Revisions

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NOTES:

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6. Printed two sides: Yes [X] No [ ]
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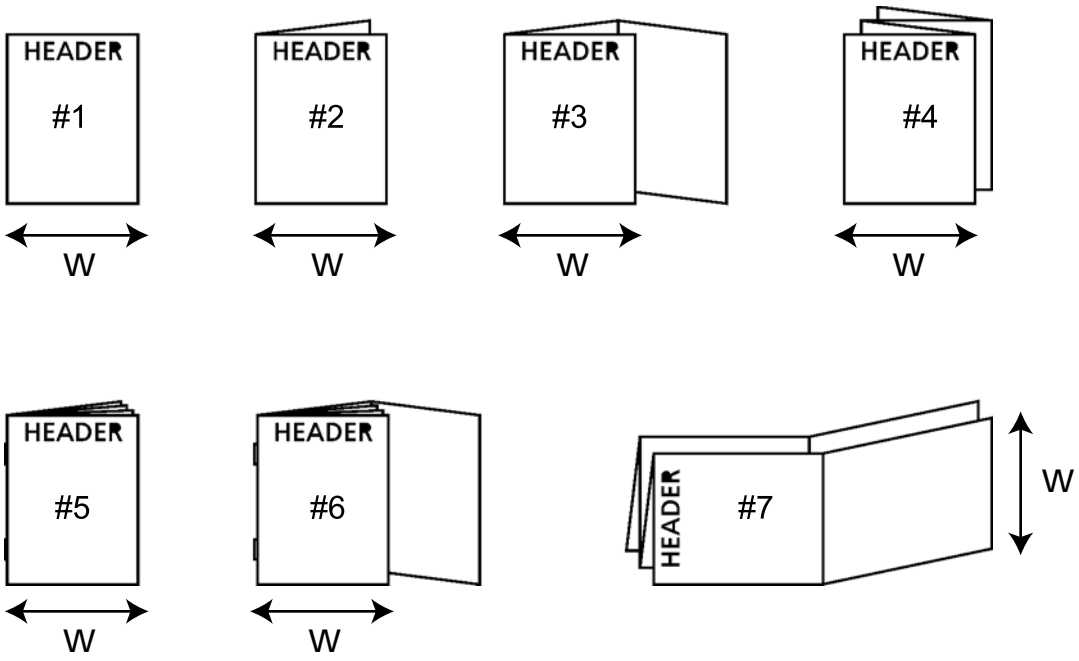


8. See Specification Control Number N/A for Material Information.
9. Graphics are approved by Becton, Dickinson and Company. Supplier has the responsibility for using the most current approved revision level.

Label Design	Date		BD Becton, Dickinson and Company 7 Loveton Circle Sparks, MD 21152 USA	
Proofer	Date			
Checked By	Date	Category and Description: Package Insert, BD MAX GBS	Sheet: 1 of 21	A
Part Number: P0091			Scale: N/A	

BD MAX™ GBS

REF 441772

P0091(06)

2014-01

For In Vitro Diagnostic Use

For use with the BD MAX™ System

CE IVD

INTENDED USE

The BD MAX™ GBS assay as implemented on the BD MAX™ System is a qualitative *in vitro* diagnostic test designed to detect Group B *Streptococcus* (GBS) DNA in Lim Broth cultures, after incubation for greater than or equal to (≥)18 hours, obtained from vaginal-rectal swab specimens from antepartum pregnant women. The test incorporates automated DNA extraction to isolate the target nucleic acid from the specimen and real-time polymerase chain reaction (PCR) to detect a 124 bp region of the *cfb* gene sequence of the *Streptococcus agalactiae* chromosome. Results from the BD MAX GBS assay can be used as an aid in determining colonization status in antepartum women.

The BD MAX GBS assay does not provide susceptibility results. Cultured isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women. Subculture to solid media for additional testing when indicated.

SUMMARY AND EXPLANATION OF THE PROCEDURE

A vaginal-rectal swab is collected and transported to the laboratory using standard bacterial swab transport systems containing a non-nutritive transport medium (e.g. Amies or Stuart). In the lab, the swab is removed from the transport medium and placed into selective Lim Broth [Todd-Hewitt Broth supplemented with colistin (10 µg/mL) and nalidixic acid (15 µg/mL)]. After incubation of inoculated Lim Broth culture for ≥18 hours at 37 °C in ambient air or 5% CO_2, a 15 µL aliquot of the broth is mixed with BD MAX GBS Sample Preparation Reagent and processed on the BD MAX System using the BD MAX GBS assay. The BD MAX System automatically extracts the target nucleic acid and amplifies a section of the *cfb* gene sequence of the GBS chromosome, if present. The BD MAX GBS assay includes an Internal Process Control to monitor for the presence of potential inhibitory substances as well as system or reagent failures that may be encountered during the entire process.

Group B *Streptococcus* (GBS) is a Gram positive bacterium that causes invasive disease primarily in infants, pregnant or postpartum women, and older adults, with the highest incidence among young infants. GBS is the leading infectious cause of morbidity and mortality among infants in the United States. As a result of prevention efforts, incidence of GBS has declined dramatically over the past 15 years, from 1.7 cases per 1,000 live births in the early 1990s to 0.34 – 0.37 cases per 1,000 live births in recent years. CDC estimates that in recent years, GBS has caused approximately 1,200 cases of early-onset invasive disease per year; approximately 70% of cases are among babies born at term (≥ 37 weeks' gestation).[1]

Early-onset infections are acquired vertically through exposure to GBS from the vagina of a colonized woman. Neonatal infection occurs primarily when GBS ascends from the vagina to the amniotic fluid after onset of labor or rupture of membranes, although GBS also can invade through intact membranes. Infants with early-onset GBS disease generally present with respiratory distress, apnea, or other signs of sepsis within the first 24 – 48 hours of life. The most common clinical syndromes of early -onset disease are sepsis and pneumonia; less frequently, early-onset infections can lead to meningitis. Mortality is higher among preterm infants, with case-fatality rates of approximately 20% and as high as 30% among those ≤33 weeks' gestation, compared with 2% – 3% among full-term infants.[1]

The current standard of care for preventing neonatal GBS disease is screening pregnant women at 35-37 weeks of gestation to determine their GBS colonization status. Most GBS testing is performed by culture and can take up to 48 hours for definitive identification of GBS following the initial ≥18 hour incubation of vaginal-rectal swabs in a selective broth medium. The BD MAX GBS assay, as implemented on the BD MAX System, can provide results from up to 24 specimens in approximately two and a half hours after the initial ≥18 hour incubation/enrichment step. The BD MAX GBS assay streamlines and simplifies the testing process by eliminating the need for operator intervention from the time the sample is placed onto the BD MAX System until results are available.

