GeneXpert
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Xpert® GBS LB

REF **GXGBS-LB-10**
GXGBS-LB-120

Cepheid

In Vitro Diagnostic Medical Device

IVD

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Xpert® GBS LB

For *In Vitro* Diagnostic Use Only.

1 Proprietary Name

Xpert® GBS LB

2 Common or Usual Name

Xpert GBS LB Assay

3 Intended Use

The Cepheid Xpert GBS LB Assay, performed on the GeneXpert® Instrument Systems, is a qualitative in vitro diagnostic test designed to detect Group B *Streptococcus* (GBS) DNA from enriched vaginal/rectal swab specimens, using fully automated real-time polymerase chain reaction (PCR) with fluorogenic detection of the amplified DNA. Xpert GBS LB Assay testing is indicated as an aid in determining GBS colonization status in antepartum women.

- The Xpert GBS LB Assay is used for antepartum testing on enriched Lim broth cultures of vaginal/rectal swabs after 18–24 hours of incubation
- The Xpert GBS LB assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women

4 Summary and Explanation

GBS bacterial infection is associated with serious illness in newborns born to women who are colonized with the microorganism. Transmission of GBS occurs from GBS-colonized women to their newborn before birth (antepartum) or during birth (intrapartum). In the United States, GBS infection is the major cause of death in newborns who develop sepsis, pneumonia, or meningitis.[1,2,3]

Currently, the standard of care for preventing neonatal GBS disease is screening pregnant women at 35–37 weeks of gestation to determine their GBS colonization status.[1,2,4,5] In November 2010, CDC published a revised guideline recommending that in addition to culture, the vaginal/rectal specimens could be tested using a nucleic acid amplification test (NAAT) after 18–24 hour incubation at 35–37 °C in an appropriate enrichment broth medium such as Lim broth to enhance the detection of GBS for antepartum specimens.[4,6] Most antepartum GBS testing is performed by culture and typically takes two to three days to finalize results. The Xpert GBS LB Assay developed by Cepheid for detecting GBS from enriched vaginal/rectal swab specimens takes approximately 55 minutes after the initial 18–24 hour enrichment step.

5 Principle of the Procedure

The GeneXpert Instrument Systems automate and integrate sample lysis, nucleic acid purification and amplification, and detection of the target sequence in complex samples using real-time and reverse transcription Polymerase Chain Reaction (RT-PCR) and PCR assays. The systems consist of an instrument, personal computer, and preloaded software for running tests and viewing the results. The systems require the use of single-use disposable GeneXpert cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination concerns are minimized. For a full description of the systems, refer to the appropriate GeneXpert Instrument System Operator Manual.

The Xpert GBS LB Assay includes reagents for the simultaneous detection of the target GBS DNA, a sample-processing control (SPC) to monitor processing conditions, and an internal control (IC) to monitor PCR conditions and the absence of reaction inhibition. The probe check feature verifies reagent rehydration, PCR-tube filling in the cartridge, probe integrity, and dye stability. The GBS primers and probe detect a target within a 3' DNA region adjacent to the *cfb* gene of *S. agalactiae*.

After collecting and transporting a swab sample to the laboratory, the swab is placed in Lim broth for enrichment overnight at 35–37 °C. A clean swab is dipped into the Lim broth after enrichment and is then transferred to the designated chamber of the cartridge. The GeneXpert System performs sample preparation by eluting the specimen material from the swab, mixing the sample reagent with the SPC (*Bacillus globigii* in the form of a bead within the cartridge) and treatment reagent, capturing cellular material on a filter, lysing the cells, and eluting the DNA. The DNA solution is then mixed with dry PCR reagents and transferred into the integrated reaction tube for real-time PCR and detection. The results are interpolated by the GeneXpert System from measured fluorescent signals and embedded calculation algorithms. Results may be viewed and may be printed. The test process takes approximately 55 minutes or less.

6 Reagents and Instruments

6.1 Material Provided

The Xpert GBS LB kit (GXGBS-LB-10) contains sufficient reagents to process 10 patient or quality-control specimens. The Xpert GBS LB kit (GXGBS-LB-120) contains sufficient reagents to process 120 patient or quality-control specimens. The kits contain the following:

	10 per kit	120 per kit
Xpert GBS LB Assay Cartridges with integrated reaction tubes		
• Bead 1, Bead 2, and Bead 3	3 per cartridge	3 per cartridge
• Reagent 1	3.0 mL per cartridge	3.0 mL per cartridge
• Reagent 2	3.0 mL per cartridge	3.0 mL per cartridge
CD	**1 per kit**	**1 per kit**
• Assay Definition File (ADF)		
• Instructions to import ADF into GeneXpert software		
• Instructions for Use (Package Insert)		

Note Safety Data Sheets (SDS) are available at www.cepheid.com or www.cepheidinternational.com under the **SUPPORT** tab.

Note The bovine serum albumin (BSA) in the beads within this product was produced and manufactured exclusively from bovine plasma sourced in the United States. No ruminant protein or other animal protein was fed to the animals; the animals passed ante- and post-mortem testing. During processing, there was no mixing of the material with other animal materials.

7 Storage and Handling

- Store the Xpert GBS LB Assay cartridges and reagents at 2 °C to 28 °C.
- Do not use reagents or cartridges that have passed the expiration date.
- Do not use a cartridge that has leaked.

8 Materials Required but Not Provided

- GeneXpert Instrument System (catalog number varies by configuration): GeneXpert instrument, computer, barcode wand reader, and operator manual
- Printer If a printer is required, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.
- Cepheid Collection Device (part number 900-0370)
- Lim broth 5mL (Todd Hewitt broth supplemented with 15 µg/mL of nalidixic acid and 10 µg/mL colistin)
- Single use disposable swabs (part number SDPS-120) for processing Lim broth specimens

9 Materials Available but Not Provided

- Inactivated bacterial controls from ZeptoMetrix, cat. no. NATSAg-MC (*S. agalactiae*) as positive control and cat. no. NATLAc-MC (*L. acidophilus*) as negative control.

