MAY 27 2010

K090191
510k Summary BD MAX GBS Assay

Per 21 CFR Sec. 807.92

Supplement Date: May 24, 2010

Submitted by: HandyLab, Inc.(a wholly owned subsidiary of Becton, Dickinson and Company)
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The name of the device:

Trade name: **BD MAX™ GBS Assay**

Common or usual name: Group B Strep Assay

Product Codes: **NJR**
Classification name: NUCLEIC ACID AMPLIFICATION ASSAY SYSTEM, GROUP B STREPTOCOCCUS, DIRECT SPECIMEN TEST
Regulation number: 866.3740

CLASS I

Classification Panel **MICROBIOLOGY**

Predicate Device(s): K062948 Cepheid Smart GBS Assay

DEVICE DESCRIPTION

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 and 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 necessary 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 and 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 (10µg/mL) and nalidixic acid (15µg/mL)]. After incubation of inoculated Lim Broth culture for >18 hours at 37 °C in ambient air or 5 % CO2, 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 found in the lower intestinal tract of 10-30 % of all healthy adults. A person who carries GBS but does not show signs of GBS disease is said to be "colonized" with GBS. GBS colonization is not contagious and GBS are commonly found bacteria associated with the human body. Under certain circumstances, GBS can invade the body and cause serious infection; this is referred to as Group B streptococcal disease. GBS can cause severe disease in a newborn and is known to be the leading cause of life threatening bacterial infections in newborns. A number of strains of the pathogen circulate in the community, and approximately 80 % of newborn infections are acquired during birth by vertical (mother-to-baby) transmission. Research has shown that GBS colonizes the anogenital mucosa of 25-40 % of healthy women, and despite the introduction of antibiotic prophylaxis in the US, GBS still causes approximately 2,500 cases of newborn infections per year. Of those infected, 25 % incur serious long-term consequences such as deafness, blindness and neurological damage. Approximately 100 babies die annually in the U.S. in the first three months of life as a result of GBS infection and half of these deaths occur during the first week of life.[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.[1] 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 and 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 120 minutes 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.

Substantial Equivalence Table

Item Being Compared	BD MAX GBS Assay	Smart GBS Assay	Same	Different
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 and 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.	Same - Assay testing is indicated for identification of GBS colonization in antepartum women Smart GBS Assay testing is also indicated for in intrapartum women The Smart GBS Assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.	x	x
Analyte	Group B *Streptococcus* DNA	Same	x	
Specimen Type	Vaginal and Rectal	Same	x	
Specimen collection media type	Amies or Stuart	Copan or Stuart	x	
Sample Preparation Method	Sample Preparation for Nucleic Acid extraction is automated on BD MAX System	Incorporates a manual sample preparation process		x
Sample Processing	Enriched in overnight LIM	Direct swab method or Enriched in overnight LIM	x	x

Platform	BD MAX System (random access)	Cepheid SmartCylcer Dx (batch)		x
Assay Format	Real Time Fluorogenic detection of PCR amplification	Same	x	
Probes	Scorpion	Taqman		x
Single Use	Yes	yes	x	
User / skill required	Moderately complex - no special skills required - built in protocol - no data interpretation required.	Highly complex (Smart Cycle) Moderately complex (Gene Expert)	x	x
Automatic Assay	Yes – built-in result interpretation	Yes	x	
Internal Process Control	Extraction and PCR internal process control is a process monitor	Probe Check		x
External Control	Materials available commercially but not required to run the test	Materials available commercially but not required to run the test	x	

PERFORMANCE DATA

Precision

Qualitative testing was performed over a 12 day period in order to determine within laboratory precision using the BD MAX GBS Assay. Precision was determined within instrument as well as across instruments. 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.

Reproducibility

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 levels, which included three 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

~100 fold dilution of the LoD. Six replicates of each panel member were tested at 3 sites, across 5 runs over a minimum of a 3 day period.

Carry over/Cross Contamination
A study was conducted to investigate within-run carry-over and between-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 or Process control were 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.

Effectiveness of Control
The BD MAX GBS Assay was performed with variations to critical assay and/or process conditions on the automated BD MAX System to demonstrate the effectiveness of the internal process controls incorporated as part of the assay. The BD MAX GBS Assay was also performed in the presence of known inhibitory factors to demonstrate the effectiveness of the internal process control to monitor for inhibition. Of the 4 critical assay conditions that were tested on the automated Jaguar system, the BD MAX GBS Assay will fail if any one of the following 3 critical assay conditions fail – (i) absence of Reagent 1, (ii) absence of Reagent 2, and (iii) absence of Reagent 3 from the strip. As a result the incorporation of the internal process control controls for the occurrence of errors due to the use of 'bad' reagents or errors due to some fluidic system malfunction resulting in the non-aspiration of these reagents from the reservoirs. In addition, the presence of an inhibitory agent (spermicidal jelly) leads to inhibition of the internal process control resulting in a higher Ct value than a sample without the agent. The data demonstrates the effectiveness of the internal process control to monitor for inhibition that may prevent detection of low levels of target and potentially lead to False negative errors. For the samples that had the Specimen omitted, the internal process control was still detected at normal levels because the internal process control pellet present in the test strip (and exogenous to the specimen) amplified to give a valid result.

Interfering Substances
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 concentration tested are the same as listed in 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 (15µl) 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 marcescans* 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.

Analytical Sensitivity Limit of Detection Study
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). Hit rate (95% positivity) method was used to determine the LoD. Pooled Clinical Negative samples spiked with GBS culture was used and individual clinical negative specimen spiked with GBS culture were used in the determination of LoD.

Microbial Variants
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 4.
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).

Analytical Specificity
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 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.

Clinical Performance
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 Centers for Disease Control and Prevention that is described 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 and 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]

To perform the culture based analysis, the enriched 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 (Table 2).

Table 2: Clinical performance statistics using the BD MAX GBS Assay

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

	SENSITIVITY	SPECIFICITY	PREVALENCE [1]
Site 1	97.4 % (37/38)	96.6 % (141/146)	20.0 % (39/195)
Site 2	92.0 % (46/50)	95.9 % (142/148)	25.1 % (50/199)
Site 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.

The conclusions drawn from the nonclinical and clinical tests demonstrate that the device is safe, effective, and performs as well as or better than the legally marketed predicate device identified in paragraph (a)(3) of this section.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center – WO66-0609
Silver Spring, MD 20993-0002

Ms. Martha J. Rumford
Director QA/RA
BD Diagnostics
5230 S. State Rd.
Ann Arbor, MI 48108

MAY 27 2010

Re: K090191
Trade/Device Name: BD MAX™ GBS Assay
Regulation Number: 21 CFR § 866.3740
Regulation Name: Nucleic Acid Amplification Assay System, Group B Streptococcus, Direct Specimen Test
Regulatory Class: Class II
Product Codes: NJR, OOI
Dated: May 24, 2010
Received: May 26, 2010

Dear Ms. Rumford:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

for Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Indications for Use Form

510(k) Number (if known): K090191

Device Name: BD MAX™ GBS ASSAY

Indications for Use:

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Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K090191