GeneXpert
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Xpert® Xpress GBS

REF XPRSGBS-CE-10

Instructions for Use

CE 2797 IVD

Cepheid

In Vitro Diagnostic Medical Device

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Trademark, Patents, and Copyright Statements

See Section 29, Revision History for a description of changes.

Xpert® Xpress GBS

In Vitro Diagnostic Use Only

1 Proprietary Name

Xpert® Xpress GBS

2 Common or Usual Name

Xpert Xpress GBS

3 Intended Purpose

3.1 Intended Use

The Xpert® Xpress GBS test, performed on GeneXpert® systems, is an automated qualitative *in vitro* diagnostic real-time polymerase chain reaction (PCR) test for the detection of DNA from Group B *Streptococcus* (GBS). The test is performed using a dual vaginal/rectal swab specimen collected from pregnant patients during antepartum or intrapartum.

The Xpert Xpress GBS test is intended to aid in the detection of GBS colonization to identify candidates for antibiotic prophylaxis.

The Xpert Xpress GBS test does not provide antimicrobial susceptibility test results. Culture is necessary to obtain isolates to perform susceptibility testing as recommended for penicillin-allergic patients.

3.2 Intended User/Environment

The Xpert Xpress GBS is intended to be performed by healthcare professionals trained on the use of the test. This test is for use in a laboratory or near-patient testing environment.

4 Summary and Explanation

GBS bacterial infection is associated with serious illness in newborns born to GBS-colonized pregnant patients. GBS usually colonizes the rectal and/or vaginal mucosae in adults and colonization may be chronic as well as transient or intermittent. GBS infection is the major cause of death in newborns who develop sepsis, pneumonia, or meningitis.[1, 2] About half of patients who are colonized with GBS will transmit the bacteria to their newborns. Transmission of GBS usually occurs during labor or after rupture of membranes.

Currently, the standard of care for preventing neonatal GBS disease is either antepartum screening of pregnant patients or intrapartum screening during labor to determine their GBS colonization status. Intrapartum antibiotic prophylaxis (IAP) is then administered to GBS-colonized women to reduce vertical transmission of GBS and to lower the risk of neonatal infections.[1, 2] Most antepartum GBS testing is performed by culture, or a nucleic acid amplification test (NAAT) performed on an enrichment broth culture after 18–24 hour incubation[3], and typically takes one to three days to finalize results. This timing might be adequate for obtaining antepartum GBS results; however, some patients may not have GBS results available at the onset of labor. For patients who have had no prenatal care, or who might deliver preterm, or whose GBS test results are unknown at the time of delivery, intrapartum testing performed directly from a non-enriched swab specimen can provide results in time to decide whether to administer antibiotics before delivery. In addition, the transient or intermittent colonization feature of GBS can lead to a change in colonization status during pregnancy which is in turn associated to a 70% sensitivity of the antenatal culture when compared to intrapartum strategies. This indicates that 3 out of 10 women

may be falsely identified as non-colonized and therefore may not receive IAP.[4] Another study showed that only 40% of antenatally colonized women are confirmed GBS positive intrapartum, suggesting an overuse of antibiotics when relying on antenatal culture results only.[5]

The potential impact of intrapartum testing is decreased use of unnecessary antibiotics in patients not otherwise indicated for prophylaxis and reduced potential effect on the intestinal microbiota of infants[6], while providing adequate prophylaxis of GBS-colonized patients with the resulting decreased risk of neonatal sepsis or meningitis.[7]

5 Principle of the Procedure

The Xpert Xpress GBS test is an automated *in vitro* diagnostic test for qualitative detection of DNA from Group B Streptococcus (GBS). The test is performed on the Cepheid GeneXpert Instrument Systems (Dx or Infinity Systems). The primers and probes in the Xpert Xpress GBS test are designed to amplify and detect unique sequences in two GBS chromosomal targets – the first is a target within a coding region for a glycosyl transferase family protein and the second target is within a coding region for a *LysR* family transcriptional regulator of *Streptococcus agalactiae* DNA.

The GeneXpert Instrument Systems automate and integrate sample processing, nucleic acid purification and amplification, and detection of target sequences in simple or complex samples using real-time PCR Polymerase Chain Reaction (PCR). The GeneXpert systems consist of an instrument, computer, and preloaded software for running tests and viewing the results. The systems require the use of single-use disposable cartridges that contain the PCR reagents and host the PCR process. Because the cartridges are self-contained, cross-contamination between samples is minimized. For a full description of the systems, refer to the *GeneXpert Dx System Operator Manual* or the *GeneXpert Infinity System Operator Manual*.