10 Warnings and Precautions

- For *In Vitro* Diagnostic Use Only.
- Treat all biological specimens, including used cartridges and reagents, as if capable of transmitting infectious agents. Because it is often impossible to know which might be infectious, all biological specimens should be treated with standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention[7] and the Clinical and Laboratory Standards Institute.[8]
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- The Xpert GBS LB Assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.
- Do not open the Xpert GBS LB Assay cartridge lid except when adding sample.
- Do not use a cartridge that has been dropped after removing it from the packaging.
- Do not shake the cartridge. Shaking or dropping the cartridge after opening the lid may yield invalid results.
- Do not use a cartridge that has a damaged reaction tube.
- Do not place the sample ID label on the cartridge lid or on the bar code label.
- Each single-use Xpert GBS LB Assay cartridge is used to process one test. Do not reuse cartridges.
- Reagent 2 contains sodium hydroxide (pH > 12.5); (H302, H315, H319) which is irritating to eyes and skin requiring eye and skin protection.
- Clean the work surface/areas with 10% bleach after processing Xpert GBS LB specimens.
- Specimens can contain high levels of organisms. Ensure that specimen containers do not contact one another. Change gloves if they come in direct contact with the specimen and after the processing of each specimen to avoid contaminating other specimens.
- Biological specimens, transfer devices, and used cartridges should be considered capable of transmitting infectious agents requiring standard precautions. Follow your institution's environmental waste procedures for proper disposal of used cartridges and unused reagents. These materials may exhibit characteristics of chemical hazardous waste requiring specific national or regional disposal procedures. If national or regional regulations do not provide clear direction on proper disposal, biological specimens and used cartridges should be disposed per WHO [World Health Organization] medical waste handling and disposal guidelines.

11 Specimen Collection and Transport

To obtain adequate specimen, follow the instructions in this section closely.

Using the Cepheid Collection Device, or swab in a non-nutritive transport medium collect a vaginal/rectal swab specimen according to CDC recommendations.[2] Transport swab specimen to the laboratory for Lim broth enrichment.

If the swab specimens will be processed in Lim broth for enrichment within 24 hours, store at room temperature. If the specimens will be processed in Lim broth after 24 hours, store swabs at 2-8 °C for up to six days.

For Lim broth enrichment, follow CDC recommendations for sample enrichment.[2] Place swab in Lim broth and incubate for 18–24 hours at 35–37 °C. The enriched Lim broth is stable at 2–8 °C for up to 72 hours.

12 Chemical Hazards[9,10]

- UN GHS Hazard Pictogram:
- Signal Word: WARNING
- **UN GHS Hazard Statements**
  - Causes skin irritation
  - Causes serious eye irritation

- **Precautionary Statements**
  - **Prevention**
    - Wash thoroughly after handling.
    - Wear protective gloves/protective clothing/eye protection/face protection
  - **Response**
    - IF ON SKIN: Wash with plenty of soap and water.
    - Take off contaminated clothing and wash before reuse.
    - Specific treatment, see supplemental first aid information.
    - If skin irritation occurs: Get medical advice/attention
    - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
    - If eye irritation persists: Get medical advice/attention
  - **Storage/Disposal**
    - Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

13 Procedure

13.1 Preparing the Cartridge

Important **Start the test within 15 minutes of adding the sample to the cartridge.**

Note Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.

To add the sample into the cartridge (Xpert GBS LB):

1. Remove the cartridge from the package.
2. Open the cartridge lid.
3. Prepare the swab as follows:
   A. Invert the enriched Lim broth tube three times to mix.
   B. Dip a clean single use disposable swab in the Lim broth.
   C. Transfer the swab into the Xpert GBS LB cartridge sample chamber. See Figure 1.
4. Raise the swab so that the score mark is centered in the notch.
5. Break the swab by snapping the shaft to the right.
6. Close the cartridge lid.

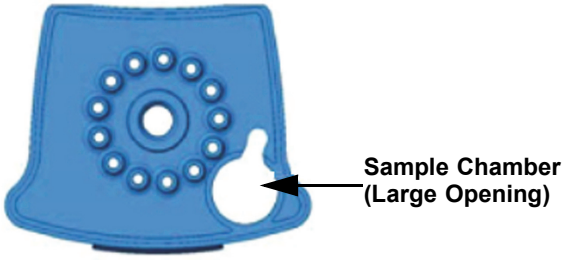

Figure 1. Xpert GBS LB Assay Cartridge (Top View)

13.2 Starting the Test

Important **Before you start the test, ensure that the GeneXpert Instrument System is equipped with the appropriate software, and the Xpert GBS LB Assay is imported into the software.**

This section lists the basic steps of running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*, depending on the model that is being used.

1. Turn on the computer, and then turn on the GeneXpert Instrument System.
2. On the desktop, double-click the GeneXpert software icon.
3. Log on to the GeneXpert Instrument System software using your user name and password.
4. In the GeneXpert Dx Systems window, click **Create Test**.

   In the GeneXpert Infinity Systems, click **Orders** > **Order Test**.

   The Scan Cartridge Barcode dialog box appears.
5. Scan the barcode on the Xpert GBS LB cartridge. Using the barcode information, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date.
6. In the Sample ID box, scan or type the Sample ID. Make sure you type the correct Sample ID. The Sample ID is associated with the test results and is shown in the View Results window and all the reports.
7. Scan or type in the Patient ID (optional).
8. In the GeneXpert Dx Systems window, click **Start Test**.

   In the GeneXpert Infinity Systems, click **Submit**.

   When prompted, enter your password.
9. For the GeneXpert Infinity Systems, place the cartridge on the conveyor belt.

   For the GeneXpert Dx Systems:

   A. Open the instrument module door with the blinking green light and load the cartridge.

   B. Close the door. The test starts and the green light stops blinking. When the test is finished, the light turns off.

   C. Wait until the system releases the door lock before opening the module door and removing the cartridge.

   D. Dispose of used cartridges in the appropriate specimen waste containers according to your institution's standard practices.

14 Viewing and Printing Results

This section lists the basic steps for viewing and printing results. For more detailed instructions on how to view and print the results, see the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

1. Click the **View Results** icon to view results.
2. Upon completion of the test, click the **Report** button of the View Results window to view and/or generate a PDF report file.

15 Quality Control

CONTROL

Each test includes the following internal controls and a probe check.

