K111860
510(k) Summary BD MAX GBS Assay

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Per 21 CFR Sec. 807.92

Supplement Date: TBD

Submitted by:

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The name of the device:

Trade names:	**BD MAX™ GBS Assay, BD MAX™ GBS System**
Common or usual names:	Group B Strep Assay, BD MAX
Product Codes:	NJR; OOI
Classification Names:	Streptococcus spp. Serological reagents; Instrumentation for clinical multiplex test systems
Regulation Numbers:	21 CFR §866.3740; 21 CFR §862.2570
Class:	Class I (BD MAX GBS Assay); Class II (BD MAX System)
Classification Panel:	Microbiology, Clinical Chemistry

Predicate Device(s): K090191 Nucleic Acid Amplification Assay System, Group B Streptococcus, Direct Specimen Test

DEVICE DESCRIPTION

INTENDED USE

BD MAX™ GBS Assay:
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 to 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.

BD MAX™ System:
The BD MAX™ System is intended for *in vitro* diagnostic (IVD) use in performing FDA cleared or approved nucleic acid testing in clinical laboratories. The BD MAX System is capable of automated extraction and purification of nucleic acids from multiple specimen types, as well as the automated amplification and detection of target nucleic acid sequences by fluorescence-based PCR.

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 (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% 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 1990's 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.

REFERENCES

[1] Centers for Disease Control and Prevention. *Prevention of Perinatal Group B Streptococcal Disease: Revised Guideline from CDC.* Morbidity and Mortality Weekly Report, November 19, 2010;59(No. RR-10);1-23

SUBSTANTIAL EQUIVALENCE

The BD MAX GBS Assay when performed in conjunction with the 2nd Generation BD MAX (6 channel) System is substantially equivalent to the BD MAX GBS Assay performed on the predicate device; the 1st Generation BD MAX (2 channel) System. Both systems detect Group B Streptococcus DNA; both systems use an automatic analysis system to determine the presence of GBS DNA through real time PCR and fluorogenic detection of the *cfb* gene. The types of probe are the same and both systems use an automated preparation method. Table 1 provides an upper-level comparison of the two systems.

Table 1: Substantial Equivalence

Item Being Compared	GBS assay on 2nd Generation BD MAX (6 channel) System (K111860)	GBS assay on 1st Generation BD MAX (2 channel) System (K090191 - Predicate Device)
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 necessary for performing susceptibility testing as recommended for penicillin-allergic women. Subculture to solid media for additional testing when indicated.	Same
Analyte	Group B Streptococcus DNA *Cfb* gene	Same
Specimen Type	Vaginal-Rectal Swab	Same
Recommended Specimen Collection Media Type	Amies or Stuart	Same
Sample Preparation Method	DNA extraction is automated on BD MAX instrument	Same
Sample Processing	Enriched in Lim broth (≥18 hours)	Same
Platform	2nd Generation BD MAX 6 channel System	1st Generation BD MAX 2 channel System
Assay Format	Amplification: Real Time PCR Detection: Fluorogenic	Same
Probe Design	Scorpion®	Same
Automatic Assay	Yes – result interpretation	Same
Internal Process Control	Extraction and PCR internal control is a process monitor	Same
External Control	Materials available commercially but not required to run the test	Same

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 on the 2nd Generation BD MAX (6 channel) System. Precision was determined across instruments as well. 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 on the 2nd Generation BD MAX (6 channel) System. 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 Moderation 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 3 sites across 6 runs over a minimum of a 3 day period.

Carry Over/ Cross Contamination

A study was conducted using the BD MAX GBS Assay on the 2nd Generation BD MAX (6 channel) System to investigate within-run carry over, between-run carry over and Top/Bottom PCR Cartridge Row carry over. All High Positive samples that gave a valid result were accurately identified as positive while all of the True Negative samples that gave a valid result were accurately identified as negative.

Interfering Substances

In order to characterize the ability of the BD MAX GBS assay to detect GBS DNA in the presence of both endogenous and exogenous interfering agents, the assay was tested using the 2nd Generation BD MAX (6 channel) System. 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 following exogenous interfering substances were tested: miconazole (fungicide), hemorrhoid cooling 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 uL) 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), mucus (one swab in Lim), amniotic fluid (10% in Lim), and feces (one swab in Lim).

In all cases, the BD MAX GBS Assay detected GBS at concentrations of 300 CFU/mL and 3000 CFU/mL of Sample Preparation Reagent in the presence of the endogenous and exogenous substances tested. Three non-target organisms, *Achromobacter xerosis*, *Enterobacter cloacae* and *Haemophilus influenza* did; however, demonstrate potential interference in the initial study. An expanded study was conducted in which twenty (20) replicates of each potential interferent was 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. cloaecae* when tested at a GBS target concentration of 300 CFU/mL of Sample Preparation Reagent.

