100.0% (1/1)	(20.7%, 100.0%)
		*stx*1 and *stx*2	100.0% (1/1)	(20.7%, 100.0%)
	Retrospective (Frozen)	*stx*1	100.0% (5/5)	(56.6%, 100.0%)
		*stx*2	100.0% (6/6)	(61.0%, 100.0%)
		*stx*1 and *stx*2	100.0% (14/14)	(78.5%, 100.0%)

[a] Two (2) prospective specimens were also tested using a validated PCR assay followed by bi-directional sequencing and gave a negative result.

Table 11 below shows the co-infections detected by the BD MAX Enteric Bacterial Panel during the prospective segment of the clinical trial. Note that there were no co-infections detected by the reference method during the prospective segment of the clinical trial.

Table 11: Co-infections Observed During the BD MAX Enteric Bacterial Panel Prospective Clinical Trial

Distinct Co-infection Combinations Detected by BD MAX Enteric Bacterial Panel		Number of Discrepant Co-Infections	Discrepant Analyte(s)[a]
Analyte 1	**Analyte 2**		
Shigella	*stx*	1	*stx*[b]
stx	*Campylobacter*	1	*stx*[c]
stx	*Salmonella*	2	*stx* (2) and *Salmonella* (1)[d]
Campylobacter	*Salmonella*	2	*Campylobacter* (2), *Salmonella* (1)[e]

[a] A discrepant co-infection or discrepant analyte was defined as one that was detected by the BD MAX assay but not detected by the reference method.

[b] One (1) discrepant *stx* was investigated using an alternate method; bi-directional sequence analysis identified the analyte in 0/1 cases.

[c] One (1) discrepant *stx* was investigated using an alternate method; bi-directional sequence analysis identified the analyte in 1/1 cases.

[d] Two (2) discrepant *stx* were investigated using an alternate method; bi-directional sequence analysis identified the analyte in 0/2 cases. One (1) discrepant *Salmonella* was investigated using an alternate method; bi-directional sequence analysis identified the analyte in 1/1 cases.

[e] Two (2) discrepant *Campylobacter* were investigated using an alternate method; bi-directional sequence analysis identified the analyte in 0/2 cases. One (1) discrepant *Salmonella* was investigated using an alternate method; bi-directional sequence analysis identified the analyte in 0/1 cases.

Of the 3,183 prospective specimens initially evaluated with the BD MAX Enteric Bacterial Panel, 4.0% of the Cary-Blair preserved and 7.8% of the unpreserved specimens initially reported as Unresolved. Following a valid repeat test, 0.1% of the Cary-Blair preserved and 1.0% of the unpreserved specimens remained Unresolved. Of the 783 retrospective specimens initially evaluated with the BD MAX Enteric Bacterial Panel, 2.2% of the Cary-Blair preserved and 4.1% of the unpreserved specimens initially reported as Unresolved. Following a valid repeat test, 0.2% of the Cary-Blair preserved and 0.6% of the unpreserved specimens remained Unresolved (refer to Table 12). The total numbers provided in Table 12 are based on compliant specimens and BD MAX Enteric Bacterial Panel results.

Table 12: Unresolved Rates

		Initial Unresolved Rates		Unresolved Rates After Repeat	
Specimen Type	**Specimen Origin**	**Percent**	**95% CI**	**Percent**	**95% CI**
Cary-Blair	Prospective (Fresh)	4.0% (77/1,905)	(3.2%, 5.0%)	0.1% (2/1,897)	(0.0%, 0.4%)
	Retrospective (Frozen)	2.2% (10/464)	(1.2%, 3.9%)	0.2% (1/463)	(0.0%, 1.2%)
Unpreserved	Prospective (Fresh)	7.8% (100/1,278)	(6.5%, 9.4%)	1.0% (13/1,251)	(0.6%, 1.8%)
	Retrospective (Frozen)	4.1% (13/319)	(2.4%, 6.8%)	0.6% (2/317)	(0.2%, 2.3%)

Of the 3,183 prospective specimens initially evaluated with the BD MAX Enteric Bacterial Panel, 1.7% of the Cary-Blair preserved and 1.6% of the unpreserved specimens initially reported as Indeterminate. Following a valid repeat test, 0% of the Cary-Blair preserved and 0.2% of the unpreserved specimens remained Indeterminate. Of the 783 retrospective specimens initially evaluated with the BD MAX Enteric Bacterial Panel, 1.5% of the Cary-Blair preserved and 1.9% of the unpreserved specimens initially reported as Indeterminate. Following a valid repeat test, 0% of the Cary-Blair preserved and 0% of the unpreserved specimens remained Indeterminate (refer to Table 13). The total numbers provided in Table 13 are based on compliant specimens and BD MAX Enteric Bacterial Panel results.

Table 13: Indeterminate Rates

		Initial Indeterminate Rates		Final Indeterminate Rates After Repeat	
Specimen Type	**Specimen Origin**	**Percent**	**95% CI**	**Percent**	**95% CI**
Cary-Blair	Prospective (Fresh)	1.7% (33/1,905)	(1.2%, 2.4%)	0.0% (0/1,897)	(0.0%, 0.2%)
	Retrospective (Frozen)	1.5% (7/464)	(0.7%, 3.1%)	0.0% (0/463)	(0.0%, 0.8%)
Unpreserved	Prospective (Fresh)	1.6% (20/1,278)	(1.0%, 2.4%)	0.2% (2/1,251)	(0.0%, 0.6%)
	Retrospective (Frozen)	1.9% (6/319)	(0.9%, 4.0%)	0.0% (0/317)	(0.0%, 1.2%)

Of the 3,183 prospective specimens initially evaluated with the BD MAX Enteric Bacterial Panel, 1.3% of the Cary-Blair preserved and 2.0% of the unpreserved specimens initially reported as Incomplete. Following a valid repeat test, 0% of the Cary-Blair preserved and 0% of the unpreserved specimens remained Incomplete. Of the 783 retrospective specimens initially evaluated with the BD MAX Enteric Bacterial Panel, 1.3% of the Cary-Blair preserved and 0% of the unpreserved specimens initially reported as Incomplete. Following a valid repeat test, 0% of the Cary-Blair preserved specimens remained Incomplete (refer to Table 14). The total numbers provided in Table 14 are based on compliant specimens and BD MAX Enteric Bacterial Panel results.