- **Sample processing control (SPC)**: Ensures the sample was correctly processed. The SPC is B. *globigii* in the form of a dry bead and is included in each cartridge. The SPC monitors the lysis and elution processing. The SPC should pass—generate a valid cycle threshold (Ct) in a negative sample—and may not amplify in a high-positive sample. The SPC passes if it meets the assigned acceptance criteria.
- **Internal control (IC)**: Verifies functional PCR reagents and the absence of inhibition that would prevent PCR amplification. The IC should pass—generate a valid Ct in a negative sample—and may not amplify in a high-positive sample. The IC passes if it meets the assigned acceptance criteria.
- **Probe check**: Before the start of the PCR reaction, the GeneXpert Instrument System measures the fluorescence signal from the probes to monitor bead rehydration, reaction-tube filling, probe integrity and dye stability. Probe Check passes if it meets the assigned acceptance criteria.
- **External controls**: External controls (one positive and one negative) may be used in accordance with local, state, and federal accrediting organizations, as applicable, according to the appropriate procedure below:

For ZeptoMetrix controls:

A. Insert single use disposable swab into the external control vial (each vial contains 0.5 mL).

B. Insert swab into Xpert GBS LB cartridge chamber S.

C. The swab is now ready for Xpert GBS testing.

16 Interpretation of Results

The results are interpolated by the GeneXpert Instrument Systems from measured fluorescent signals and embedded calculation algorithms and will be shown in the View Results window. Possible results are shown in Table 1. Examples of Xpert GBS LB Assay results are provided in Figure 2, Figure 3 and Figure 4.

Table 1. GBS Results and Interpretation

Result	Interpretation
POSITIVE See Figure 2.	GBS target nucleic acid is detected • SPC—NA (not applicable) • IC—NA (not applicable) • Probe check—PASS
NEGATIVE See Figure 3.	GBS target nucleic acid is not detected • GBS—NEG • SPC—PASS • IC—PASS • Probe Check—PASS
INVALID See Figure 4.	Presence or absence of GBS cannot be determined. IC and/or SPC does not meet acceptance criteria. • GBS—INVALID • SPC—FAIL* • IC—FAIL* • Probe Check—PASS * The SPC and/or the IC failed.
ERROR	Presence or absence of GBS cannot be determined. A system component failed, the maximum pressure was reached, or the probe check failed. • GBS—NO RESULT • SPC—NO RESULT • IC—NO RESULT • Probe Check—FAIL* * If the probe check passed, the error is caused by a system component failure.
NO RESULT	Presence or absence of GBS cannot be determined. The operator stopped the test, a power failure occurred during the test, or problems were detected in the cartridge. • GBS—NO RESULT • SPC—NO RESULT • IC—NO RESULT Probe Check—NA (not applicable)

