K060540

5.0 510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (408) 400-8230 Fax number: (408) 541-6439
Contact:	Russel K. Enns, Ph.D.
Date of Preparation:	February 28, 2006
Device:	
Trade name:	Xpert GBS™
Common name:	Group B Strep (GBS) Assay
Classification name:	Nucleic Acid Amplification Assay System, Group B Streptococcus, Direct Specimen Test
Regulation number:	866.3740
Procode:	NJR
Classification Advisory Committee:	Microbiology
Predicate Device:	IDI-Strep B™ Assay [510(k) no. K022504]

JUL 25 2006

Device Description:

The Xpert GBS™ is a rapid, fully-automated DNA test for detecting GBS directly from vaginal/rectal swab specimens from pregnant women. A swab containing the specimen is inserted into an individual single-use multi-chambered cartridge (the Xpert GBS™ cartridge) along with the specified single-use reagents (Reagent 1 and Reagent 2) that are provided with the assay. The user initiates a test from the system user interface, the instrument signals the user where to place the cartridge by flashing a green light, and the cartridge is placed into the indicated module in the GeneXpert Dx System instrument. The GeneXpert Dx System has 1 to 4 randomly accessible modules, each of which can process one sample. The instrument moves the sample and reagents to and from different chambers within the Xpert GBS™ cartridge for sample preparation, hydrates dry reagent beads containing critical components, fills the reaction tube with the final reaction mixture, and performs optical probe checks to ensure proper tube fill and presence of probes. The reaction mixture is then subjected to PCR thermal cycling and real-time detection of DNA. The Xpert GBS™ completes sample preparation and real-time PCR for GBS in approximately 75 minutes.

Device Intended Use:

The Cepheid® Xpert GBS™ performed on the GeneXpert Dx System is a qualitative *in vitro* diagnostic test designed to detect Group B streptococcus (GBS) DNA in vaginal/rectal specimens. The test utilizes automated real-time polymerase chain reaction (PCR) for a unique gene specific sequence amplification of *Streptococcus agalactiae* recovered from clinical samples and fluorogenic target-specific hybridization for the detection of the amplified DNA. Results from the Xpert GBS™ are intended for use as a method for rapid detection of GBS colonization in antepartum and intrapartum women.

Substantial Equivalence:

The Xpert GBS™ is substantially equivalent to the Infectio Diagnostic Inc. IDI-Strep B™ Assay (K022504). Both assays detect Group B Streptococcus; both assays recommend the use of Copan Collection and Transport Liquid Stuarts medium for specimen collection; both assays determine the presence of GBS through real-time PCR amplification and fluorogenic target-specific hybridization detection.

The Xpert GBS™ is fully-automated using the Cepheid GeneXpert Dx System instrument. The IDI-Strep B™ Assay is semi-automated using the Cepheid SmartCycler® System instrument. Both instruments employ the same principle I-CORE® design for controlling the real-time PCR amplification and fluorogenic target-specific hybridization detection.

A multi-center study (Protocol 101, Rev. 5) was conducted on vaginal/rectal swab specimens collected from 418 women admitted for delivery (intrapartum) and from 366 women at 35-37 weeks gestation (antepartum). The samples were evaluated with the Xpert GBS™ and the IDI-Strep B™ Assay. Broth culture was also performed for informational purposes. The test results showed the two assays to be substantially equivalent.

Table 5-1 shows the similarities and differences between the Xpert GBS™ and the IDI-Strep B™ Assay.

Table 5-1

Similarities and Differences Between the Xpert GBS™ and the IDI-Strep B™ Assay

	Xpert GBS™	**IDI-Strep B™ Assay**
Regulation no. /Procode	21 CFR 866.3740 / NJR	same
Device Classification Name	Nucleic Acid Amplification Assay System, Group B Streptococcus, Direct Specimen Test	same