Table 14: Incomplete Rates

		Initial Incomplete Rates		Final Incomplete Rates After Repeat	
Specimen Type	**Specimen Origin**	**Percent**	**95% CI**	**Percent**	**95% CI**
Cary-Blair	Prospective (Fresh)	1.3% (24/1,905)	(0.8%, 1.9%)	0.0% (0/1,897)	(0.0%, 0.2%)
	Retrospective (Frozen)	1.3% (6/464)	(0.6%, 2.8%)	0.0% (0/463)	(0.0%, 0.8%)
Unpreserved	Prospective (Fresh)	2.0% (26/1,278)	(1.4%, 3.0%)	0.0% (0/1,251)	(0.0%, 0.3%)
	Retrospective (Frozen)	0.0% (0/319)	(0.0%, 1.2%)	0.0% (0/317)	(0.0%, 1.2%)

Analytical Inclusivity

A variety of BD MAX Enteric Bacterial Panel assay target strains were included in this study. Strain selection criteria included prevalence, serotype and motility, where appropriate. One hundred twenty-one (121) strains were tested, including strains from public collections and well-characterized clinical isolates.

Inclusivity testing included 30 strains of *Campylobacter* spp. (*jejuni* and *coli*), 30 strains of *Salmonella* spp. (*enterica* and *bongori*), 31 strains of *Shigella* spp. / Enteroinvasive *Escherichia coli* (EIEC) and 35 strains found to be positive for Shiga toxin types 1 or 2 (including 30 *E. coli* strains of which 20 were non-O157, and 5 *Shigella dysenteriae* strains). The strains were tested as target pools containing three or four assay targets each at the LoD for the assay in unpreserved stool matrix. The assay correctly identified 120 of the 121 strains tested at the LoD. One strain of *Shigella sonnei* (ENF 15987) demonstrated 79.17% positivity at a concentration of 56.1 CFU/mL. The isolate was further evaluated and yielded 100% positivity at a concentration of 405 CFU/mL. Seven (7) other strains of *Shigella sonnei* were evaluated during the analytical inclusivity study and met the study acceptance criteria at a concentration of 56.1 CFU/mL.

Analytical Sensitivity

The analytical sensitivity (Limit of Detection or LoD) for the BD MAX Enteric Bacterial Panel was determined as follows: Two (2) individual Target Mixes were prepared, each of which contained a bacterial suspension that was comprised of a representative strain for each of the target organisms detected by the BD MAX Enteric Bacterial Panel, including one strain bearing a variation of a gene coding for a Shiga-like toxin. Each target organism was prepared and quantified from culture prior to inclusion in the relevant Target Mix. Individual inoculating loops were dipped into each of the two Target Mixes and each inoculating loop was then transferred to a Sample Buffer Tube, already containing fecal matrix (preserved or unpreserved) that was pre-determined to be negative for all the targets detected by the BD MAX Enteric Bacterial Panel. Each Target Mix was tested in replicates of 30 per sample type (preserved or unpreserved), by a single operator, using 3 different production lots of the BD MAX Enteric Bacterial Panel. Analytical sensitivity (LoD), defined as the lowest concentration at which greater than 95% of all replicates are expected to test positive with 95% confidence, ranged from 10 to 653 CFU/mL (in Sample Buffer Tube) and 1,500 to 97,950 CFU/mL (in stool) for preserved specimens and 42 to 910 CFU/mL (in Sample Buffer Tube) and 6,300 to 136,500 CFU/mL (in stool) for unpreserved specimens (refer to Table 15).

Table 15: BD MAX Enteric Bacterial Panel Limit of Detection

	Unpreserved	Cary-Blair Preserved
***Salmonella* Typhimurium (ATCC 14028)**		
LoD (CFU/mL in SBT) [95% CI]	**296 [233–376]**	**193 [142–263]**
LoD (CFU/mL in stool) [95% CI]	**44,400 [34,950–56,400]**	**28,950 [21,300–39,450]**
***Salmonella enteriditis* (ATCC 13076)**		
LoD (CFU/mL in SBT) [95% CI]	**620 [403–954]**	**502 [345–729]**
LoD (CFU/mL in stool) [95% CI]	**93,000 [60,450–143,100]**	**75,300 [51,750–109,350]**
***Campylobacter coli* (ATCC 43134)**		
LoD (CFU/mL in SBT) [95% CI]	**95 [70–128]**	**55 [41–76]**
LoD (CFU/mL in stool) [95% CI]	**14,250 [10,500–19,200]**	**8,250 [6,150–11,400]**
***Campylobacter jejuni* (ATCC 43429)**		
LoD (CFU/mL in SBT) [95% CI]	**42 [36–49]**	**10 [9–10]**
LoD (CFU/mL in stool) [95% CI]	**6,300 [5,400–7,350]**	**1,500 [1,350–1,500]**
***Shigella flexneri* (ATCC 700930)**		
LoD (CFU/mL in SBT) [95% CI]	**374 [249–561]**	**229 [151–347]**
LoD (CFU/mL in stool) [95% CI]	**56,100 [37,350–84,150]**	**34,350 [22,650–52,050]**