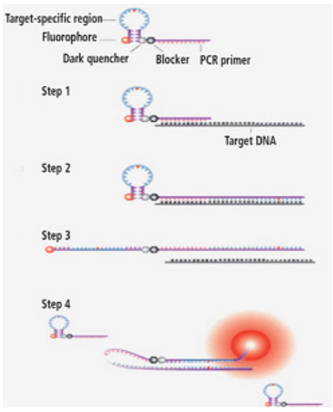
PRINCIPLES OF THE PROCEDURE

Vaginal-rectal swabs are inoculated into Lim Broth. Following incubation for ≥18 hours at 37 °C in ambient air or 5% CO_2, a 15 µL aliquot of Lim Broth is used for detecting the presence of GBS. The aliquot of broth is added to BD MAX™ GBS Sample Preparation Reagent and processed using the BD MAX System. The BD MAX System automates and integrates DNA extraction and concentration, reagent preparation, and nucleic acid amplification and detection of the target sequence using real-time PCR. An Internal Process Control is also incorporated into the lysis, extraction, concentration and amplification steps to monitor for the presence of potential inhibitory substances as well as system or reagent failures.

The BD MAX System uses a combination of lytic and extraction reagents to perform cell lysis, DNA extraction and removal of inhibitors. Following cell lysis, with a combination of heat and lytic enzymes, the released nucleic acids are captured by magnetic affinity beads. The beads, with the bound nucleic acids, are washed and the nucleic acids are eluted using release solution and prepared for PCR by addition of neutralization reagent. The BD MAX System then uses the PCR-ready DNA solution to rehydrate a freeze-dried PCR pellet containing all the reagents necessary for amplification of the GBS-specific target. The freeze-dried PCR pellet also contains reagents to amplify a section of the Internal Process Control sequence to enable simultaneous amplification and detection of both target and Internal Process Control DNA sequences. After reconstitution of the freeze-dried amplification reagents, the BD MAX System dispenses the prepared PCR-ready solution into one lane (per specimen) of the BD MAX™ Microfluidic Cartridge. Microvalves in the BD MAX Microfluidic Cartridge are sealed by the system prior to initiating PCR to prevent evaporation as well as amplicon contamination.

The amplified targets are detected in real time using Scorpions® chemistry-based fluorogenic oligonucleotide probe molecules specific to the amplicons for the respective targets. Scorpions chemistry features a bi-functional molecule which includes a PCR primer covalently attached to a probe. The Scorpions primers used in the BD MAX GBS assay have a fluorophore and quencher held together by an internal stem loop. Figure 1 is a diagrammatic representation of Scorpions functionality. In Steps 1 and 2, the Scorpions primer is extended on the target DNA. In Step 3, the extended primer is heat-denatured, along with the stem loop of the probe, thereby causing the quencher and the fluorophore to disassociate. In Step 4, the extended Scorpions primer is rearranged and binds to the newly extended DNA strand as it cools and begins to fluoresce in a target-specific manner, while the un-extended primer is quenched. The difference between Scorpions chemistry and other detection systems is that the probe and primer are on the same molecule so that signal generation is through a uni-molecular rearrangement, as opposed to a bimolecular collision. This results in extremely rapid signal generation kinetics for Scorpions reactions.

Figure 1: Mechanism of action of Scorpions® chemistry



A Scorpions probe labeled with a fluorophore (Excitation: 490 nanometers and Emission: 521 nanometers) at the 5' end, and a dark quencher at the 3' end, is used to detect GBS DNA. For detection of the Internal Process Control, the Scorpions probe is labeled with an alternate fluorescent dye (Excitation: 590 nanometers and Emission: 610 nanometers) at the 5' end, and a dark quencher at the 3' end. The BD MAX System monitors the fluorescent signal emitted by the Scorpions probes at the end of each amplification cycle. When amplification is complete, the BD MAX System analyzes the data and provides a final result (POSITIVE/NEGATIVE/ INDETERMINATE).

REAGENTS

EQUIPMENT AND MATERIALS REQUIRED BUT NOT PROVIDED

1. BD MAX System
   1st Generation (2 channel) – REF 441769 or REF 441856
   or
   2nd Generation (6 channel) – REF 441916 or REF 441917
2. BD MAX Microfluidic Cartridges REF 441770 (12 Lane) or REF 437519 (24 Lane) for 1st Generation BD MAX (2 channel) or 2nd Generation BD MAX (6 channel) Systems, respectively
3. Vortex Genie 2 (Fisher) or equivalent
4. Micropipettor (recommend P100, accurate between 10-100 µL)
5. Aerosol resistant extended length micropipette tips
6. Lab coat and disposable gloves
7. BBL™ Lim Broth REF 292209 or REF 296266
8. Swabs compatible with vaginal-rectal specimen collection and recommended transport media (e.g. Amies or Stuart)

REF	Contents	Quantity
441772	**BD MAX™ GBS Master Mix (GB)** *Freeze-dried PCR Master Mix containing GBS-specific Scorpions® probe and primers along with Internal Process Control-specific Scorpions probe and primers.*	24 tests (2 x 12 tubes)
	BD MAX™ DNA Unitized Reagent Strips *Unitized reagent strip containing all the liquid reagents and disposable pipette tips necessary for DNA Extraction.*	24 strips
	BD MAX™ GBS Extraction Reagent (E3) *Freeze-dried DNA magnetic affinity beads* *Freeze-dried Mutanolysin* *Freeze-dried Protease reagents* *Freeze-dried Internal Process Control*	24 tests (2 x 12 tubes)
	BD MAX™ GBS Sample Preparation Reagent	24 tests (2 x 12 tubes)

WARNINGS AND PRECAUTIONS

- This test is for *in vitro* diagnostic use only.
- Do not use the kit if the packaging is damaged upon arrival.
- Do not use the kit after the expiration date.
- Do not use reagents if the protective pouch is open or broken upon arrival.
- Protect reagents against heat and humidity. Prolonged exposure to humidity will affect product performance.
- Avoid microbial and deoxyribonuclease (DNase) contamination of reagents at all times. The use of sterile DNase-free disposable filter-blocked or positive displacement pipette tips is recommended. Use a new tip for each specimen.
- Good molecular laboratory technique should be used to avoid contaminating the workspace or environment.
- To avoid contamination of the environment with GBS amplicons, do not break apart the BD MAX Microfluidic Cartridges post-amplification. The seals of the BD MAX Microfluidic Cartridges prevent contamination.
- In cases where open-tube PCR tests are also conducted in the laboratory, care must be taken to ensure that the BD MAX GBS assay, the additional reagents required for testing, and the BD MAX System are not contaminated.
- To minimize risk of contamination, only one Lim Broth specimen and one sample preparation tube should be open at one time.
- Performing the BD MAX GBS assay outside the time ranges recommended for specimen storage can produce invalid results.
- Good laboratory practices and changing gloves between handling patient specimens are recommended to avoid contamination of specimens.
- Always handle specimens as if they are infectious and in accordance with safe laboratory procedures such as those described in Biosafety in Microbiological and Biomedical Laboratories[2] and in CLSI Document M29-A[3].
- 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, or eat in areas where specimens or kit reagents are being handled.
- Dispose of unused reagents and waste in accordance with country, federal, provincial, state and local regulations.
- The BD MAX Microfluidic Cartridges REF 441770 (12 Lane) for 1st Generation BD MAX (2 channel) Systems are not re-usable and should be discarded properly after each run whether empty lanes remain or not.