	Xpert GBS™	**IDI-Strep B™ Assay**
Intended Use	The Cepheid® Xpert GBS™ performed on the GeneXpert Dx System is a qualitative *in vitro* diagnostic test designed to detect Group B streptococcus (GBS) DNA in vaginal/rectal specimens. The test utilizes automated real-time polymerase chain reaction (PCR) for a unique gene specific sequence amplification of *Streptococcus agalactiae* recovered from clinical samples and fluorogenic target-specific hybridization for the detection of the amplified DNA. Results from the Xpert GBS™ are intended for use as a method for rapid detection of GBS colonization in antepartum and intrapartum women.	A qualitative *in vitro* diagnostic test for the rapid detection of Group B streptococcus (GBS) in vaginal/rectal specimens from antepartum or intrapartum women. The test performed on the SmartCycler® automated analyzer utilizes polymerase chain reaction (PCR) for the amplification of a *cfb* gene sequence of GBS recovered from clinical samples and fluorogenic target-specific hybridization for the detection of the amplified DNA. IDI-Strep B™ Assay can be used to establish GBS colonization status of antepartum and intrapartum women.
Organism Detection	Group B streptococcus DNA	Same
Specimen Type	Direct from Vaginal/rectal swab	Same
Collection and Transport Medium	Copan with Liquid Stuart Medium	Same
Assay Platform	Cepheid GeneXpert Dx System	Cepheid SmartCycler System
Assay Format	Amplification: PCR with I-CORE heating and cooling module. Detection: Fluorogenic target-specific hybridization	Same
Self-contained system assay	Yes	No
Single use	Yes; single-use Cepheid cartridge includes integrated reaction tube	Yes; single-use Cepheid reaction tube
Fully automated assay	Yes: Sample Preparation, amplification, detection and result interpretation	No: Sample Preparation is manual.
Time to result	≤ 75 minutes total	Approximately 60 minutes
Built in Lysis control	Yes	No
External Assay Controls	Materials available, but not required.	Required.

	Xpert GBS™	IDI-Strep B™ Assay
Internal Assay Controls	Sample Processing Control; Cepheid Internal Control; Probe Check (all optical channels) Failures result in single sample repeat.	Internal control Site check (1 optical channel) Same
Fluidics	Self-contained after two single-dose reagent additions (dispense entire contents of each).	Multiple manual pipetting, fluid transfers, vortexing, centrifugation steps.
Criteria for Ct determination	Primary growth curve	2nd derivative analysis
Amplification verification	Yes: curve fit check (protects against false positives due to optical noise)	None
Users	Labor and Delivery Nurses and moderate complexity laboratory technologists	Lab technologists
Performance Characteristics as determined in the Cepheid Clinical Study (Protocol 101, Rev. 5.0) in comparison to culture technique (CDC) at intrapartum	Sensitivity: 94.6% Specificity: 94.8%	As determined in the Cepheid Clinical study using the same subjects as tested with the Xpert GBS™: Sensitivity: 82.4% Specificity: 94.8%
Probes	TaqMan® Probes	Molecular beacons

Non-Clinical Studies:

Analytical Specificity

Genomic DNA from 101 strains representing 28 Streptococci, 73 other species including strains phylogenetically related to *Streptococcus agalactiae*, other microflora (bacteria and yeasts) commonly found in vaginal and anal flora, and human DNA were tested. Replicates of three were tested at 1.5 ng/25 µL reaction (~2×10^5 equivalent genome copies per reaction). None of the 28 Streptococcal isolates (non-GBS) tested positive. Of the remaining 73 strains, four (*Enterococcus gallinarium*, *Staphylococcus simulans*, *Micrococcus luteus*, and *Propionibacterium acnes*) were weakly positive in one of six replicates.

Analytical Sensitivity

The analytical sensitivity, or limit of detection (LoD), was determined using 11 *Streptococcus agalactiae* strains representing nine known serotypes. Quantitated culture and purified genomic DNA were tested in four replicates. The LoD is 25 genome copies per reaction, or stated another way as about 4-8 CFU per reaction depending upon strain type.

Clinical Study:

Performance characteristics of the Xpert GBS Assay were determined in a multi-site prospective investigational study at six institutions with maternity services in the United States. Each institution had a culture-based or nucleic acid test (NAT) based screening program. Testing was done in clinical laboratories affiliated with each institution as well as the labor and delivery area. Both intrapartum and antepartum subjects were included in the study. To be enrolled in the intrapartum portion of the study, women had to provide written consent, be in labor, and have no contraindication to vaginal examination (for example, bleeding). To be enrolled in the antepartum portion of the study, women had to provide written consent, be at 35-37 weeks gestation, and have no contraindication to vaginal examination (for example, bleeding). There was also no evidence of placenta previa, no urgent indication to proceed to delivery, and no antibiotic used in the week prior to admission for all subjects.

The method of reference used was the culture technique recommended by the Centers for Disease Control and Prevention (CDC): microbiological culture in selective broth medium (LIM broth, which is Todd-Hewitt broth supplemented with 15 μg/*mL* of nalidixic acid, and 10 μg/*mL* of colistin), followed by overnight incubation and subculture onto solid blood agar medium. Specific identification of colonies suggestive of GBS was done with slide agglutination tests.

The performance characteristics of the Xpert GBS Assay were determined from the results of 784 maternity patients: 366 antepartum and 418 intrapartum.