	Unpreserved	Cary-Blair Preserved
***Shigella sonnei* (BD ENF 7142)**		
LoD (CFU/mL in SBT) [95% CI]	**84 [59–118]**	**124 [67–229]**
LoD (CFU/mL in stool) [95% CI]	**12,600 [8,850–17,700]**	**18,600 [10,050–34,350]**
***E. coli stx*1 (ATCC 43890)**		
LoD (CFU/mL in SBT) [95% CI]	**255 [195–332]**	**223 [167–299]**
LoD (CFU/mL in stool) [95% CI]	**38,202 [29,259–49,865]**	**33,495 [25,026–44,817]**
***E. coli stx*1 / *stx*2 (BD ENF 10513)**		
LoD (CFU/mL in SBT) [95% CI]	**910 [550–1,505]**	**653 [384–1,111]**
LoD (CFU/mL in stool) [95% CI]	**136,500 [82,500–225,750]**	**97,950 [57,600–166,650]**
***E. coli stx*2 (ATCC 43889)**		
LoD (CFU/mL in SBT) [95% CI]	**722 [519–1,006]**	**599 [291–1,231]**
LoD (CFU/mL in stool) [95% CI]	**108,300 [77,850–150,900]**	**89,850 [43,650–184,650]**

SBT: Sample Buffer Tube

Analytical Specificity

The BD MAX Enteric Bacterial Panel was performed on samples containing phylogenetically related species and other organisms (bacteria, viruses, parasites and yeast) likely to be found in stool specimens.

- Nine (9) out of 9 *Campylobacter* strains (*Campylobacter* species other than *jejuni* or *coli*) with undetectable *tuf* gene sequences, tested at a concentration ≥1 x 10^6 CFU/mL in the Sample Buffer Tube, produced negative results with the BD MAX Enteric Bacterial Panel.
- Six (6) out of 6 *Escherichia coli* strains other than Shiga toxin-producing strains, tested at a concentration ≥1 x 10^6 CFU/mL in the Sample Buffer Tube, produced negative results with the BD MAX Enteric Bacterial Panel.
- Ninety-eight (98) out of 99 other bacterial strains (including 53 species and subspecies), tested at a concentration ≥1 x 10^6 CFU/mL in the Sample Buffer Tube (or ~1 x 10^8 genomic DNA cp/mL or 1 x 10^8 elementary bodies/mL in the Sample Buffer Tube), produced negative results with the BD MAX Enteric Bacterial Panel. *Shigella boydii* (ATCC 12028) produced 1 replicate out of 3 as positive for the presence of s*tx*.
- Fifteen (15) out of 15 viruses, tested at a concentration ≥1 x 10^4 PFU/mL in the Sample Buffer Tube, produced negative results with the BD MAX Enteric Bacterial Panel.
- Three (3) out of 3 ova and parasites, tested at a concentration ≥1 x 10^5 cysts/mL in the Sample Buffer Tube, produced negative results with the BD MAX Enteric Bacterial Panel.
- Two (2) out of 2 *Candida* species tested at a concentration ≥1 x 10^5 organisms/mL in the Sample Buffer Tube, produced negative results with the BD MAX Enteric Bacterial Panel.
- Sixteen (16) Enteric organisms representing each target of the BD MAX Enteric Bacterial Panel were tested, with results as follows:
    - Three (3) of 3 *Campylobacter* spp.; one *Campylobacter coli*, one *Campylobacter jejuni*, subsp. *doylei* and one *Campylobacter jejuni*, subsp. *jejuni* bearing the *tuf* gene tested at a concentration ≥1 x 10^6 CFU/mL in the Sample Buffer Tube, produced positive results for *Campylobacter* and negative results for all other targets with the BD MAX Enteric Bacterial Panel.
    - Four (4) of 4 *E. coli*; two O157 and two non-O157 strains bearing the *stx* gene tested at a concentration ≥1 x 10^6 CFU/mL in the Sample Buffer Tube, produced positive results for *E. coli* and negative results for all other targets with the BD MAX Enteric Bacterial Panel.
    - Five (5) of 5 *Salmonella* spp. bearing the *spaO* gene tested at a concentration ≥1 x 10^6 CFU/mL in the Sample Buffer Tube, produced positive results for *Salmonella* and negative results for all other targets with the BD MAX Enteric Bacterial Panel.
    - Three (3) of 4 *Shigella* spp.; one *Shigella sonnei*, one *Shigella boydii*, one *Shgiella flexneri* and *Shigella dysentariae* bearing the *ipaH* gene tested at a concentration ≥1 x 10^6 CFU/mL in the Sample Buffer Tube, produced positive results for *ipaH* and negative results for all other targets with the BD MAX Enteric Bacterial Panel.
        - Initial testing of *Shigella boydii* (ATCC 12028) produced 1 replicate out of 3 as positive for the presence of s*tx*. Subsequent testing of this strain produced positive results with 8 out of 20 replicates for the presence of *stx*.

Interfering Substances

Nineteen (19) biological and chemical substances occasionally used or found in stool specimens were evaluated for potential interference with the BD MAX Enteric Bacterial Panel. Included in this study was an Antibiotics Mixture, which consisted of a combination of 8 different antibiotics tested simultaneously, with each antibiotic at a concentration that may be excreted in a stool sample. Vagisil was identified as a potentially interfering substance at a concentration of 9.2% Vagisil in a stool specimen or 0.92 mg/mL in the Sample Buffer Tube. Nystatin cream and spermicidal lubricant both demonstrated potential interference at a concentration of 50% (5.0 mg/mL of interferent in the Sample Buffer Tube). The BD MAX Enteric Bacterial Panel demonstrated acceptable performance with nystatin cream at a concentration of 31% (3.1 mg/mL of nystatin cream in the Sample Buffer Tube) and spermicidal lubricant at 34% (3.4 mg/mL of spermicidal lubricant in the Sample Buffer Tube). Results demonstrated no reportable interference with any other substance tested (refer to Table 16).