- The BD MAX Microfluidic Cartridges REF 437519 (24 Lane) for 2nd Generation BD MAX (6 channel) Systems may be used for up to two (2) runs. After two runs, the cartridge should be properly discarded whether empty lanes remain or not.
- Consult the BD MAX System User's Manual for additional warnings, precautions and procedures.

STORAGE AND STABILITY

- Collected specimens should be kept between 2-30 °C during transport.
- Enriched Lim Broth specimens should be stored at 2-8 °C for no longer than 7 days before testing.
- Enriched Lim Broth specimens mixed with the BD MAX GBS Sample Preparation Reagent should be used within 4 hours of preparation.
- BD MAX GBS assay Kits are stable at 2-25 °C through the stated expiration date. Do not use kits or kit components that have passed their stated expiration date(s).
- BD MAX™ GBS Master Mix (GB) and Extraction Reagents (E3) are provided in a nitrogen-sealed pouch. To protect product from humidity, immediately re-seal after opening. Pouch contents are stable for up to 7 days after initial opening and re-sealing.

INSTRUCTIONS FOR USE - Specimen Collection/Transport/Incubation

1. Collect the vaginal-rectal swab specimen using the CDC recommended clinical procedure.[1] Transport the specimen to the laboratory in a non-nutritive transport medium (e.g. Amies or Stuart).
2. If vaginal-rectal swabs are collected separately from the same patient, both swabs can be placed in the same transport container.
3. Label specimens clearly for GBS testing.
4. Remove swab(s) from transport medium and inoculate swabs into selective Lim Broth [Todd Hewitt Broth supplemented with colistin (10µg/mL) and nalidixic acid (15 µg/mL)].
5. Incubate inoculated Lim Broth for ≥18 hours at 37 °C in ambient air or 5% CO_2.
6. Proceed to Test Preparation.

Test Preparation

1. Vortex the enriched Lim Broth specimen to achieve uniform distribution.
2. Using a calibrated P100 micropipettor and an extended length pipette tip (so as to not contaminate the micropipettor with the enriched specimen) aspirate 15 µL of the enriched specimen into the pipette tip.
3. Remove the cap on a BD MAX GBS Sample Preparation Reagent tube and dispense the 15 µL of enriched specimen into the tube, taking care not to aerosolize the specimen. Pipette liquid up and down to ensure complete transfer of specimen.

BD MAX Operation
(Refer to BD MAX System User's Manual for programming and setup instructions)

1. For each specimen to be tested, place one (1) DNA Unitized Reagent Strip on the BD MAX System Rack.
2. Snap the BD MAX GBS Extraction Reagent tube (E3) into the DNA Unitized Reagent Strip in Position 1 as shown in Figure 2.
3. Snap the BD MAX GBS Master Mix tube (GB) into the DNA Unitized Reagent Strip in Position 2 as shown in Figure 2.
4. Select the 'Work List' tab in the 'Run' screen on the BD MAX System monitor.
5. Enter the specimen/patient identification number into the BD MAX System, using either the barcode scanner or manual entry. Start with Position 1 of Rack A (Rack A is positioned on the left side of the BD MAX System and Rack B is on the right, Figure 3).

6. Enter the barcode from each BD MAX GBS Sample Preparation Reagent tube using the barcode scanner or manual entry. Start with Position 1 of Rack A and ensure that each patient/specimen ID and each BD MAX GBS Sample Preparation Reagent tube is accurately matched.
7. Place the BD MAX GBS Sample Preparation Reagent tube (containing the specimen) on the BD MAX System Rack according to the Work List location ensuring that no positions are skipped.

   Note: Place the tubes into the sample rack with 1D barcode labels facing outward (this makes scanning tubes easier during sample login)
8. Repeat Steps (1-7) for all specimens.
9. Define the test to be run by choosing 'BD MAX GBS' from the pull down menu under the 'Test' tab in the Work List creation window on the BD MAX System monitor.
10. Select 'Swab' as Specimen Type.
11. Place appropriate number (1 or 2) of BD MAX Microfluidic Cartridge(s) into the BD MAX System.
12. Load Rack(s) into the BD MAX System (Figure 3). Ensure that the placement of Rack(s) corresponds to the Work List definition.
13. Close the BD MAX System lid and start processing the test run.

Figure 2: DNA Unitized Reagent Strips

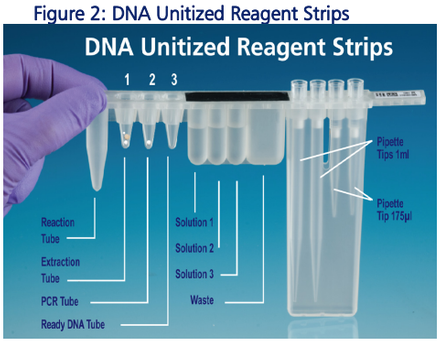


Figure 3: BD Max System

QUALITY CONTROL

Quality control procedures monitor the accuracy and precision of the analytical process. Laboratories must establish the number, type, and frequency of testing control materials according to guidelines or requirements of country, provincial, state and local regulations or accreditation organizations.

1. External control materials are not provided by BD. Commercially available control material may be used or a ≥18 hour GBS culture in Lim Broth may be utilized as positive control material. GBS (*Streptococcus agalactiae* ATCC® BAA-22) is a recommended strain to use as a control. An uninoculated GBS Sample Preparation Reagent tube or a 15 µL aliquot of pure Lim Broth is recommended for use as an external negative control.
2. An Internal Process Control is provided in each BD MAX GBS assay. This Internal Process Control monitors the efficacy of the DNA extraction and PCR amplification processes.
3. One (1) external positive control and one (1) external negative control should be run daily until adequate process validation is achieved on the BD MAX System. Reduced frequency of control testing should be based on adequate data and determined by the individual laboratory.
4. An external negative control that yields a positive test result is indicative of a specimen handling and/or a contamination problem. Review the specimen handling technique to avoid mix-up and/or contamination.
5. An external positive control that yields a negative or indeterminate test result is indicative of a reagent failure or BD MAX System error. Repeat with additional controls. Check the BD MAX System monitor for any error messages. If the problem persists, use unopened reagents or a new BD MAX GBS assay Kit.