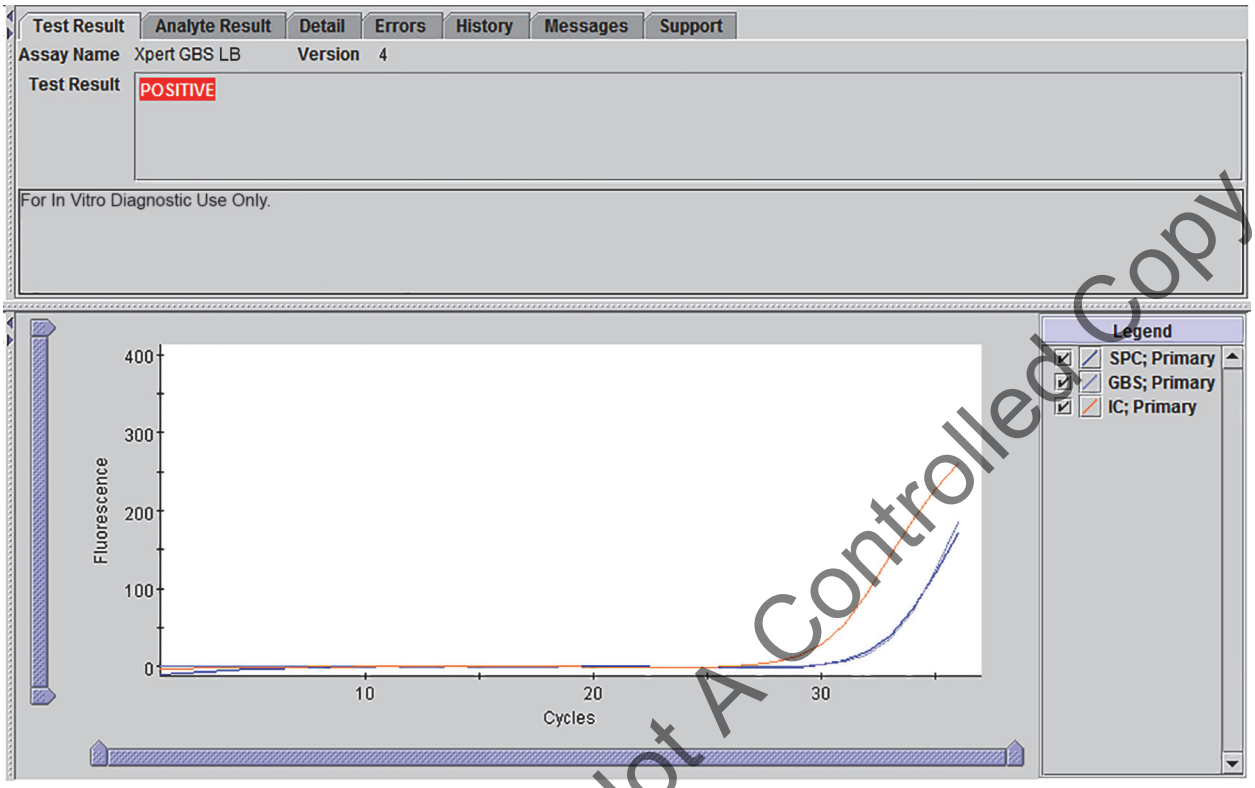

Figure 2. An Example of a Positive Result

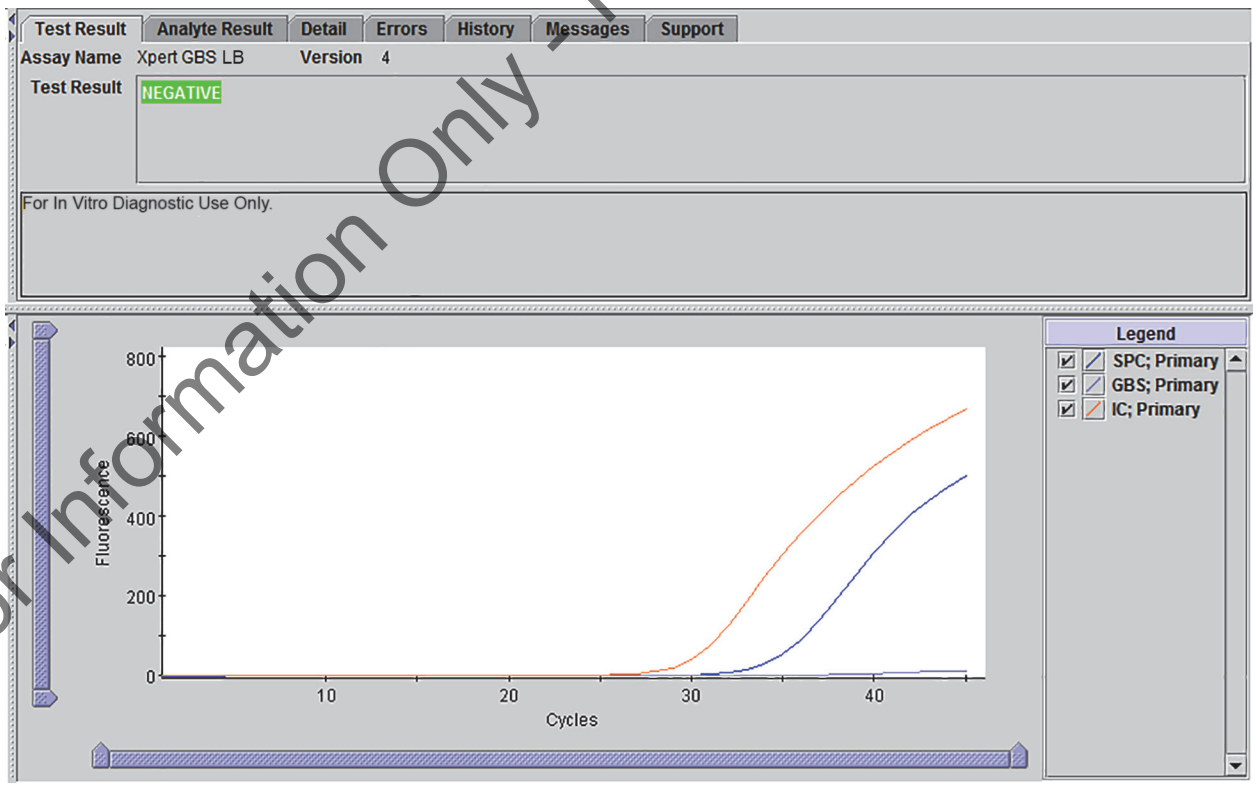

Figure 3. An Example of a Negative Result

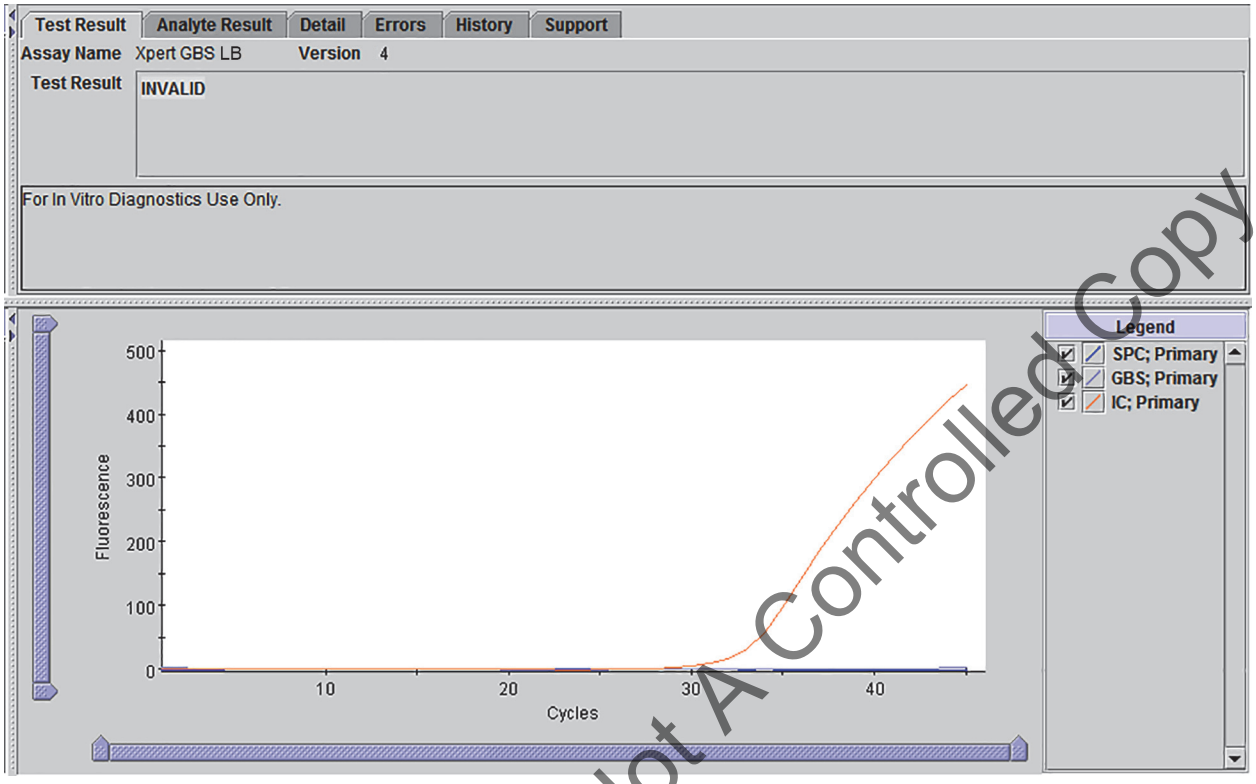

Figure 4. An Example of an Invalid Result

17 Reasons to Repeat the Assay

If any of the test results mentioned below occur, repeat the test according to the instructions in Section 18, Retest Procedure.