Table 16: Endogenous and Commercial Exogenous Substances Tested with the BD MAX Enteric Bacterial Panel

Brand Name or Description	Result	Brand Name or Description	Result
Fecal Fat	NI	Spermicidal Lubricant	P
Human DNA	NI	Diaper Rash Cream	NI
Mucus	NI	Vagisil	I
Whole human blood	NI	Laxatives	NI
Hydrocortisone Cream	NI	Anti-Diarrheal (liquid)	NI
Antiseptic Towelettes	NI	Anti-Diarrheal (pill)	NI
Enema	NI	Antibiotics Mixture	NI
Hemorrhoidal Gel	NI	Antacids	NI
Nystatin Cream	P	Non-Steroidal Anti-Inflammatory (NSAID)	NI
Topical Antibiotic	NI	–	–

I: Interference with the BD MAX Enteric Bacterial Panel.

P: Potential interference with the BD MAX Enteric Bacterial Panel at high concentrations

NI: No reportable interference with the BD MAX Enteric Bacterial Panel.

Mixed Infection/Competitive Interference

The mixed infection/competitive interference study was designed to evaluate the ability of the BD MAX Enteric Bacterial Panel to detect low positive results in the presence of other targets at high concentrations. Four (4) organisms (*Salmonella* Typhimurium, *Campylobacter coli*, *Shigella sonnei* and *Escherichia coli* O157:H7) were individually prepared at 1.5x their respective LoD to serve as a low target in the BD MAX Enteric Bacterial Panel Sample Buffer Tube. A high target mix comprised of the organisms representative of the other three BD MAX Enteric Bacterial Panel analytes was spiked into the Sample Buffer Tube at a concentration of >1 x 10^6 CFU/mL along with 10 µL of unpreserved stool and tested to simulate mixed infections. All four low target organisms were successfully detected by the BD MAX Enteric Bacterial Panel when combined with their respective simulated high target concentration mixed infection preparations.

Precision

Within-laboratory precision was evaluated for the BD MAX Enteric Bacterial Panel at one (1) site. Testing was performed over 12 days, with 2 runs per day (one each by 2 technologists), for a total of 24 runs.

Four specific target organisms, at different concentrations, were used to create the panel members for this study. The panel members contained *Escherichia coli stx* 1, *Salmonella* Typhimurium, *Shigella sonnei* and *Campylobacter coli.*

The following values were used as spike levels and tested in triplicate for the target organisms contained in each panel member:

- Moderate Positive (MP): 3x LoD
- Low Positive (LP): 1.5x LoD
- High Negative (HN): $C_{20\text{-}80}$ LoD
- True Negative (TN): No Target

Each sample contained negative unpreserved stool matrix. True Negative (TN) samples contained no target. High Negative (HN) samples were spiked with target organisms below the analytical LoD of the assay; however, the HN samples were expected to yield a positive result in approximately 20% to 80% of the replicates due to the inherent sensitivity of PCR assays. Results are summarized by target and concentration in Table 17.

Table 17: Precision Study Results Using One Lot of the BD MAX Enteric Bacterial Panel

	Percent Agreement by Analyte				
Category	***E. coli stx*1**	***Salmonella***	***Shigella***	***Campylobacter***	**Expected Values**
TN[a]	100.00%	100.00%	100.00%	100.00%	100.00%
HN[a]	27.78%	25.00%	30.56%	54.17%	20% to 80%
LP	98.61%	100.00%	98.61%	100.00%	≥95.00%
MP	100.00%	100.00%	98.61%	98.61%	100.00%

[a] For the True Negative (TN) and High Negative (HN) categories, the expected assay result was deemed to be negative. Therefore, percent agreement was calculated for negative results.

Reproducibility

For the Site-to-Site reproducibility study, three (3) clinical sites were provided with a total of ten (10) panels, each consisting of 12 tubes. The panels used were the same as described under the Precision heading, above. Each site was asked to perform the study on five (5) distinct days (consecutive or not), wherein each day, two (2) panels were tested, one (1) for each of two (2) technologists.

The overall Site-to-Site Reproducibility percent agreement was 100% for the TN category for all targets, and ranged from 41.1% to 77.8%, 96.7% to 100% and 98.9% to 100% for the HN, LP and MP categories, respectively (refer to Table 18). The qualitative and quantitative reproducibility across sites and by target is presented below in Tables 19 through 26. Ct.Score is an internal criterion used to determine final assay results and was selected as an additional means of assessing assay reproducibility. Overall mean Ct.Score values with variance components (SD and %CV) are shown in Tables 20, 22, 24 and 26.

Table 18: Site-to-Site Reproducibility Study Results Using One Lot of the BD MAX Enteric Bacterial Panel

Category	*Campylobacter* (*coli* and *jejuni*) [n], (95% CI)	*Salmonella* spp. [n], (95% CI)	*Shigella* spp. [n], (95% CI)	Shiga toxins (*stx*1 and *stx*2) [n], (95% CI)
TN[a]	100.0%, [90/90], (95.9%, 100.0%)	100.0%, [90/90], (95.9%, 100.0%)	100.0%, [90/90], (95.9%, 100.0%)	100.0%, [90/90], (95.9%, 100.0%)
HN[a]	77.8%, [70/90], (68.2%, 85.1%)	44.4%, [40/90], (34.6%, 54.7%)	41.1%, [37/90], (31.5%, 51.4%)	50.0%, [45/90], (39.9%, 60.1%)
LP	100.0%, [90/90], (95.9%, 100.0%)	96.7%, [87/90], (90.7%, 98.9%)	97.8%, [88/90], (92.3%, 99.4%)	100.0%, [90/90], (95.9%, 100.0%)
MP	100.0%, [90/90], (95.9%, 100.0%)	98.9%, [89/90], (94.0%, 99.8%)	100.0%, [90/90], (95.9%, 100.0%)	98.9%, [89/90], (94.0%, 99.8%)

[a] For the True Negative (TN) and High Negative (HN) categories, the expected assay result was deemed to be negative. Therefore, percent agreement was calculated for negative results.