RESULTS INTERPRETATION

Results are available on the 'Results' tab in the 'Results' window on the BD MAX System monitor. Test results are automatically interpreted by the BD MAX System software. A test result may be called as NEG (negative), POS (positive), or IND (Indeterminate) based on the amplification status of the target and Internal Process Control. Results are interpreted based on the following decision algorithm (Table 1). If the patient has signs or symptoms of infection, other laboratory tests and clinical information should be used to confirm a negative result.

Table 1: BD MAX GBS assay Decision Algorithm

Test Result		Amplification Status	
		GBS	IPC*
Positive	IF	0 < Ct ≤ 37	N/A
Negative	IF	Ct# = -1 OR Ct > 37	0 < Ct < 36
Indeterminate		All other cases	All other cases

*Internal Process Control; #Cycle Threshold

Indeterminate Results Procedure

In case of an IND (Indeterminate) result, a retest is required. IND results occur due to inhibition of the PCR reaction, reagent failure or system errors. Be sure to check the BD MAX System for error messages. If IND results persist, use unopened reagents or a new BD MAX GBS assay Kit. If all of these attempts do not resolve the problem, contact BD Technical Service.

LIMITATIONS OF THE PROCEDURE

1. The BD MAX GBS assay can only be used on the BD MAX System by trained personnel.
2. Performance of the BD MAX GBS assay was established with vaginal- rectal specimens collected from antepartum women using swabs in non-nutritive transport medium (e.g. Amies or Stuart) and enriched in Lim Broth. Use of the BD MAX GBS assay for clinical specimen types other than those specified has not been evaluated and performance characteristics are not established.
3. The BD MAX GBS assay has been validated with Lim Broth media only. Performance of the BD MAX GBS assay with other types of selective broth media has not been evaluated.
4. The BD MAX GBS assay has been validated with Lim Broth cultures obtained from vaginal-rectal swab specimens incubated for ≥18 hours. Performance of the BD MAX GBS assay with Lim Broth cultures incubated for less than 18 hours has not been evaluated.
5. 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.
6. The presence of feces and body powder can potentially inhibit the detection of GBS at low concentration levels (300 CFU/mL of Sample Preparation Reagent). No interference by these substances was observed at moderate GBS concentration levels (3000 CFU/mL of Sample Preparation Reagent).
7. The presence of *Corynebacterium xerosis, Serratia marcescens* and EBV can potentially inhibit the detection of GBS at low concentration levels (300 CFU/mL of Sample Preparation Reagent) when running the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) system.
8. The presence of *Enterobacter cloacae* can potentially inhibit the detection of GBS at low concentration levels (300 CFU/mL of Sample Preparation Reagent) when running the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) system.

9. False negative results will likely occur if specimen was not added to the BD MAX GBS Sample Preparation Reagent tube.
10. If the BD MAX GBS assay result is IND then the test should be repeated.
11. A positive test result does not necessarily indicate the presence of viable organisms. It is, however, presumptive for the presence of Group B *Streptococcus* DNA.
12. While there are no known strains/isolates of GBS lacking the *cfb* gene, the occurrence of such a strain could lead to an erroneous result using the BD MAX GBS assay.
13. If *Moraxella osloensis* is present in the specimen, there exists a potential for a false positive result because this organism cross reacted in four (4) of nine (9) replicates when running the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) system.
14. The potential for a false positive result exists in the presence of *Aerococcus viridans, Enterococcus durans, Pseudomonas aeruginosa, Providencia stuartii* and *Proteus vulgaris*. Cross-reactivity was observed with each of these organisms when running the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) system: *A. viridans* (1 of 20 replicates), *E. durans* (1/20), *P. aeruginosa* (1/20), *P. stuartii* (2/20) and *P. vulgaris* (4/20).
15. Mutations in primer/probe binding regions may affect detection using the BD MAX GBS assay.
16. Results from the BD MAX GBS assay should be used as an adjunct to clinical observations and other information available to the physician.
17. A negative result does not rule out the possibility of GBS colonization. False negative results may occur when the GBS concentration in the specimen is below the LoD of 200 CFU/mL of Sample Preparation Reagent. If the patient has signs or symptoms of infection, other laboratory tests and clinical information should be used to confirm the negative result.
18. The test is not intended to differentiate carriers of Group B *Streptococcus* from those with streptococcal disease.
19. Test results may be affected by concurrent antimicrobial therapy as GBS DNA may continue to be detected.

EXPECTED VALUES

Approximately 25–40% of healthy women are colonized with GBS. Culture screening of both the vagina and rectum for GBS late in gestation, during prenatal care, can detect women who are likely to be colonized with GBS at the time of delivery. In the investigational study for the BD MAX GBS assay, the overall GBS prevalence rate as determined by culture was 23.0% (143/623) with a 95% CI of 19.7 – 26.5%. Prevalence is based on all compliant reference culture results.

PERFORMANCE CHARACTERISTICS

Clinical Performance [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

Performance characteristics of the BD MAX GBS assay were determined in a 3-site prospective investigational study. Specimens were collected by health care providers using the procedure recommended by the Centers for Disease Control and Prevention as follows: "Swab the lower vagina (vaginal introitus), followed by the rectum (i.e., insert swab through the anal sphincter) using the same swab or two different swabs." Swabs were sent for culture-based analysis to be performed by laboratories at three separate metropolitan locations in the U.S. Following incubation of the vaginal-rectal swab specimens for ≥18 hours in selective Lim Broth medium, a 15 µL aliquot of this enriched broth was tested using the BD MAX GBS assay to ascertain the clinical sensitivity and specificity of the BD MAX GBS assay as compared to the reference culture method based on CDC recommendations.[1]

The vaginal-rectal swab specimens were inoculated in Lim Broth and incubated ≥18 hours. The Lim Broth specimens were then subcultured to a sheep blood agar plate and incubated up to 48 hours. Colonies suggestive of GBS were then Gram stained and tested for catalase production. Gram positive/catalase negative colonies were then specifically identified by the appropriate confirmatory method. Beta hemolytic GBS colonies were confirmed using a latex agglutination test method and gamma hemolytic GBS colonies were confirmed by performing a CAMP reaction. Of the 631 clinical specimens enrolled in the study, 601 were compliant and included in the statistical analyses (Tables 2 and 3).

Table 2: Clinical performance statistics using the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System

All Sites		REFERENCE (CULTURE)		
		Positive	Negative	Total
BD MAX GBS assay	Positive	133	15	148
	Negative	7	446	453
	Total	140	461	601

Table 3: Summary of Clinical performance statistics using the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System

SITE	SENSITIVITY	SPECIFICITY	PREVALENCE [1]
1	97.4% (37/38)	96.6% (141/146)	20.0% (39/195)
2	92.0% (46/50)	95.9% (142/148)	25.1% (50/199)
3	96.2% (50/52)	97.6% (163/167)	23.6% (54/229)
Total (95 % CI)	95.0% (133/140)	96.7% (446/461)	23.0% (143/623)
	CI (90.0 – 98.0%)	CI (94.7 – 98.2%)	CI (19.7 – 26.5%)

[1]Prevalence is based on all specimens with compliant culture reference method results.