Total Results:

Vaginal/rectal specimens were collected from each subject using two sets of double-marked swabs (Cepheid GBS Collection Devices). One of the swabs from the first set was used in the CDC-recommended culture technique. The second set of double-marked swabs was divided: one swab was used in the Xpert GBS Assay on the GeneXpert Dx System, the other was used in the IDI Strep B™ Assay on the SmartCycler® System.

To minimize swab-to-swab variation, the swabs remaining from the Xpert GBS Assay and the IDI Strep B Assay were both cultured. Sensitivity and specificity were calculated relative to the culture results.

Table 5-2 compares the overall results from the Xpert GBS Assay run on the GeneXpert Dx System and the CDC-recommended culture technique. The sensitivity and specificity data are shown below the table.

Table 5-2

Comparison of Xpert GBS Assay and the CDC culture technique.

		Culture		
		Positive	**Negative**	**Total**
GeneXpert	**Positive**	173	24	197
	Negative	17	570	587
	Total	190	594	784

Sensitivity: 91.1% (95% CI = 86.1–94.7%)
Specificity: 96.0% (95% CI = 94.0–97.4%)
Accuracy: 94.8% (95% CI = 93.0–96.2%)
Prevalence: 24.2% (95% CI = 21.3–27.4%)

Intrapartum Results:

Table 5-3 compares the intrapartum culture results from the Xpert GBS Assay run on the GeneXpert Dx System and the CDC recommended culture technique. The sensitivity and specificity data are shown below the table.

Table 5-3

Comparison of Xpert GBS Assay and the CDC culture technique.

		Culture		
		Positive	**Negative**	**Total**
GeneXpert	**Positive**	88	17	105
	Negative	5	308	313
	Total	93	325	418

Sensitivity: 94.6% (95% CI = 87.9–98.2%)
Specificity: 94.8% (95% CI = 91.8–96.9%)
Accuracy: 94.7% (95% CI = 92.1–96.7%)
Prevalence: 22.2% (95% CI = 18.4–26.5%)

Antepartum Results:

Table 5-4 compares the antepartum culture results from the Xpert GBS Assay run on the GeneXpert Dx System and the CDC-recommended culture technique. The sensitivity and specificity data are shown below the table.

Table 5-4

Comparison of Xpert GBS Assay and the CDC culture technique

		Culture		
		Positive	**Negative**	**Total**
GeneXpert	**Positive**	85	7	92
	Negative	12	262	274
	Total	97	269	366

Sensitivity: 87.6% (95% CI = 79.4–93.4%)
Specificity: 97.4% (95% CI = 94.7–98.9%)
Accuracy: 94.8% (95% CI = 92.0–96.8%)
Prevalence: 26.5% (95% CI = 22.1–31.3%)

Reproducibility:

A panel of four simulated specimens with varying concentrations of GBS were tested in triplicate on 10 different days at each of the three sites (4 specimens × 3 × 10 days × 3 sites). One lot of reagent was used for the study.

Table 5-5

Summary of reproducibility results

Specimen ID	Site 1	Site 2	Site 3	Total Agreement	Total % Agreement
Negative	30/30	30/30	30/30	90/90	100%
Weak Positive	30/30	30/30	30/30	90/90	100%
Positive	30/30	30/30	30/30	90/90	100%
Strong Positive	30/30	30/30	30/30	90/90	100%
Total Agreement	120/120	120/120	120/120	360/360	100%
% Agreement	100%	100%	100%	100%	100%

Conclusions:

The results of the nonclinical and clinical studies discussed above demonstrate that the device is as safe, as effective, and performs as well or better than the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

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JUL 25 2006

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Re: k060540
Trade/Device Name: Xpert GBS™
Regulation Number: 21 CFR 866.3740
Regulation Name: Streptococcus spp. serological test reagents
Regulatory Class: Class I
Product Code: NJR
Dated: May 17, 2006
Received: May 18, 2006

Dear Dr. Enns:

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 either class II (Special Controls) or class III (PMA), 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); 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240)276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

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

Indications for Use

510(k) Number (if known): K060540 ~~k06540~~

Device Name: Xpert GBS Assay

Indications For Use:

The Cepheid Xpert GBS performed on the GeneXpert Dx System is a qualitative *in vitro* diagnostic test designed to detect Group B Streptococcus (GBS) DNA from vaginal/rectal swab specimens, using fully automated real-time polymerase chain reaction (PCR) with fluorogenic detection of the amplified DNA. Xpert GBS Assay testing is indicated for rapid identification of antepartum and intrapartum GBS colonization.

- The use of the Xpert GBS for intrapartum screening should not preclude the use of other strategies (e.g., antepartum testing). Intrapartum Xpert GBS results are useful to identify candidates for intrapartum antibiotic prophylaxis when administration of intravenous antibiotics is not delayed pending results.
- The Xpert GBS assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF 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) K060540