Table 19: *Campylobacter* Site-to-Site Qualitative Reproducibility Across Sites With Pooled Days, Runs and Replicates

Category	Concentration	SITE												Total			
		2				3				5							
		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
TN	Blank	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0
HN	5 CFU/mL	22	73.3	8	26.7	24	80.0	6	20.0	24	80.0	6	20.0	70	77.8	20	22.2
LP	≥1 and <2 x LoD	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0
MP	≥2 and ≤5 x LoD	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0

Table 20: *Campylobacter* Site-to-Site Quantitative Reproducibility Across Sites, Days, Runs and Within Run

				Within Run Within Day		Between Run Within Day		Between Day Within Site		Between Site		Total	
Variable	Category	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ct.Score	HN	20	36.2	0.54	1.5%	1.18	3.2%	0.00	0.0%	0.00	0.0%	1.30	3.6%
	LP	90	32.7	0.49	1.5%	0.28	0.9%	0.00	0.0%	0.00	0.0%	0.57	1.7%
	MP	90	32.2	0.60	1.8%	0.14	0.4%	0.00	0.0%	0.00	0.0%	0.61	1.9%

Table 21: *Salmonella* Site-to-Site Qualitative Reproducibility Across Sites With Pooled Days, Runs and Replicates

Category	Concentration	SITE												Total			
		2				3				5							
		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
TN	Blank	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0
HN	75 CFU/mL	10	33.3	20	66.7	16	53.3	14	46.7	14	46.7	16	53.3	40	44.4	50	55.6
LP	≥1 and <2 x LoD	30	100.0	0	0	28	93.3	2	6.7	29	96.7	1	3.3	87	96.7	3	3.3
MP	≥2 and ≤5 x LoD	30	100.0	0	0	30	100.0	0	0	29	96.7	1	3.3	89	98.9	1	1.1

Table 22: *Salmonella* Site-to-Site Quantitative Reproducibility Across Sites, Days, Runs and Within Run

				Within Run Within Day		Between Run Within Day		Between Day Within Site		Between Site		Total	
Variable	Category	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ct.Score	HN	50	36.4	0.92	2.5%	0.00	0.0%	0.00	0.0%	0.43	1.2%	1.01	2.8%
	LP	87	34.6	0.99	2.9%	0.00	0.0%	0.00	0.0%	0.61	1.8%	1.16	3.4%
	MP	89	33.2	0.61	1.9%	0.34	1.0%	0.23	0.7%	0.43	1.3%	0.85	2.6%

Table 23: *Shigella* Site-to-Site Qualitative Reproducibility Across Sites With Pooled Days, Runs and Replicates

Category	Concentration	SITE												Total			
		2				3				5							
		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
TN	Blank	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0
HN	9 CFU/mL	12	40.0	18	60.0	13	43.3	17	56.7	12	40.0	18	60.0	37	41.1	53	58.9
LP	≥1 and <2 x LoD	29	96.7	1	3.3	30	100.0	0	0	29	96.7	1	3.3	88	97.8	2	2.2
MP	≥2 and ≤5 x LoD	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0

Table 24: *Shigella* Site-to-Site Quantitative Reproducibility Across Sites, Days, Runs and Within Run

				Within Run Within Day		Between Run Within Day		Between Day Within Site		Between Site		Total	
Variable	Category	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ct.Score	HN	53	34.8	0.99	2.8%	0.57	1.6%	0.52	1.5%	0.29	0.8%	1.29	3.7%
	LP	88	33.1	0.79	2.4%	0.35	1.1%	0.23	0.7%	0.47	1.4%	1.01	3.1%
	MP	90	32.5	0.80	2.5%	0.39	1.2%	0.00	0.0%	0.50	1.5%	1.03	3.2%

Table 25: Shiga toxin Site-to-Site Qualitative Reproducibility Across Sites With Pooled Days, Runs and Replicates

Category	Concentration	SITE												Total			
		2				3				5							
		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect		Correct		Incorrect	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
TN	Blank	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0
HN	100 CFU/mL	16	53.3	14	46.7	15	50.0	15	50.0	14	46.7	16	53.3	45	50.0	45	50.0
LP	≥1 and <2 x LoD	30	100.0	0	0	30	100.0	0	0	30	100.0	0	0	90	100.0	0	0
MP	≥2 and ≤5 x LoD	30	100.0	0	0	30	100.0	0	0	29	96.7	1	3.3	89	98.9	1	1.1

Table 26: Shiga toxin Site-to-Site Quantitative Reproducibility Across Sites, Days, Runs and Within Run

				Within Run Within Day		Between Run Within Day		Between Day Within Site		Between Site		Total	
Variable	Category	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Ct.Score	HN	45	35.9	1.78	5.0%	0.00	0.0%	0.00	0.0%	1.03	2.9%	2.06	5.7%
	LP	90	31.8	0.65	2.0%	0.00	0.0%	0.00	0.0%	0.36	1.1%	0.74	2.3%
	MP	89	31.3	0.62	2.0%	0.22	0.7%	0.07	0.2%	0.24	0.8%	0.70	2.2%

For the Lot-to-Lot reproducibility study, two users each completed a single run of 12 panel members on a single instrument for each of two lots of reagents over a 5-day period. The panels used were the same as described under the Precision heading, above. Results from 5 days of the accuracy and precision study were used to comprise data for one lot of reagents for the Lot-to-Lot study.

The overall Lot-to-Lot reproducibility percent agreement was 100% for the TN category for all targets, and ranged from 13.33% to 62.22%, 95.56% to 100% and 97.78% to 100% for the HN, LP and MP categories, respectively (refer to Table 27).