- An **INVALID** result indicates one or more of the following:
  - GBS is not detected and the control SPC and/or IC failed
  - The sample was not properly processed or PCR was inhibited
- An **ERROR** result indicates that the assay was aborted. Possible causes include: the reaction tube was filled improperly; a reagent probe integrity problem was detected; or the maximum pressure limit was exceeded.
- A **NO RESULT** indicates that insufficient data were collected. For example, the operator stopped a test that was in progress, or a power failure occurred.

18 Retest Procedure

For retest of a **NO RESULT**, **INVALID**, or **ERROR** result, use the remaining enriched Lim broth, invert tube three times to mix. Insert single use disposable swab into the Lim broth. Insert swab into the sample chamber of a new Xpert GBS LB cartridge and then rerun the test. Continue with subsequent testing steps starting at Section 13.2, Starting the Test.

19 Limitations

- Erroneous test results might occur from improper specimen collection, technical error, sample mix-up, or because the number of organisms in the specimen is not detected by the test. Careful compliance to the instructions in this insert and to the Vaginal/Rectal Specimen Collection Protocol instructions document is necessary to avoid erroneous results. Swabbing both the lower vagina and rectum increases the yield substantially compared with sampling the cervix or sampling the vagina without also swabbing the rectum.
- The performance of the Xpert GBS LB Assay was validated using the procedures provided in this package insert only. Modifications to these procedures may alter the performance of the test.
- The Xpert LB Assay has been validated with Lim broth medium only. Performance of the assay has not been validated with other GBS selective broth enrichment media.

- Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women. Use remaining enriched Lim broth to obtain culture isolates. Laboratories must validate their own culturing procedures.
- Good laboratory practices should be followed and gloves should be changed between handling each patient specimen in order to avoid contamination of specimens or reagents.
- Regularly clean the work surface/areas with 10% bleach before and after processing Xpert GBS LB specimens.
- Patients who have used systemic or topical (vaginal) antibiotic treatment in the week prior as well as patients diagnosed with placenta previa should not be tested with Xpert GBS LB assay.
- A positive result does not necessarily indicate the presence of viable organisms.
- Mutations or polymorphisms in primer or probe binding regions may affect detection of new or unknown variants and may result in a false negative result.
- 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 limit of detection (LOD).

20 Expected Values

Approximately 10–30% of pregnant women are colonized with GBS in the vagina or rectum. GBS colonization can be transient, chronic, or intermittent. 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.[2,3,4] During this clinical evaluation for the Xpert GBS LB Assay, 28.7% (237/826) of women were colonized with GBS by Xpert GBS LB Assay.

21 Performance Characteristics

21.1 Clinical Performance

Performance characteristics of the Xpert GBS LB Assay were evaluated at three institutions in the U.S. using the GeneXpert Dx, Infinity-48, and the Infinity-80 instrument systems. Subjects included individuals whose routine care called for collection of vaginal/rectal swab specimens for GBS testing. For eligible subjects, aliquots of leftover Lim broth sample were obtained for testing with the Xpert GBS LB Assay and reference culture testing, and patient management continued at the site per the standard practice. The Xpert GBS LB Assay performance was compared to culture.

21.2 Overall Results

A total of 826 enriched Lim broth specimens were tested for GBS by the Xpert GBS LB Assay, and culture. The Xpert GBS LB Assay demonstrated a sensitivity and specificity for detection GBS colonization of 99.0% and 92.4%, respectively, relative to culture (Table 2).

Table 2. Xpert GBS LB Assay Performance vs. Culture

		Culture		
		Pos	**Neg**	**Total**
Xpert GBS	**Pos**	189	48[a]	237
	Neg	2[b]	587	589
	Total	191	635	826
Sensitivity: 99.0% (95% CI: 96.3-99.9) Specificity: 92.4% (95% CI: 90.1-94.4) PPV: 79.7% (95% CI: 74.1-84.7) NPV: 99.7% (95% CI: 98.8-100.0)				

a. Testing result by sequencing: 47 of 48 GBS specimens were sequenced, 42 were GBS positive, 5 were GBS negative and one Lim broth was not sequenced.
b. Testing result by sequencing: 2 of 2 GBS specimens were sequenced, both were GBS negative.

Xpert GBS LB Assays for 98.1% (810/826) of eligible specimens were successful on the first attempt. The indeterminate cases included twelve **ERROR** results, two **INVALID** results, and two **NO RESULT** outcomes. All of the 16 indeterminate cases were retested and yielded valid results upon repeat assay. The overall rate of assay success was 100% (826/826).

22 Analytical Performance

22.1 Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical limit of detection (LoD) of 11 GBS strains representing nine known serotypes. All GBS strains used were procured from ATCC or CDC. The LoD is defined as the lowest concentration per sample that can be reproducibly distinguished from negative samples with 95% confidence or the lowest concentration at which 19 of 20 replicates were positive. Each strain was tested in replicates of 20 per concentration of bacteria.

The LoD was determined empirically as the lowest concentration that had 19/20 or 20/20 positive results. The LoD point estimates for each strain tested are summarized in Table 3. The overall LoD for the assay is 333 CFU/mL.

Table 3. Confirmed LoD—GBS Serotypes

Strain Id	Confirmed LoD (CFU/swab) [at least 19/20 positive]	Confirmed LoD (CFU/mL of Lim Broth) [at least 19/20 positive]	LoD Estimate (Logistic Regression) (CFU/swab)		
			Lower 95% CI	Lod Estimate	Upper 95% CI
Serotype Ia	13 (20/20)	173	8.0	10.0	14.2
Serotype Ib	25 (20/20)	333	8.7	11.1	15.7
Serotype II	25 (20/20)	333	10.4	13.3	20.1
Serotype II	25 (20/20)	333	20.1	23.6	32.1
Serotype III	25 (19/20)	333	16.3	21	35.4
Serotype IV	25 (20/20)	333	10.7	14.4	23.7
Serotype IVc	5 (20/20)	67	2.4	3.1	4.8
Serotype V	25 (20/20)	333	14.2	18.2	26.1
Serotype VI	25 (20/20)	333	7.6	10.4	17.8
Serotype VI	25 (20/20)	333	10.2	13.4	20.7
Serotype VIII	10 (20/20)	133	4.3	5.6	8.4

22.2 Analytical Specificity (Exclusivity)

The analytical specificity of the Xpert GBS LB Assay was evaluated by testing a panel of 100 strains representing 24 Streptococci, 76 other species including strains phylogenetically related to *S. agalactiae*, other microflora (bacteria and yeasts) commonly found in vaginal/anal flora, and human DNA. Replicates of three were tested at concentrations of 4.5 to 9.5 × 10^8 CFU/mL or 1.7–3.2 McFarland units in Lim broth. The analytical specificity was 100%.