The Xpert Xpress GBS test includes reagents for the direct detection of GBS target DNA from vaginal/rectal swabs specimens. A Sample Processing Control (SPC), a Sample Adequacy Control (SAC) and a Probe Check Control (PCC) are also included in the cartridge utilized by the GeneXpert instrument. The SPC is present to control for adequate processing of the sample and to monitor for the presence of potential inhibitor(s) in the PCR reaction. The SPC also ensures that the PCR reaction conditions (temperature and time) are appropriate for the amplification reaction and that the PCR reagents are functional. The SAC detects the presence of the human hydroxymethylbilane synthase (HMBS) gene and ensures that sufficient sample is collected and contains adequate human DNA. The PCC verifies reagent rehydration, PCR tube filling, and confirms that all reaction components are present in the cartridge including monitoring probe integrity and dye stability.

The dual vaginal/rectal swab specimen is collected from pregnant patients at intrapartum/antepartum and placed into a transport tube containing Liquid Stuart Medium. After collecting and transporting a swab specimen to the GeneXpert testing area, testing is performed by directly inserting the swab into the sample chamber of the Xpert Xpress GBS cartridge. The GeneXpert cartridge is loaded onto the GeneXpert Instrument System platform, which performs hands-off, automated sample processing, and real-time PCR for detection of GBS DNA.

The Xpert Xpress GBS test has an Early Assay Termination (EAT) function that provides earlier time to result in high titer specimens if the signal from the GBS target reaches a pre-determined threshold before all the PCR cycles have been completed. When GBS titers are high enough to initiate the EAT function, the SPC and SAC amplification curves may not be seen, and their results may not be reported.

6 Reagents and Materials

6.1 Materials Provided

The Xpert Xpress GBS test kit (XPRSGBS-CE-10) contains sufficient reagents to process 10 patient or quality-control specimens. The kit contains the following:

Xpert Xpress GBS Cartridges with Integrated Reaction Tubes **10 per kit**

Component/Reagent	Ingredient	Amount
Beads (freeze-dried)	Enzyme: polymerase < 5%	3 per cartridge
	dNTPs < 5%	
	Primer and probes < 5%	
	Internal control - bacterial origin < 5%	
	Protein stabilizer - bovine origin < 5%	
	PCR buffer < 5%	
Reagents	Chelating agent < 5%	4.5 mL per cartridge
	Tris buffer < 5%	
	Detergent < 5%	
	Sodium hydroxide < 5%	

Abbreviated Instructions for Use **1 per kit**

CD **1 per kit**

- Assay Definition Files (ADF)
- Instructions to import ADF into GeneXpert software
- Instructions for Use (IFU) (For use with the GeneXpert Dx and Infinity Systems only)

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

Note The protein stabilizer 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.

7 Storage and Handling

- Store the Xpert Xpress GBS cartridges at 2 °C to 28 °C.
- Do not use cartridges that have passed the expiration date on the label.
- Do not use a cartridge that has leaked.
- Do not open the cartridge lid until you are ready to perform testing.

8 Materials Required but Not Provided

- Cepheid Collection Device (part number 900-0370)
- GeneXpert Dx System or GeneXpert Infinity System (catalog number varies by configuration): GeneXpert instrument, computer, barcode scanner, and operator manual.

- For *GeneXpert Dx System*: GeneXpert Dx software version 5.3 or higher
- For *GeneXpert Infinity-80* and *Infinity-48s systems*: Xpertise software version 6.8 or higher

9 Materials Available but Not Provided

Printer: If a printer is required, contact Cepheid Technical Support to arrange for the purchase of a recommended printer.

10 Warnings and Precautions

10.1 General

- For *in vitro* diagnostic use.
- For single-use only. Each single-use cartridge is used to process one test. Do not reuse spent cartridges.
- Follow your institution's safety procedures for working with chemicals and handling biological samples.
- Treat all biological specimens, including used cartridges, 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 Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work (seventh individual directive within the meaning of Article 16(1) of Directive 89/391/EEC).[8] 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.[9]
- Follow good laboratory practices. Change gloves between handling each patient specimen in order to avoid contamination of specimens or reagents. Regularly clean the work surface/areas.
- Wear protective disposable gloves, laboratory coats and eye protection when handling specimens and reagents. Wash hands thoroughly after handling specimens and test reagents.
- 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.
- In the event of contamination of the work area or equipment with samples or controls, thoroughly clean the contaminated area with a freshly prepared solution of 0.5% sodium hypochlorite (or a 1:10 dilution of household chlorine bleach). Follow by wiping the surface with 70% ethanol. Let work surfaces dry completely before proceeding.
- Clean the work surface/areas with 10% bleach before and after processing Xpert Xpress GBS 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.