Table 27: Lot-to-Lot Reproducibility Study Results Using Three Lots of the BD MAX Enteric Bacterial Panel

Target	Level	Correct	Total	% Correct	95% CI	
					Lower CI	Upper CI
STEC	TN[a]	90	90	100.00%	95.91%	100.00%
	HN[a]	27	90	30.00%	21.51%	40.13%
	LP	89	90	98.89%	93.97%	99.80%
	MP	90	90	100.00%	95.91%	100.00%
Campy	TN	90	90	100.00%	95.91%	100.00%
	HN	56	90	62.22%	51.90%	71.54%
	LP	90	90	100.00%	95.91%	100.00%
	MP	88	90	97.78%	92.26%	99.39%
Shig	TN	90	90	100.00%	95.91%	100.00%
	HN	15	90	16.67%	10.37%	25.69%
	LP	86	90	95.56%	89.12%	98.26%
	MP	89	90	98.89%	93.97%	99.80%
Sal	TN	90	90	100.00%	95.91%	100.00%
	HN	12	90	13.33%	7.79%	21.87%
	LP	89	90	98.89%	93.97%	99.80%
	MP	90	90	100.00%	95.91%	100.00%

[a] For the True Negative (TN) and High Negative (HN) categories, the expected assay result was deemed to be negative. Therefore, percent agreement was calculated for negative results.

Carryover / Cross-Contamination

A study was conducted to investigate within-run carryover and between-run carryover while processing samples with high bacterial loads of *Salmonella enterica*, *Shigella sonnei*, *Campylobacter jejuni* and Shiga toxin-producing *Escherichia coli* in the BD MAX Enteric Bacterial Panel. A panel made of one high positive member containing the four target organisms and one negative member was used to prepare numerous samples. Strains of *Salmonella enterica* (*SpaO*, ATCC 13076), *Shigella sonnei* (*ipaH*, ATCC 10523), *Campylobacter jejuni* (*tuf*, ATCC 29428) and Shiga toxin-producing *Escherichia coli* (*stx*1 and *stx*2, ENF 10513) were used for the high positive panel member (~1 x 10^6 CFU/mL). The negative member did not contain any target analyte. Twelve (12) replicates of the high positive panel member and 12 replicates of the negative panel member were tested in each run by alternating negative and positive samples. One (1) operator performed 16 consecutive runs, with 15 runs containing 24 samples and 1 run containing 4 samples.

Carryover contamination was assessed for each target in the BD MAX Enteric Bacterial Panel. A total of 167 Sample Buffer Tubes, each containing the 4 BD MAX Enteric Bacterial Panel targets, were assessed in the carryover contamination study. Of the 668 readings across all targets, one Sample Buffer Tube was positive for all 4 panel targets.

Expected Values

In the BD MAX Enteric Bacterial Panel clinical study, reportable results from compliant specimens, were obtained from 8 geographically diverse sites and compared to the reference methods. The study population was grouped based on specimen type. The number and percentage of positive cases by target, as determined by the BD MAX Enteric Bacterial Panel during the prospective segment of the clinical trial, are presented below in Table 28.

Table 28: Prevalence Values Observed during the BD MAX Enteric Bacterial Panel Clinical Trial

		Prevalence			
Specimen Type	**Site**	***Salmonella***	***Shigella***	***Campylobacter***	**Shiga toxins**
Cary-Blair Preserved	1	0.0% (0/186)	0.0% (0/186)	1.1% (2/188)	0.0% (0/185)
	2	0.8% (3/377)	0.3% (1/377)	1.6% (6/368)	0.8% (3/391)
	3	0.9% (5/548)	0.2% (1/548)	0.8% (4/528)	0.2% (1/551)
	4	3.9% (6/152)	11.2% (17/152)	2.0% (3/152)	0.0% (0/135)
	5	0.3% (1/339)	0.0% (0/339)	1.5% (5/340)	0.3% (1/320)
	6	1.4% (6/431)	0.0% (0/431)	1.9% (8/431)	0.7% (3/411)
	Total	1.0% (21/2,033)	0.9% (19/2,033)	1.4% (28/2,007)	0.4% (8/1,993)
Unpreserved	1	1.6% (6/376)	0.3% (1/376)	0.8% (3/376)	0.0% (0/176)
	7	1.6% (5/305)	0.0% (0/305)	2.0% (6/304)	0.0% (0/229)
	8	1.4% (4/284)	0.0% (0/284)	1.1% (3/284)	0.4% (1/265)
	4	2.9% (9/314)	6.7% (21/314)	3.5% (11/314)	0.4% (1/266)
	Total	1.9% (24/1,279)	1.7% (22/1,279)	1.8% (23/1,278)	0.2% (2/936)

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Change History

Revision	Date	Change Summary
(04)	2019-11	Converted printed instructions for use to electronic format and added access information to obtain the document from bd.com/e-labeling. Updated pictures in Figures 2 and 3. Removed expired legal disclaimers pertaining to use of the product for amplification and detection of nucleic acid sequences, for diagnostic research purposes, and rights to use the product for certain blood and tissue screening applications.

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Method of sterilization: ethylene oxide / Метод на стерилизация: етиленов оксид / Způsob sterilizace: etylenoxid / Steriliseringsmetode: ethylenoxid / Sterilisationsmethode: Ethylenoxid / Μέθοδος αποστείρωσης: αιθυλενοξείδιο / Método de esterilización: óxido de etileno / Steriliseerimismeetod: etüleenoksiid / Méthode de stérilisation : oxyde d'éthylène / Metoda sterilizacije: etilen oksid / Sterilizálás módszere: etilén-oxid / Metodo di sterilizzazione: ossido di etilene / Стерилизация әдici – этилен тотығы / 소독 방법: 에틸렌옥사이드 / Sterilizavimo būdas: etileno oksidas / Sterilizēšanas metode: etilēnoksīds / Gesteriliseerd met behulp van ethyleenoxide / Steriliseringsmetode: etylenoksid / Metoda sterylizacji: tlenek etylu / Método de esterilização: óxido de etileno / Metodă de sterilizare: oxid de etilenă / Метод стерилизации: этиленоксид / Metóda sterilizácie: etylénoxid / Metoda sterilizacije: etilen oksid / Steriliseringsmetod: etenoxid / Sterilizasyon yöntemi: etilen oksit / Метод стерилізації: етиленоксидом / 灭菌方法：环氧乙烷