Analytical Sensitivity/Limit of Detection Study

The Limit of Detection (LoD) of the BD MAX GBS Assay with the 1st Generation BD MAX (2 channel) System is 200 CFU/mL of Sample Preparation Reagent as determined by the hit rate (95% positivity) method. Pooled Clinical Negative samples spiked with GBS culture (ATCC Strain 27579) and individual clinical negative specimens spiked with GBS culture were used in the determination of LoD. To confirm the analytical sensitivity of the BD MAX GBS Assay with the 2nd Generation BD MAX (6 channel) System, 64 replicates of ATCC Strain 27579 were tested at concentrations of 200 CFU/mL and 165 CFU/mL of Sample Preparation Reagent. The detection rate was 100% and 98%, respectively.

An additional study, using the methods described previously, 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 New System demonstrated a LoD of 160 CFU/mL of Sample Preparation Reagent.

Microbial Variants

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 with the 2nd Generation BD MAX (6 channel) System was able to detect all major serotypes of GBS at 300 CFU/mL of Sample Preparation Reagent (3×10^4 CFU/mL incubated Lim broth culture).

Analytical Specificity

To confirm the analytical specificity of the BD MAX GBS Assay when performed on the 2nd Generation BD MAX (6 channel) System, the assay was tested on samples containing high levels of non-target organisms. A total of 127 organisms were tested, 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 of 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. In the initial study, potential cross-reactivity was observed with nine (9) organisms (*Aerococcus viridians*, *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 (0/20) was observed with the *C. albicans, D. radiodurans, L. jensenii, S. pyogenes* or human DNA samples. Reactivity was observed with *A. viridians* (1/20), *E. durans* (1/20), *P. aeruginosa* (1/20), *P. stuartii* (2/20) and *P. vulgaris* (4/20). *P. aeruginosa*, *P. stuartii* and *P. vulgaris* are gram negative organisms. Lim broth enrichment is designed to suppress growth of gram negative organisms.

Clinical Performance/Comparison Study

Performance characteristics of the BD MAX GBS Assay on the 2nd Generation BD MAX (6 channel) System were compared to the characteristics of the assay on the 1st Generation BD MAX (2 channel) System in a 3-site Comparison Study. The Comparison Study panel was comprised of 214 non-contrived, clinical samples prepared internally from residual, clinical Lim Broth specimens obtained from five (5) clinical laboratories that had inoculated each vaginal-rectal swab specimen in Lim Broth and then incubated overnight for >18 hours. The panel was 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 generated by 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) 1st Generation instruments determined the GBS status. Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) were calculated. Results are presented in Table 2.

Table 2: Summary of Study Comparing 2nd Generation BD MAX System to 1st Generation BD MAX System using the BD MAX GBS Assay

	PPA with 95% CI	NPA with 95% CI
Site A	100% (110/110) (96.8% - 100%)	98.1% (102/104) (93.3% - 99.5%)
Site B	100% (110/110) (96.6% - 100%)	99.0% (103/104) (94.8% - 99.8%)
Site C	100% (110/110) (96.6% - 100%)	100% (104/104) (96.4% - 100%)
Combined	100% (330/330) (100% – 100%)	99.0% (309/312) CI (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.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

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BD Diagnostics
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Manager, Regulatory Affairs
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Sparks, MD 21152

FEB 16 2012

Re: K111860
Trade Name: BD MAX™GBS Assay, BD MAX™ System
Regulation Number: 21 CFR §866.3740
Regulation Name: Streptococcal spp. Serological Reagents
Regulatory Class: Class I, II
Product Code: NJR, OOI
Dated: February 6, 2012
Received: February 8, 2012

Dear Ms. Williams:

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 the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

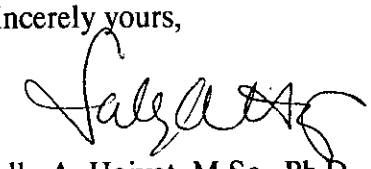
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050. 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 Part 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,



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Enclosure

1.2 Indications for Use Statement

510(k) Number (if known): K111860

Device Name: BD MAX™ GBS Assay, BD MAX™ System

Indication(s) for use:

BD MAX™ GBS Assay:

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.

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BD MAX™ System:
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Prescription Use XXX AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (Part 21 CFR 801 Subpart C)

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

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

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

510(k) K111860