Analytical Sensitivity [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

The Limit of Detection (LoD) of the BD MAX GBS assay is 200 CFU/mL Sample Preparation Reagent ($2x10^4$ CFU/mL enriched Lim Broth).* Both pooled and individual clinical negative specimens spiked with GBS culture were used in the determination of LoD.

*15 µL of Lim Broth at 2 x 10^4 CFU/mL added to 1.5mL of Sample Preparation Reagent = 300 CFU/1.5mL Sample Preparation Reagent.

Final concentration of GBS per 1mL of Sample Preparation Reagent = 200 CFU/mL Sample Preparation Reagent.

Table 4: Summary of Analytical Sensitivity

CFU/mL Sample Preparation Reagent	No. of Valid Tests (No IND)	No. of Positive	No. of Negative	No. IND (No Result)	Hit Rate
BD MAX GBS assay with pooled clinical negative specimens					
200	20	20	0	2	100%
150	22	22	0	0	100%
100	21	11	10	1	52%
75	21	14	7	1	67%
50	22	8	14	0	36%
BD MAX GBS assay with individual clinical negative specimens					
300	20	19	1	2	95%
200	22	22	0	0	100%
100	22	20	2	0	91%

Microbial Variants [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

The ability of the BD MAX GBS assay to detect multiple GBS serotypes was demonstrated using 12 different strains of GBS bacteria listed in Table 5. The BD MAX GBS assay was able to detect all major serotypes of GBS at 300 CFU/mL Sample Preparation Reagent ($3x10^4$ CFU/mL incubated Lim Broth culture)

Table 5: List of GBS variants tested

GBS Serotype	Source
Ia	ATCC[1] 12400
Ib	NCS[2], blood
Ic	ATCC 27591
II	ATCC 12973
III	ATCC BAA-22
III	ATCC 12403
IV	ATCC 49446
V	ATCC BAA-611
VI	NCS, Placenta
VII	NCS, blood
VIII	Clinical Isolate, confirmed by serotype-specific Latex Agglutination
ND	ATCC 13813

[1] ATCC: American Type Culture Collection, Manassas, VA, USA
[2] NCS: National Centre for Streptococcus, Edmonton, Alberta, Canada

Analytical Specificity [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

The BD MAX GBS assay was performed on samples containing high levels of non-target organisms, using the BD MAX System, to demonstrate the specificity of the assay for detection of Group B *Streptococcus*. A total of 127 organisms were tested (119 viable organisms and 8 genomic DNA), including 11 organisms phylogenetically similar to Group B *Streptococcus* and

a wide variety of other organisms including viruses, fungi and parasites that are known to infect the urogenital tract or are part of urogenital microflora. The following concentrations of non-target organisms were tested: bacterial and fungal organisms at ~10^6 CFU/mL sample preparation reagent, viral organisms at > $2x10^{2.5}$ $TCID_{50}$/mL of Sample Preparation Reagent, and DNA stocks at ~3ng/mL of Sample Preparation Reagent. Specificity was also tested using 1.55 x 10^3 ng of human DNA per mL of sample preparation reagent. The Internal Process Control was detected in all specimens. None of the 11 phylogenetically related streptococcal isolates tested positive with the BD MAX GBS assay. Of the remaining strains tested, only one (*Moraxella osloensis*) was positive in four of nine replicates. Table 6 lists the Non-Target Organisms tested in the Analytical Specificity and Interfering Substances studies for both the 1st Generation BD MAX (2 channel) System and the 2nd Generation BD MAX (6 channel) System.

Table 6: List of Non-Target Organisms

Organisms		
Achromobacter xerosis	*Gemella haemdysans**	*Peptostreptococcus anaerobius*
Acinetobacter baumannii	*Haemophilus influenza*	*Plesiomonas shigelloides*
Aerococcus viridans	*Haemophilus influenza* type B	*Propionibacterium acnes*
Aeromonas hydrophila	*Hemophilus ducreyi*	*Proteus mirabilis*
Alcaligenes faecalis	HHV6	*Proteus vulgaris*
Bacillus cereus	HHV-6B	*Providencia stuartii*
Bacillus subtilis	HHV-7	*Pseudomonas aeruginosa*
Bacteroides fragilis	HHV-8	*Pseudomonas fluorescens*
Bifidobacterium adolescentis	HPV-16*	*Pseudomonas putida*
Bifidobacterium brevis	HSV1	*Rahnella aquatilis*
BK virus	HSV2	*Rhodospirillum rubrum**
Brevibacterium linens	JC virus	*Saccharomyces cerevisiae**
*Campylobacter jejuni**	*Kingella denitrificans*	*Salmonella enterica Minn**
Candida albicans	*Kingella kingae*	*Salmonella enterica typhi*
Candida glabrata	*Klebsiella oxytoca*	*Salmonella enterica*
Candida krusei	*Klebsiella pneumoniae*	*Salmonella newport*
Candida parapsilosis	*Lactobacillus acidophilus*	*Salmonella typhimurium*
Candida tropicalis	*Lactobacillus brevis*	*Serratia marcescens*
Chlamydia pneumoniae	*Lactobacillus casei*	*Shigella flexneri*
Chlamydia trachomatis	*Lactobacillus delbreukii*	*Shigella sonnei*
Chromobacterium violaceum	*Lactobacillus jensenii*	*Staphylococcus aureus*
Citrobacter freundii	*Lactobacillus lactis*	*Staphylococcus epidermidis*
Clostridium perfringens	*Legionella pneumophila*	*Staphylococcus saprophyticus*
CMV	*Listeria monocytogenes*	*Staphylococcus* spp
Corynebacterium genitalium	*Micrococcus luteus*	*Streptococcus anginosus* (Grp C)
Corynebacterium spp	*Mobiluncus mulieris*	*Streptococcus bovis*
Corynebacterium urealyticum	*Moraxella catarrhalis*	*Streptococcus dysgalactiae* (Grp G)
Corynebacterium xerosis	*Moraxella lacunata*	*Streptococcus haemolyticus (pyogenes)*
Cryptococcus neoformans	*Moraxella osloensis*	*Streptococcus hominis (salivarius)*
Deinococcus radiodurans	*Morganella morganii*	*Streptococcus intermedius*
Derxia gummosa	*Mycobacterium smegmatis*	*Streptococcus mitis*
EBV (HHV-4)	*Mycoplasma genitalium*	*Streptococcus oralis*
Eikenella corrodens	*Mycoplasma hominis*	*Streptococcus pneumoniae*
Enterobacter aerogenes	*Mycoplasma pneumoniae*	*Streptococcus salivarius*
Enterobacter cloacae	*Neisseria flava*	*Streptococcus sanguinis*
*Enterococcus avium**	*Neisseria flavescens*	*Streptomyces griseus*
Enterococcus dispar	*Neisseria gonorrhoeae*	*Trichomonas vaginalis*
Enterococcus durans	*Neisseria lactamica*	*Ureaplasma urealyticum*
Enterococcus faecalis	*Neisseria meningitidis* A	*Vibrio parahaemolyticus*
Enterococcus faecium	*Neisseria meningitidis* B	VZV
Enterococcus spp.	*Neisseria meningitidis* 158	*Yersinia enterocolitica*
Escherichia coli	*Neisseria meningitidis* M1883*	
Gardnerella vaginalis	*Neisseria perflava*	

*Organisms tested with genomic DNA on 1st Generation BD MAX (2 channel system).