10.2 Specimens

- The intended performance of this test is dependent on appropriate specimen collection, storage, handling, and transport to the test site.
- Maintain proper storage conditions during specimen transport to ensure the integrity of the specimen (see Section 11, Specimen Collection, Transport and Storage). Specimen stability under shipping conditions other than those recommended has not been evaluated.
- Reliable results are dependent on adequate specimen collection, transport, storage, and processing. Incorrect test results may occur from improper specimen collection, handling or storage, technical error, sample mix-up or because the number of organisms in the specimen is below the limit of detection of the test. Careful compliance with the Instructions for Use and the *GeneXpert Dx System Operator Manual* or *GeneXpert Infinity System Operator Manual* are necessary to avoid erroneous results.

10.3 Test/Reagent

- Do not open the Xpert Xpress GBS cartridge lid except when adding specimen.
- 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 non-determinate results.
- Do not place the sample ID label on the cartridge lid or on the barcode label on the cartridge.
- Do not use a cartridge with a damaged barcode label.
- Do not substitute reagents with other reagents.
- Do not use a cartridge that has a damaged reaction tube.
- Do not use a visibly damaged cartridge.
- Each single-use Xpert Xpress GBS cartridge is used to process one test. Do not reuse processed cartridges.
- Do not use a cartridge if it appears wet or if the lid seal appears to have been broken.

11 Specimen Collection, Transport, and Storage

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

Collect vaginal/rectal swab specimens according to ACOG, European or local recommendations[1-3] using the Cepheid Collection Device (part number 900-0370).

1. Use gauze to wipe away excessive amounts of secretion or discharge from vaginal and rectal area.
2. Remove the Collection Device, a double swab, from the pouch.
3. Carefully insert the double swab into the patient's vagina. Sample secretions from the mucosa of the lower one-third part of the vagina. Rotate the swabs three times to ensure uniform sample on both swabs. Do not collect cervical sample.
4. Using the same double swab, carefully insert the swab approximately 2.5 cm beyond the anal sphincter, and gently rotate to sample anal crypts.

Important **Keep swabs attached to the red cap throughout the procedure.**

5. Remove and discard the clear cap on the transport tube and place swabs into the transport tube, labeled with Sample ID, pushing the red cap down completely.
6. When possible, store specimens at 2–8 °C when not being processed.
   - If the specimens will be processed *within 24 hours*, storage at up to 25 °C is acceptable.
   - If the specimens will be tested *after 24 hours*, refrigerate until testing is performed. Specimens may be stored up to six days at 2–8 °C.

12 Chemical Hazards[8]

Signal Word: Warning

Hazard Pictogram:

CLP Hazard Statements

- Causes skin irritation
- Causes serious eye irritation

CLP Precautionary Statements

- Wash face, hands and any exposed skin thoroughly after handling
- Wear protective gloves and eye/face protection
- Specific treatment (see supplemental first aid information)
- If skin irritation occurs: Get medical advice/attention
- If eye irritation persists: Get medical advice/attention
- Take off contaminated clothing and wash it before reuse

13 Procedure

13.1 Preparing the Cartridge

Important **Start the test within 30 minutes of adding the sample to the cartridge.**

Note Do not add two swabs to one cartridge. Only one swab is required. The second swab is extra and can be used for susceptibility or repeat testing. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic patients.

To add the specimen to the cartridge:

1. Wear protective disposable gloves.
2. Remove the cartridge from the package.
3. Inspect the test cartridge for damage. If damaged, do not use it.
4. If cartridge has been stored refrigerated ensure equilibration to room temperature prior to use.
5. Label the cartridge with sample identification.

Note Write on the side of the cartridge or affix an ID label. Do not put the label on the lid of the cartridge or over the existing 2D barcode on the cartridge.

6. Open the cartridge lid by lifting the front of the cartridge lid.
7. Open the cap of the specimen transport tube.
8. Remove the swabs from the transport tube.
9. Remove one swab from cap and gently brush the two swabs together using a twirling motion for five seconds (see Figure 1).