Method of sterilization: irradiation / Метод на стерилизация: ирадиация / Způsob sterilizace: záření / Steriliseringsmetode: bestråling / Sterilisationsmethode: Bestrahlung / Μέθοδος αποστείρωσης: ακτινοβολία / Método de esterilización: irradiación / Steriliseerimismeetod: kiirgus / Méthode de stérilisation : irradiation / Metoda sterilizacije: zračenje / Sterilizálás módszere: besugárzás / Metodo di sterilizzazione: irradiazione / Стерилизация әдici – сәуле түсipy / 소독 방법: 방사 / Sterilizavimo būdas: radiacija / Sterilizēšanas metode: apstarošana / Gesteriliseerd met behulp van bestraling / Steriliseringsmetode: bestråling / Metoda sterylizacji: napromienianie / Método de esterilização: irradiação / Metodă de sterilizare: iradiere / Метод стерилизации: облучение / Metóda sterilizácie: ožiarenie / Metoda sterilizacije: ozračavanje / Steriliseringsmetod: strålning / Sterilizasyon yöntemi: irradyasyon / Метод стерилізації: опроміненням / 灭菌方法：辐射

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Upper limit of temperature / Горен лимит на температурата / Horní hranice teploty / Øvre temperaturgrænse / Temperaturobergrenze / Ανώτερο όριο θερμοκρασίας / Límite superior de temperatura / Ülemine temperatuuripiir / Limite supérieure de température / Gornja dozvoljena temperatura / Felső hőmérsékleti határ / Limite superiore di temperatura / Температураның руқсат етілген жоғарғы шеги / 상한 온도 / Aukščiausia laikymo temperatūra / Augšējā temperatūras robeža / Hoogste temperatuurlimiet / Øvre temperaturgrense / Górna granica temperatury / Limite máximo de temperatura / Limită maximă de temperatură / Верхний предел температуры / Horná hranica teploty / Gornja granica temperature / Övre temperaturgräns / Sıcaklık üst sınırı / Максимальна температура / 温度上限

Keep dry / Пазете сухо / Skladujte v suchém prostředí / Opbevares tørt / Trocklagern / Φυλάξτε το στεγνό / Mantener seco / Hoida kuivas / Conserver au sec / Držati na suhom / Száraz helyen tartandó / Tenere all'asciutto / Құрғақ күйінде ұста / 건조 상태 유지 / Laikykite sausai / Uzglabāt sausu / Droog houden / Holdes tørt / Przechowywać w stanie suchym / Manter seco / A se feri de umezeală / Не допускать попадания влаги / Uchovávajte v suchu / Držite na suvom mestu / Förvaras torrt / Kuru bir şekilde muhafaza edin / Берегти від вологи / 请保持干燥

Collection time / Време на събиране / Čas odběru / Opsamlingstidspunkt / Entnahmeuhrzeit / Ώρα συλλογής / Hora de recogida / Kogumisaeg / Heure de prélèvement / Sati prikupljanja / Mintavétel időpontja / Ora di raccolta / Жинау уақыты / 수집 시간 / Paėmimo laikas / Savākšanas laiks / Verzameltijd / Tid prøvetaking / Godzina pobrania / Hora de colheita / Ora colectării / Время сбора / Doba odberu / Vreme prikupljanja / Uppsamlingstid / Toplama zamanı / Час забору / 采集时间

Peel / Обелете / Otevřete zde / Åbn / Abziehen / Αποκολλήστε / Desprender / Koorida / Décoller / Otvoriti skini / Húzza le / Staccare / Ұстіңгі қабатын алып таста / 벗기기 / Plėšti čia / Atlīmēt / Schillen / Trekk av / Oderwać / Destacar / Se dezlipeşte / Отклеить / Odtrhnite / Oljuštiti / Dra isär / Ayırma / Відклеїти / 撕下

Perforation / Перфорация / Perforace / Perforering / Διάτρηση / Perforación / Perforatsioon / Perforacija / Perforálás / Perforazione / Тесік тесу / 절취선 / Perforacija / Perforācija / Perforatie / Perforacja / Perfuração / Perforare / Перфорация / Perforácia / Perforasyon / Перфорація / 穿孔

Do not use if package damaged / Не използвайте, ако опаковката е повредена / Nepoužívejte, je-li obal poškozený / Må ikke anvendes hvis emballagen er beskadiget / Inhal beschädigter Packungnicht verwenden / Μη χρησιμοποιείτε εάν η συσκευασία έχει υποστεί ζημιά. / No usar si el paquete está dañado / Mitte kasutada, kui pakend on kahjustatud / Ne pas l'utiliser si l'emballage est endommagé / Ne koristiti ako je oštećeno pakiranje / Ne használja, ha a csomagolás sérült / Non usare se la confezione è danneggiata / Егер пакет бұзылған болса, пайдаланба / 패키지가 손상된 경우 사용 금지 / Jei pakuotė pažeista, nenaudoti / Nelietot, ja iepakojums bojāts / Niet gebruiken indien de verpakking beschadigd is / Må ikke brukes hvis pakke er skadet / Nie używać, jeśli opakowanie jest uszkodzone / Não usar se a embalagem estiver danificada / A nu se folosi dacă pachetul este deteriorat / Не использовать при повреждении упаковки / Nepoužívajte, ak je obal poškodený / Ne koristite ako je pakovanje oštećeno / Använd ej om förpackningen är skadad / Ambalaj hasar görmüşse kullanmayın / Не використовувати за пошкодженої упаковки / 如果包装破损，请勿使用