Interfering Substances [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

The BD MAX GBS assay was tested in the presence of both endogenous and exogenous interfering agents to characterize the ability of the assay to detect GBS DNA under these conditions. The study was performed at GBS concentrations of 300 CFU/mL and 3000 CFU/mL of Sample Preparation Reagent. Interference was also studied in the presence of high concentrations of 127 relevant non-target organisms to determine if the detection of GBS at 300 CFU/mL was affected by the presence of these organisms. The list of organisms and concentrations tested are the same as listed in the Analytical Specificity section. The following exogenous interfering substances were tested: miconazole (fungicide), hemorrhoid cooling gel, spermicidal foam (nonoxynol 9), spermicidal gel (nonoxynol 9), contraceptive gel, deodorant spray, lubricating gel, moisturizing lotion, body oil and body powder. A complete swab of exogenous agent, similar to the collection of a GBS swab, was added to negative Lim Broth and released into the specimen. The specimen (15 µL) with the interfering agent was added to the Sample Preparation Reagent tube. The following endogenous substances were tested: human DNA (1.55×10^3 ng /mL Sample Preparation Reagent), whole blood (10% in Lim), urine (30% in Lim), mucous (one swab in Lim), amniotic fluid (10% in Lim), and feces (one swab in Lim).

Interference (1/3 replicates) was observed in the presence of *Corynebacterium xerosis*, *Serratia marcescens* and EBV when tested at a GBS target concentration of 300 CFU/mL of Sample Preparation Reagent.

The BD MAX GBS assay was able to detect GBS at a concentration of 300 CFU/mL of Sample Preparation Reagent in the presence of all interfering agents tested except body powder and feces where one of the three replicates was called negative. At 3000 CFU/mL of Sample Preparation Reagent no interference was observed with these agents.

Precision [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

Qualitative testing was performed over a 12 day period in order to determine within laboratory precision using the BD MAX GBS assay. For consistency, testing was performed using the same lot of BD MAX GBS assay. Panel members were prepared at five levels, which included four concentrations of GBS along with True Negative (TN) samples. The levels of the panel members were determined by relation to the Limit of Detection (LoD) of the assay. The Moderate Positive (MP) sample was at a concentration of ~3X LoD, the Low Positive (LP) sample was at a level of ~1.5X LoD, the High Negative 2 (HN-2) sample was at a ~10 fold dilution of the LoD and the High Negative 1 (HN-1) sample was at a ~100 fold dilution of the LoD. Four replicates of each panel member were tested over a 12 day period with two runs per day on three different instruments by multiple operators. Precision results within and across instruments are shown in Table 7. Variance component analysis results are presented in Table 8.

Table 7: Precision Results Within and Across Instruments on 1st Generation BD MAX (2 channel) System

Level	Instrument 1	Instrument 2	Instrument 3	Overall
	Percent Positive	Percent Positive	Percent Positive	Percent Positive
MP	98.9% (92/93)	94.7% (90/95)	100% (95/95)	97.9% (277/283)
LP	95.7% (90/94)	95.7% (90/94)	97.9% (92/94)	96.5% (272/282)
	Percent Negative	Percent Negative	Percent Negative	Percent Negative
TN	100% (94/94)	100% (93/93)	100% (94/94)	100% (281/281)
HN-2 (1:10)	95.7% (90/94)	92.6% (88/95)	88.3% (83/94)	92.2% (261/283)
HN-1 (1:100)	97.9% (93/95)	100% (95/95)	100% (95/95)	99.3% (283/285)

1590 tests were run in the precision study, 26 results were IND (1.6%).

Table 8: Variance Component Analysis of 1st Generation BD MAX (2 channel) System

			Within Run Within Day Within Instrument	Between Run Within Day	Between Day Within Instrument	Between Instruments	Total
Level	N	Mean Ct	CV	CV	CV	CV	CV
GBS: Variance Component Analysis Positive Results							
MP	277	28.7	2.5%	0.0%	0.5%	0.4%	2.6%
LP	272	28.9	3.2%	2.5%	0.0%	0.0%	4.0%
IPC: Variance Component Analysis Negative Results							
HN-2 (1:10)	261	28.4	2.4%	0.5%	0.0%	1.2%	2.7%
HN-1 (1:100)	283	28.4	1.5%	0.4%	0.0%	1.1%	1.9%
TN	281	28.4	1.6%	0.0%	0.4%	1.1%	1.9%

Reproducibility [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

Qualitative testing was performed in order to determine reproducibility using the BD MAX GBS assay. Reproducibility was determined within site as well as across sites. Panel members were prepared at four (4) levels, which included three (3) concentrations of GBS along with True Negative (TN) samples. The levels of the panel members were determined by relation to the Limit of Detection (LoD) of the assay. The Moderate Positive (MP) sample was at a concentration of ~2X LoD, the Low Positive (LP) sample was at a level of ~1X LoD, the High Negative (HN) sample was at a concentration of ~50 fold dilution of the LoD. Six (6) replicates of each panel member were tested at three (3) sites, across five (5) runs over a minimum of a three (3) day period. Reproducibility results within and across sites are shown in Table 9.

Table 9: Reproducibility Results Within and Across Sites on 1st Generation BD MAX (2 channel) System

Level	Site 1	Site 2	Site 3	Overall
	Percent Positive	Percent Positive	Percent Positive	Percent Positive
MP	100% (28/28)	100% (27/27)	100% (29/29)	100% (84/84)
LP	93.1% (27/29)	100% (29/29)	100% (29/29)	97.7% (85/87)
	Percent Negative	Percent Negative	Percent Negative	Percent Negative
TN	100% (28/28)	100% (30/30)	100% (30/30)	100% (88/88)
HN(1:50)	92.9% (26/28)	69.0% (20/29)	83.3% (25/30)	81.6% (71/87)
Level	Site 1	Site 2	Site 3	Overall
	Average Ct (CV%) GBS Target			
MP	29 (2.3%)	29 (3.9%)	28 (3.0%)	29 (3.2%)
LP	31 (5.5%)	30 (14.1%)	30 (2.8%)	30 (8.9%)
Level	Average Ct (CV%) IPC			
TN	27 (2.7%)	26 (2.4%)	27 (3.0%)	27 (3.0%)
HN(1:50)	26 (2.5%)	26 (3.2%)	28 (6.0%)	27 (5.0%)

Carry-Over and Cross-Contamination [determined with the BD MAX GBS assay on the 1st Generation BD MAX (2 channel) System]

A study was conducted to investigate within run carry-over and across run carry-over. All High Positive samples that gave a valid result were accurately identified as positive while all of the True Negative samples were accurately identified as negative. IND results were due to PCR failure as neither Target nor Process control was amplified. This study demonstrated the absence of carry-over and cross-contamination either within a run or between successive runs using the GBS assay on the BD Max System.