22.3 Interfering Substances Study

In a non-clinical study, potentially interfering substances that may be present in vaginal/rectal specimens were evaluated directly relative to the performance of the Xpert GBS LB Assay. Potentially interfering endogenous and exogenous substances include, but are not limited to: human amniotic fluid, meconium, serum, urine, fecal material, human blood, lubricating gel, vaginal anti-itch medications, vaginal antifungal medications, anti-diarrheal medications, laxatives, stool softeners, topical hemorrhoid ointments, body oil, body powder, deodorant sprays, enema solutions, and spermicidal foam. Substances were tested at concentrations close to saturation. These substances are listed in Table 4 with active ingredients. None of the substances tested had a statistically significant effect on the assay performance. All positive samples were correctly reported as GBS positive, and all negative samples were correctly reported as GBS negative.

Table 4. Potentially Interfering Substances in Xpert GBS LB Assay

Category	Substance/Supplier	Final Concentration
Lim Broth (Control)	Becton, Dickinson and Company	-
Human Amniotic Fluid	New England Life Sciences	2.0% (v/v)
Human Whole Blood (EDTA)	Stanford Blood Center	2.0% (v/v)
Human Whole Blood (NaCitrate)	Stanford Blood Center	2.0% (v/v)
Human Serum	Stanford Blood Center	2.0% (v/v)
Human Urine Sample	In-house	2.0% (v/v)
Human Fecal Sample	In-house	0.47% (w/v)
Human Meconium Sample	LEE BioSolutions	1.75% (w/v)
Personal Lubricant	K-Y® Jelly Personal Lubricant (Personal Products Company, Skillman, NJ)	1.22% (w/v)
Lubricating Gel	AquaGel® Lubricating Gel (Parker Laboratories, Inc., Fairfield, NJ)	0.57% (w/v)
Vaginal Anti-Itch Medication	Vagisil Cream	0.41% (w/v)
Vaginal Anti-Fungal Medication	Monistat Cream	0.29% (w/v)
	Yeast Gard (Douche)	1.89% (w/v)
Topical Hemorrhoid Ointments	Preparation H Cream	0.26% (w/v)
Anti-Diarrheal Medications	Pepto Bismol	1.00% (w/v)
	Kaopectate	1.33% (w/v)
Deodorant Powder	Vagisil Powder	0.31% (w/v)
Deodorant Suppositories	Norforms Suppositories	0.30% (w/v)
Deodorant Spray	FDS Deodorant Spray	0.53% (w/v)
Baby Powder	Gold Bond Powder	0.40% (w/v)
Body Oil	Neutrogena Body Oil	1.41% (w/v)
Spermicidal Foam	Delfen Contraceptive Foam	0.59% (w/v)
Oral Laxatives	Metamucil Fiber Supplement	0.33% (w/v)
	Exlax (Chocolate Pieces)	0.60% (w/v)
	Phillips Milk of Magnesia	1.78% (w/v)
Stool Softener	Dulcolax Suppositories	0.25% (w/v)
Enema Solution	Fleet Enema	1.93% (w/v)

22.4 Carry-over Contamination Study

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination in negative samples run following very high positive samples in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately following a very high GBS positive sample (roughly $1x10^6$ CFU/swab) Lim broth consisting of GBS serotype II or GBS serotype IV cells. This testing scheme was repeated 20 times on four GeneXpert modules for a total of 88 runs resulting in 40 positive and 48 negative specimens. All 40 positive samples were correctly reported as GBS positive. All 48 negative samples were correctly reported as GBS negative.

23 Reproducibility

A panel of seven specimens with varying concentrations of two different GBS strains were tested by two operators each in triplicate on five different days at three sites (7 specimens × 2 operators × 3 times/day × 5 days × 3 sites). One lot of Xpert GBS LB Assay was used at each of the three testing sites. The three levels were moderate positive (~3–4 × LOD), low positive (~1 × LOD) and high negative (below LOD). Xpert GBS LB Assays were performed on the GeneXpert Instrument Systems according to the Xpert GBS LB Assay procedure. Results are summarized in Table 5. A comparison of Ct value results by target in each sample level between the GeneXpert Dx, Infinity-48 and Infinity-80 instruments and their overall results are provided in Table 6.

Table 5. Summary of Reproducibility Results

Specimen ID	Site 1 (Infinity-48)	Site 2 (GeneXpert Dx)	Site 3 (Infinity-80)	% Total Agreement by Sample
GBS strain 1 moderate positive	100% (30/30)	100% (30/30)	100% (30/30)	100% (90/90)
GBS strain 1 low positive	100% (30/30)	96.7% (29/30)	100% (30/30)	98.9% (89/90)
GBS strain 1 high negative	73.3% (22/30)	80% (24/30)	63.3% (19/30)	72.2% (65/90)
GBS strain 2 moderate positive	100% (30/30)	100% (30/30)	100% (30/30)	100% (90/90)
GBS strain 2 low positive	100% (30/30)	100% (30/30)	100% (30/30)	100% (90/90)
GBS strain 2 high negative	80% (24/30)	83.3% (25/30)	76.7% (23/30)	80.0% (72/90)
Negative	100% (30/30)	100% (29/29)[a]	100% (30/30)	100% (89/89)[a]

a. One negative sample had indeterminate result on initial test but was not retested by mistake.