Keep away from heat / Пазете от топлина / Nevystavujte přílišnému teplu / Må ikke udsættes for varme / Vor Wärme schützen / Κρατήστε το μακριά από τη θερμότητα / Mantener alejado de fuentes de calor / Hoida eemal valgusest / Protéger de la chaleur / Držati dalje od izvora topline / Óvja a melegtől / Tenere lontano dal calore / Салқын жерде сақта / 열을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no karstuma / Beschermen tegen warmte / Må ikke utsettes for varme / Przechowywać z dala od źródeł ciepła / Manter ao abrigo do calor / A se feri de căldură / Не нагревать / Uchovávajte mimo zdroja tepla / Držite dalje od toplote / Får ej utsättas för värme / Isıdan uzak tutun / Берегти від дії тепла / 请远离热源

Cut / Срежете / Odstřihněte / Klip / Schneiden / Κόψτε / Cortar / Lõigata / Découper / Reži / Vágja ki / Tagliare / Кесіңіз / 잘라내기 / Kirpti / Nogriezt / Knippen / Kutt / Odciąć / Cortar / Decupaţi / Отрезать / Odstrihnite / Iseći / Klipp / Kesme / Розрізати / 剪下

Collection date / Дата на събиране / Datum odběru / Opsamlingsdato / Entnahmedatum / Ημερομηνία συλλογής / Fecha de recogida / Kogumiskuupäev / Date de prélèvement / Dani prikupljanja / Mintavétel dátuma / Data di raccolta / Жинаған тізбекүні / 수집 날짜 / Paėmimo data / Savākšanas datums / Verzameldatum / Dato prøvetaking / Data pobrania / Data de colheita / Data colectării / Дата сбора / Dátum odberu / Datum prikupljanja / Uppsamlingsdatum / Toplama tarihi / Дата забору / 采集日期

µL/test / µL/тест / µL/Test / µL/εξέταση / µL/prueba / µL/teszt / µL/테스트 / мкл/тест / µL/tyrimas / µL/pārbaude / µL/teste / мкл/аналіз / µL/检测

Keep away from light / Пазете от светлина / Nevystavujte světlu / Må ikke udsættes for lys / Vor Licht schützen / Κρατήστε το μακριά από το φως / Mantener alejado de la luz / Hoida eemal valgusest / Conserver à l'abri de la lumière / Držati dalje od svjetla / Fény nem érheti / Tenere al riparo dalla luce / Қараңғыланған жерде ұста / 빛을 피해야 함 / Laikyti atokiau nuo šilumos šaltinių / Sargāt no gaismas / Niet blootstellen aan zonlicht / Må ikke utsettes for lys / Przechowywać z dala od źródeł światła / Manter ao abrigo da luz / Feriţi de lumină / Хранить в темноте / Uchovávajte mimo dosahu svetla / Držite dalje od svetlosti / Får ej utsättas för ljus / Işıktan uzak tutun / Берегти від дії світла / 请远离光线

Hydrogen gas generated / Образуван е водород газ / Možnost úniku plynného vodíku / Frembringer hydrogengas / Wasserstoffgas erzeugt / Δημιουργία αερίου υδρογόνου / Producción de gas de hidrógeno / Vesinikgaasi tekitatud / Produit de l'hydrogène gazeux / Sadrži hydrogen vodik / Hidrogén gázt fejleszt / Produzione di gas idrogeno / Газтектес сутеri пайда болды / 수소 가스 생성됨 / Išskiria vandenilio dujas / Rodas ūdeņradis / Waterstofgas gegenereerd / Hydrogengass generert / Powoduje powstawanie wodoru / Produção de gás de hidrogénio / Generare gaz de hidrogen / Выделение водорода / Vyrobené použitím vodíka / Oslobađa se vodonik / Genererad vätgas / Açığa çıkan hidrojen gazı / Реакція з виділенням водню / 会产生氢气

Patient ID number / ИД номер на пациента / ID pacienta / Patientens ID-nummer / Patienten-ID / Αριθμός αναγνώρισης ασθενούς / Número de ID del paciente / Patsiendi ID / No d'identification du patient / Identifikacijski broj pacijenta / Beteg azonosító száma / Numero ID paziente / Пациенттің идентификациялық нөмірі / 환자 ID 번호 / Paciento identifikavimo numeris / Pacienta ID numurs / Identificatienummer van de patiënt / Pasientens ID-nummer / Numer ID pacjenta / Número da ID do doente / Număr ID pacient / Идентификационный номер пациента / Identifikačné číslo pacienta / ID broj pacijenta / Patientnummer / Hasta kimlik numarası / Ідентифікатор пацієнта / 患者标识号

Fragile, Handle with Care / Чупливо, Работете с необходимото внимание. / Křehké. Při manipulaci postupujte opatrně. / Forsigtig, kan gå i stykker. / Zerbrechlich, vorsichtig handhaben. / Εύθραυστο. Χειριστείτε το με προσοχή. / Frágil. Manipular con cuidado. / Õrn, käsitsege ettevaatlikult. / Fragile. Manipuler avec précaution. / Lomljivo, rukujte pažljivo. / Törékeny! Óvatosan kezelendő. / Fragile, maneggiare con cura. / Сынғыш, абайлап пайдаланыңыз. / 조심 깨지기 쉬운 처리 / Trapu, elkitės atsargiai. / Trausls; rīkoties uzmanīgi / Breekbaar, voorzichtig behandelen. / Ømtålig, håndter forsiktig. / Krucha zawartość, przenosić ostrożnie. / Frágil, Manuseie com Cuidado. / Fragil, manipulaţi cu atenţie. / Хрупкое! Обращаться с осторожностью. / Krehké, vyžaduje sa opatrná manipulácia. / Lomljivo - rukujte pažljivo. / Bräckligt. Hantera försiktigt. / Kolay Kırılır, Dikkatli Taşıyın. / Тендітна, звертатися з обережністю / 易碎，小心轻放

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