Table 10: Summary of Carry-Over and Cross-Contamination Studies on 1st Generation BD MAX (2 channel) System

Across Run Carry-Over	
Run 1: High Positive	Carry over All High Positive 21/21 positive; 3 IND
Run 2: True Negative	Carry over All True Negative 24/24 negative
Within Run Carry-Over	
High Positive/True Negative placed every other lane 10/10 positive; 2 IND 12/12 negative	

Comparison Study [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System]

The performance of the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System was evaluated in a study conducted at three testing sites. The Comparison Study panel was comprised of 214 residual clinical Lim Broth samples. Aliquots of each sample were tested on three (3) 1st Generation BD MAX (2 channel) Systems at a single internal site and on three (3) 2nd Generation BD MAX (6 channel) Systems at each of two (2) external sites as well as one (1) internal site. The GBS status of each sample was determined by the result on the 1st Generation BD MAX (2 channel) System. In the event of a discordant or IND result, the result generated by

two (2) of the three (3) instruments determined the GBS status. Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) along with 95% confidence intervals were calculated for each site separately and all sites combined. Results are presented in Table 11 below. Among samples tested with the 2nd Generation BD MAX (6 channel) System, the overall rate of indeterminate results was 3.6%. Results are presented in Table 12 below.

Table 11: Percent Agreement for the BD MAX GBS assay when tested on the 1st and 2nd Generation BD MAX Systems

	PPA with 95% CI	NPA with 95% CI
Site A	100% (110/110) (96.6% – 100.0%)	98.1% (102/104) (93.3% – 99.5%)
Site B	100% (110/110) (96.6% – 100.0%)	99.0% (103/104) (94.8% – 99.8%)
Site C	100% (110/110) (96.6% – 100.0%)	100% (104/104) (96.4% – 100.0%)
Combined	100% (330/330) (100 – 100%)	99.0% (309/312) (97.8 – 100%)

Numerators are results from 2nd Generation BD MAX and denominators are results from 1st Generation BD MAX. The 95% CI were calculated by score method for each site and by bootstrap approach for all sites combined.

Table 12: Indeterminate Result Rates for 2nd Generation BD MAX System

Site	Initial IND Rate with 95% CI		Final IND Rate with 95% CI	
Site A	3.7% (8/214)	(1.9%, 7.2%)	0.0% (0/214)	(0.0%, 1.8%)
Site B	2.8% (6/214)	(1.3%, 6.0%)	0.0% (0/214)	(0.0%, 1.8%)
Site C	4.2% (9/214)	(2.2%, 7.8%)	0.0% (0/214)	(0.0%, 1.8%)
Combined	3.6% (23/642)	(2.2%, 5.3%)	0.0% (0/642)	(0.0%, 0.6%)

The 95% CI were calculated by score method for each site and by bootstrap approach for all sites combined.

Analytical Sensitivity [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System]

To confirm the analytical sensitivity of the BD MAX GBS assay on the 2nd Generation BD MAX System, 64 replicates of ATCC Strain 27579 were tested at concentrations of 200 CFU/mL and 165 CFU/mL Sample Preparation Reagent. The detection rate was 100% and 98%, respectively. An additional study was performed to establish and confirm the LoD of the BD MAX GBS assay with a second GBS strain. The results of this study indicated that the BD MAX GBS assay when tested with GBS Strain ATCC 13813 on the 2nd Generation BD MAX (6 channel) System demonstrated a LoD of 160 CFU/mL Sample Preparation Reagent.

Microbial Variants [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System]

The ability of the BD MAX GBS assay to detect multiple GBS serotypes was demonstrated using 12 different strains of GBS bacteria. The BD MAX GBS assay run on the 2nd Generation BD MAX (6 channel) System was able to detect all major serotypes of GBS at 300 CFU/mL Sample Preparation Reagent (3×10^4 CFU/mL incubated Lim broth culture).

Precision [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System]

To evaluate the precision of the BD MAX GBS assay when used on the 2nd Generation BD MAX System, the Precision Study performed on the 1st Generation BD MAX (2 channel) System (as described previously) was repeated. For consistency, testing was performed using one lot of

BD MAX GBS assay reagents. Panel members were prepared at five levels, which included four concentrations of GBS along with True Negative (TN) samples. The levels of the panel members were determined in relation to the Limit of Detection (LoD) of the assay. The Moderate Positive (MP) sample was at a concentration of ~3X LoD, the Low Positive (LP) sample was at a level of ~1.5X LoD, the High Negative 2 (HN-2) sample was at a ~10 fold dilution of the LoD and the High Negative 1 (HN-1) sample was at a ~100 fold dilution of the LoD. Four replicates of each panel member were tested over a 12 day period with two runs per day on three different instruments by multiple operators. Precision results within and across instruments are shown in Table 13. Variance component analysis results are presented in Table 14. Precision results for both the 1st Generation and 2nd Generation BD MAX Systems are summarized in Table 15.

Table 13: Precision Results Within and Across Instruments on 2nd Generation BD MAX System

Level	Instrument 1	Instrument 2	Instrument 3	Overall
	Percent Positive	Percent Positive	Percent Positive	Percent Positive
MP	100% (96/96)	100% (93/93)	100% (94/94)	100% (283/283)
LP	94.8% (91/96)	100% (95/95)	99.0% (95/96)	97.9% (281/287)
	Percent Negative	Percent Negative	Percent Negative	Percent Negative
TN	100% (96/96)	100% (96/96)	100% (93/93)	100% (285/285)
HN-2 (1:10)	70.5% (67/95)	79.2% (76/96)	81.1% (77/95)	76.9% (220/286)
HN-1 (1:100)	94.8% (91/96)	98.9% (93/94)	96.8% (90/93)	96.8% (274/283)

1440 tests were run in the precision study, 16 results were IND (1.1%).