Table 6. Summary of Ct Value Results by Instruments in Each Sample Level

GBS strain 1: Moderate Positive				
		SPC	**GBS**	**IC**
Infinity-48 n=30	**MEAN**	33.04	35.85	30.39
	STDEV	0.50	0.47	0.19
	CV	1.52%	1.30%	0.64%
	No. of results	29[a]	30	30
GeneXpert Dx n=30	**MEAN**	32.98	35.82	30.51
	STDEV	0.62	0.64	0.25
	CV	1.90%	1.79%	0.83%
	No. of results	30	30	30
Infinity-80 n=30	**MEAN**	32.95	36.05	30.48
	STDEV	0.61	0.96	0.22
	CV	1.85%	2.67%	0.71%
	No. of results	30	30	30
Overall n=90	**MEAN**	32.99	35.91	30.46
	STDEV	0.58	0.72	0.23
	CV	1.75%	2.00%	0.74%
	No. of results	89	90	90
	[a] One SPC CT=0 excluded due to positive for GBS			
GBS strain 1: Low Positive				
		SPC	**GBS**	**IC**
Infinity-48 n=30	**MEAN**	32.65	37.13	30.41
	STDEV	0.50	0.78	0.23
	CV	1.54%	2.10%	0.75%
	No. of results	30	30	30
GeneXpert Dx n=30	**MEAN**	32.96	37.5	30.46
	STDEV	0.61	1.25	0.33
	CV	1.84%	3.33%	1.07%
	No. of results	30	29[b]	30
Infinity-80 n=30	**MEAN**	32.8	37.41	30.54
	STDEV	0.50	0.73	0.36
	CV	1.54%	1.94%	1.19%
	No. of results	30	30	30
Overall n=90	**MEAN**	32.80	37.35	30.47
	STDEV	0.55	0.95	0.31
	CV	1.67%	2.54%	1.03%
	No. of results	90	89	90
	[b] One GBS CT=0 excluded due to negative for GBS"			

Table 6. Summary of Ct Value Results by Instruments in Each Sample Level (Continued)

GBS strain 1: High Negative				
		SPC	GBS	IC
Infinity-48 n=30	MEAN	32.77	N/A	30.43
	STDEV	0.50	N/A	0.22
	CV	1.54%	N/A	0.71%
	No. of results	30		30
GeneXpert Dx n=30	MEAN	32.82	N/A	30.47
	STDEV	0.43	N/A	0.20
	CV	1.31%	N/A	0.66%
	No. of results	30		30
Infinity-80 n=30	MEAN	32.80	N/A	30.45
	STDEV	0.49	N/A	0.24
	CV	1.51%	N/A	0.80%
	No. of results	30		30
Overall n=90	MEAN	32.79	N/A	30.45
	STDEV	0.47	N/A	0.22
	CV	1.44%	N/A	0.72%
	No. of results	90		90
GBS strain 2: Moderate Positive				
		SPC	GBS	IC
Infinity-48 n=30	MEAN	32.93	35.6	30.46
	STDEV	0.40	0.57	0.18
	CV	1.22%	1.60%	0.58%
	No. of results	30	30	30
GeneXpert Dx n=30	MEAN	32.98	35.63	30.38
	STDEV	0.51	0.63	0.23
	CV	1.56%	1.76%	0.75%
	No. of results	30	30	30
Infinity-80 n=30	MEAN	32.89	35.50	30.43
	STDEV	0.74	0.59	0.28
	CV	2.24%	1.66%	0.92%
	No. of results	30	30	30
Overall n=90	MEAN	32.93	35.58	30.42
	STDEV	0.56	0.59	0.23
	CV	1.71%	1.66%	0.76%
	No. of results	90	90	90

Table 6. Summary of Ct Value Results by Instruments in Each Sample Level (Continued)

GBS strain 2: Low Positive				
		SPC	**GBS**	**IC**
Infinity-48 n=30	**MEAN**	32.90	37.05	30.39
	STDEV	0.64	1.19	0.24
	CV	1.95%	3.20%	0.79%
	No. of results	30	30	30
GeneXpert Dx n=30	**MEAN**	33.01	36.97	30.46
	STDEV	0.66	0.75	0.29
	CV	1.99%	2.04%	0.94%
	No. of results	30	30	30
Infinity-80 n=30	**MEAN**	32.60	36.96	30.42
	STDEV	0.52	0.84	0.28
	CV	1.59%	2.26%	0.91%
	No. of results	30	30	30
Overall n=90	**MEAN**	32.84	36.99	30.42
	STDEV	0.63	0.93	0.27
	CV	1.91%	2.53%	0.88%
	No. of results	90	90	90
GBS strain 2: High Negative				
		SPC	**GBS**	**IC**
Infinity-48 n=30	**MEAN**	32.79	N/A	30.49
	STDEV	0.49	N/A	0.25
	CV	1.51%	N/A	0.82%
	No. of results	30		30
GeneXpert Dx n=30	**MEAN**	32.90	N/A	30.39
	STDEV	0.40	N/A	0.26
	CV	1.23%	N/A	0.86%
	No. of results	30		30
Infinity-80 n=30	**MEAN**	33.00	N/A	30.48
	STDEV	0.60	N/A	0.24
	CV	1.81%	N/A	0.80%
	No. of results	30		30
Overall n=90	**MEAN**	32.90	N/A	30.45
	STDEV	0.51	N/A	0.25
	CV	1.54%	N/A	0.83%
	No. of results	90		90

Table 6. Summary of Ct Value Results by Instruments in Each Sample Level (Continued)

Negative				
		SPC	**GBS**	**IC**
Infinity-48 n=30	**MEAN**	32.87	N/A	30.45
	STDEV	0.51	N/A	0.21
	CV	1.55%	N/A	0.68%
	No. of results	30		30
GeneXpert Dx n=29[C]	**MEAN**	32.85	N/A	30.39
	STDEV	0.54	N/A	0.32
	CV	1.65%	N/A	1.04%
	No. of results	29		29
Infinity-80 n=30	**MEAN**	32.83	N/A	30.47
	STDEV	0.68	N/A	0.27
	CV	2.06%	N/A	0.87%
	No. of results	30		30
Overall n=89	**MEAN**	32.85	N/A	30.44
	STDEV	0.58	N/A	0.27
	CV	1.76%	N/A	0.87%
	No. of results	89		89
	[C] One Error not retested			

24 Instrument System Precision

An in-house precision study was conducted to compare the performance of the GeneXpert Dx and the Infinity-80 instrument systems. A panel of seven specimens with varying concentrations of two different GBS strains was tested on 12 different days by two operators. Each operator conducted four runs of each panel specimen per day on each of the two instrument systems (7 specimens × 4 times/day × 12 days × 2 operators × 2 instrument systems). One lot of Xpert GBS LB Assay was used for the study. Xpert GBS LB assays were performed according to the Xpert GBS LB Assay procedure. Results are summarized in Table 7. A comparison of Ct value results by target in each sample level between the GeneXpert Dx system and Infinity-80 system instruments and their overall results are provided in Table 8.