Table 14: Variance Component Analysis of Precision Results on 2nd Generation BD MAX System

			Within Run Within Day Within Instrument		Between Run Within Day		Between Day Within Instrument		Between Instruments		Total	
Level	N	Mean Ct	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
GBS: Variance Component Analysis Positive Results												
MP	283	28.8	0.52	1.8%	0.22	0.8%	0	0.0%	0.23	0.8%	0.60	2.1%
LP	281	29.4	0.53	1.8%	0.19	0.7%	0.02	0.1%	0.27	0.9%	0.63	2.1%
IPC: Variance Component Analysis Negative Results												
HN-2 (1:10)	220	27.2	0.36	1.3%	0	0.0%	0.04	0.2%	0.25	0.9%	0.95	1.6%
HN-1 (1:100)	274	27.3	0.54	2.0%	0	0.0%	0.04	0.2%	0.17	0.6%	2.19	2.1%
TN	285	27.3	0.43	1.6%	0.22	0.8%	0	0.0%	0.14	0.5%	0.50	1.8%

Table 15: Precision Summary for 1st and 2nd Generation BD MAX Systems

Panel Level	1st Generation				2nd Generation			
	N	Mean Ct	SD	%CV	N	Mean Ct	SD	%CV
MP	277	28.7	0.74	2.6	283	28.8	0.6	2.1
LP	272	28.9	1.16	4.0	281	29.4	0.63	2.1
HN-2 (1:10)	22	29.4	0.73	2.5	66	31.1	0.95	3.0
HN-1 (1:100)	2	29.3	0.29	1.0	9	30.6	2.19	7.2

Reproducibility [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System]

To evaluate the reproducibility of the BD MAX GBS assay when tested on the 2nd Generation BD MAX System, the Reproducibility Study performed on the 1st Generation BD MAX (2 channel) System (as described previously) was repeated. Reproducibility was determined within site as well as across sites. Panel members were prepared at four (4) levels, which included three (3) concentrations of GBS along with True Negative (TN) samples. The levels of the panel members

were determined in relation to the Limit of Detection (LoD) of the assay. The Moderate Positive (MP) sample was at a concentration of ~3X LoD, the Low Positive (LP) sample was at a level of ~1X LoD, the High Negative (HN) sample was at a concentration of ~50 fold dilution of the LoD. Five replicates of each panel member were tested at three (3) sites, across six (6) runs over three (3) days. Reproducibility results within and across sites are shown in Table 16. Variance component analysis results are presented in Table 17. Reproducibility results for both the 1st and 2nd Generation BD MAX Systems are summarized in Table 18.

Table 16: Reproducibility Results Within and Across Sites on 2nd Generation BD MAX System

Level	Site 1	Site 2	Site 3	Overall
	Percent Positive	Percent Positive	Percent Positive	Percent Positive
MP	100% (30/30)	100% (30/30)	100% (35/35)	100% (95/95)
LP	100% (30/30)	96.7% (29/30)	100% (35/35)	99.0% (94/95)
	Percent Negative	Percent Negative	Percent Negative	Percent Negative
TN	100% (30/30)	100% (30/30)	100% (35/35)	100% (95/95)
HN (1:50)	83.3% (25/30)	70% (21/30)	85.7% (30/35)	80% (76/95)

Table 17: Variance Component Analysis of Reproducibility Results on 2nd Generation BD MAX System

				Within Run		Between Run Within Day		Between Day Within Site		Between Sites		Overall	
Level	N	Mean Ct	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	
GBS: Variance Component Analysis Positive Results													
MP	95	29.4	0.53	1.8%	0.22	0.8%	0	0.0%	0.46	1.6%	0.74	2.5%	
LP	94	30.6	0.73	2.4%	0.29	0.9%	0.11	0.4%	0.71	2.3%	1.07	3.5%	
IPC: Variance Component Analysis Negative Results													
HN (1:50)	76	28.5	0.47	1.7%	0	0.0%	0	0.0%	0.34	1.2%	0.58	2.0%	
TN	95	28.5	0.61	2.2%	0.27	1.0%	0.1	0.4%	0.39	1.4%	0.78	2.8%	

Table 18: Reproducibility Summary for 1st and 2nd Generation BD MAX Systems

Category	1st Generation				2nd Generation			
	N	Mean Ct	SD	%CV	N	Mean Ct	SD	%CV
MP	84	28.7	0.93	3.2	95	29.4	0.74	2.5
LP	85	30.1	2.61	8.7	94	30.6	1.07	3.5
HN	16	29.9	4.24	14.2	19	33.5	2.39	7.1

Analytical Specificity [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System]

To evaluate the specificity of the BD MAX GBS assay when performed on the 2nd Generation BD MAX (6 channel) System, the Analytical Specificity study previously performed on the 1st Generation BD MAX (2 channel) system (as described in Table 6) was repeated. Potential cross-reactivity was observed with nine (9) organisms (*Aerococcus viridans*, *Candida albicans*, *Deinococcus radiodurans, Enterococcus durans, Lactobacillus jensenii, Proteus vulgaris, Providencia stuartii, Pseudomonas aeroginosa*, and *Streptococcus pyogenes*) and with human DNA.

An expanded study was conducted in which twenty (20) replicates of each potential cross-reactant were tested on the 2nd Generation BD MAX System. No reactivity was observed with the *C. albicans, D. radiodurans, L. jensenii, S. pyogenes* or human DNA samples. Table 19

summarizes the cross-reactivity observed with the remaining samples tested in the expanded study.

Table 19: Analytical Specificity on 2nd Generation BD MAX System

Non-Target Organism	No. Positive (n=20)
A. viridans	1/20
E. durans	1/20
**P. aeruginosa*	1/20
**P. stuartii*	2/20
**P. vulgaris*	4/20

*The organisms indicated with an asterisk are gram negative. Lim broth enrichment is designed to suppress growth of gram negative organisms.

Interfering Substances [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) System]

To evaluate the performance of the BD MAX GBS assay when tested on the 2nd Generation BD MAX System, the Interfering Substances study performed on the 1st Generation BD MAX (2 channel) system (as described previously) was repeated. In all cases, the BD MAX GBS assay detected GBS at concentrations of 300 CFU/mL and 3000 CFU/mL in the presence of the endogenous and exogenous substances tested.

Of the 127 non-target organisms (Table 6) tested for potential biological interference, three (3) organisms, *Achromobacter xerosis*, *Enterobacter cloacae* and *Haemophilus influenza* demonstrated potential interference in the initial study using the 2nd Generation BD MAX (6 channel) System. An expanded study was conducted in which twenty (20) replicates of each potential interferent were tested on the 2nd Generation BD MAX System. No interference was observed across the 20 replicates of *A. xerosis* and *H. influenzae*. Interference (2/20 replicates) was observed in the presence of *E. cloacae* when tested with a GBS target concentration of 300 CFU/mL of Sample Preparation Reagent.

Carry-Over and Cross-Contamination [determined with the BD MAX GBS assay on the 2nd Generation BD MAX (6 channel) system]

Studies were performed to evaluate potential Carry-Over and Cross-Contamination of the BD MAX GBS assay when tested on the 2nd Generation BD MAX (6 channel) System. Results demonstrated the absence of carry-over and cross-contamination within a run, between successive runs, and between cartridge rows.

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Patents

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