Table 7. Summary of Instrument Precision Results

Specimen ID	GeneXpert Dx	Infinity-80	% Total Agreement by Sample
GBS strain 1 moderate positive	100% (96/96)	100% (96/96)	100% (192/192)
GBS strain 1 low positive	100% (96/96)	100% (96/96)	100% (192/192)
GBS strain 1 high negative	77.1% (74/96)	76.0% (73/96)	76.6% (147/192)
GBS strain 2 moderate positive	100% (96/96)	100% (96/96)	100% (192/192)
GBS strain 2 low positive	99.0% (95/96)	97.9% (94/96)	98.4% (189/192)
GBS strain 2 high negative	85.4% (82/96)	82.3% (79/96)	83.9% (161/192)
Negative	100% (96/96)	100% (96/96)	100% (192/192)

Table 8. Summary of Ct Value Results by Target in Each Sample Level

GBS strain 1: Moderate Positive				
		SPC	**GBS**	**IC**
Infinity-80 n=96	**MEAN**	32.83	35.93	30.45
	STDEV	0.52	0.75	0.41
	CV	1.59%	2.08%	1.35%
	No. of results	96	96	96
GeneXpert Dx n=96	**MEAN**	32.72	35.88	30.48
	STDEV	0.63	0.77	0.29
	CV	1.93%	2.14%	0.94%
	No. of results	96	96	96
Overall n=192	**MEAN**	32.77	35.90	30.47
	STDEV	0.58	0.75	0.35
	CV	1.77%	2.10%	1.16%
	No. of results	192	192	192

Table 8. Summary of Ct Value Results by Target in Each Sample Level

GBS strain 1: Low Positive				
		SPC	**GBS**	**IC**
Infinity-80 n=96	**MEAN**	32.73	37.67	30.40
	STDEV	0.49	1.08	0.28
	CV	1.51%	2.86%	0.92%
	No. of results	96	96	96
GeneXpert Dx n=96	**MEAN**	32.73	37.64	30.42
	STDEV	0.39	1.04	0.22
	CV	1.19%	2.76%	0.71
	No. of results	96	96	96
Overall n=192	**MEAN**	32.73	37.65	30.41
	STDEV	0.44	1.06	0.25
	CV	1.35%	2.81%	0.82%
	No. of results	192	192	192
GBS strain 1: High Negative				
		SPC	**GBS**	**IC**
Infinity-80 n=96	**MEAN**	32.75	N/A	30.39
	STDEV	0.64	N/A	0.25
	CV	1.95%	N/A	0.84%
	No. of results	96		96
GeneXpert Dx n=96	**MEAN**	32.61	N/A	30.42
	STDEV	0.54	N/A	0.29
	CV	1.64%	N/A	0.95%
	No. of results	96		96
Overall n=192	**MEAN**	32.68	N/A	30.4
	STDEV	0.59	N/A	0.27
	CV	1.81%	N/A	0.89%
	No. of results	192		192

Table 8. Summary of Ct Value Results by Target in Each Sample Level

GBS strain 2: Moderate Positive				
		SPC	GBS	IC
Infinity-80 n=96	MEAN	32.62	35.6	30.39
	STDEV	0.99	0.51	0.23
	CV	3.05%	1.43%	0.76%
	No. of results	96	96	96
GeneXpert Dx n=96	MEAN	32.82	35.63	30.44
	STDEV	0.49	0.52	0.29
	CV	1.51%	1.47%	0.95%
	No. of results	96	96	96
Overall n=192	MEAN	32.72	35.61	30.42
	STDEV	0.79	0.51	0.26
	CV	2.41%	1.44%	0.86%
	No. of results	192	192	192
GBS strain 2: Low Positive				
		SPC	GBS	IC
Infinity-80 n=96	MEAN	32.8	37.06	30.48
	STDEV	0.68	1.00	0.69
	CV	2.07%	2.69%	2.25%
	No. of results	96	94	96
GeneXpert Dx n=96	MEAN	32.65	36.92	30.44
	STDEV	0.56	0.94	0.28
	CV	1.72%	2.56%	0.92%
	No. of results	96	95	96
Overall n=192	MEAN	32.72	36.99	30.46
	STDEV	0.63	0.97	0.52
	CV	1.91%	2.63%	1.72%
	No. of results	192	189	192

Table 8. Summary of Ct Value Results by Target in Each Sample Level

GBS strain 2: High Negative				
		SPC	**GBS**	**IC**
Infinity-80 n=96	**MEAN**	32.7	N/A	30.39
	STDEV	0.54	N/A	0.22
	CV	1.67%	N/A	0.73%
	No. of results	96		96
GeneXpert Dx n=96	**MEAN**	32.79	N/A	30.46
	STDEV	0.58	N/A	0.26
	CV	1.78%	N/A	0.85%
	No. of results	96		96
Overall n=192	**MEAN**	32.74	N/A	30.43
	STDEV	0.56	N/A	0.24
	CV	1.72%	N/A	0.80%
	No. of results	192		192
Negative				
		SPC	**GBS**	**IC**
Infinity-80 n=96	**MEAN**	32.67	N/A	30.39
	STDEV	0.54	N/A	0.21
	CV	1.64%	N/A	0.67%
	No. of results	96		96
GeneXpert Dx n=96	**MEAN**	32.68	N/A	30.39
	STDEV	0.50	N/A	0.30
	CV	1.53%	N/A	0.97%
	No. of results	96		96
Overall n=192	**MEAN**	32.68	N/A	30.39
	STDEV	0.52	N/A	0.25
	CV	1.58%	N/A	0.84%
	No. of results	192		192

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10. Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z).

26 Cepheid Headquarters Locations

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27 Technical Assistance

Before contacting Cepheid Technical Support, collect the following information:

- Product name
- Lot number
- Serial number of the instrument
- Error messages (if any)
- Software version and, if applicable, Computer Service Tag number

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28 Table of Symbols

Symbol	Meaning
	Catalog number
	*In vitro* diagnostic medical device
	Do not reuse
	Batch code
	Consult instructions for use
	Caution
	Manufacturer
	Country of manufacture
	Contains sufficient for <n> tests
	Control
	Expiration date
	Temperature limitation
	Biological risks
	Warning

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