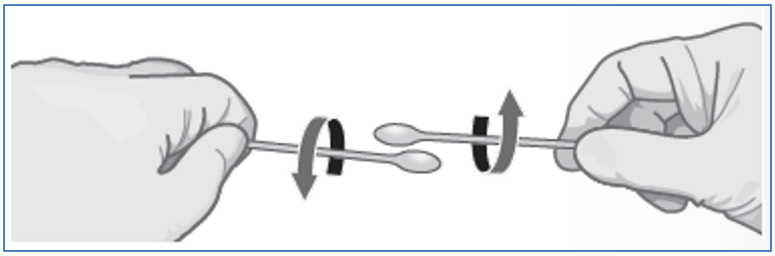

Figure 1. Swab Twirling Motion

10. Return the second swab still attached to the cap back into the transport tube.
11. Using gauze or equivalent, hold the swab to be used for testing above the score mark (see Figure 2).

Figure 2. Xpert Xpress GBS Collection Swab

12. Insert the swab into the Xpert Xpress GBS cartridge sample chamber (see Figure 3).

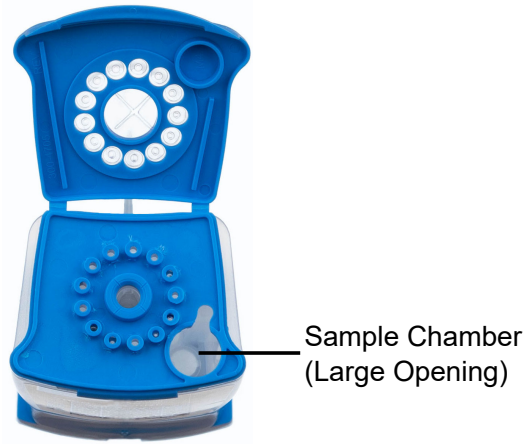

Figure 3. Xpert Xpress GBS Cartridge (Top View)

13. Raise the swab so that the score mark is centered in the notch.
14. Break the swab by snapping the shaft to the right.
15. Ensure the swab is properly positioned in the cartridge and the swab end is not in the notch of the sample chamber opening and does not prevent lid closure. If the swab is stuck in the notch, use a lint free wipe/gauze or the remaining end of the swab to release it from the notch to minimize the risk of contamination.
16. Close the cartridge lid. Start the test within 30 minutes.

13.2 External Controls

External controls may be used in accordance with local, state, and country accrediting organizations, as applicable.

14 Running the Test

- For the GeneXpert Dx System, see Section 14.1.
- For the GeneXpert Infinity System, see Section 14.2.

14.1 GeneXpert Dx System

14.1.1 Starting the Test

Before you start the test, make sure that:

Important

- The system is running the correct GeneXpert Dx software version shown in section— Materials Required but Not Provided.
- The correct assay definition file is imported into the software.

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Dx System Operator Manual*.

Note The steps you follow can be different if the system administrator changed the default workflow of the system.

1. Turn on the GeneXpert Dx System, then turn on the computer and log on. The GeneXpert software will launch automatically. If it does not, double-click the GeneXpert Dx software shortcut icon on the Windows® desktop.
2. Log on using your username and password.
3. In the **GeneXpert System** window, click **Create Test**.
   The **Create Test** window displays. The **Scan Patient ID barcode** dialog box displays.
4. Scan or type in the Patient ID. If typing the Patient ID, make sure the Patient ID is typed correctly.
   The Patient ID is associated with the test results and displays in the **View Results** window and all the reports. The **Scan Sample ID barcode** dialog box displays.
5. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly.

The Sample ID is associated with the test results and displays in the **View Results** window and all the reports. The **Scan Cartridge Barcode** dialog box displays.

6. Scan the barcode on the 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.

Note If the barcode on the cartridge does not scan, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the software and the assay definition file is not available, a screen displays indicating the assay definition file is not loaded on the system. If this screen displays, contact Cepheid Technical Support.

7. Click **Start Test**. In the dialog box that displays, type your password, if required.
8. Open the instrument module door with the blinking green light and load the cartridge.
9. Close the door. The test starts and the green light stops blinking.

   When the test is finished, the light turns off.
10. Wait until the system releases the door lock before opening the module door, then remove the cartridge.
11. Dispose of the used cartridges in the appropriate specimen waste containers according to your institution's standard practices.

14.1.2 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*.

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.

14.2 GeneXpert Infinity System

14.2.1 Starting the Test

Important

Before you start the test, make sure that:

- The system is running the correct Xpertise software version shown in section - Materials Required but Not Provided.
- The correct assay definition file is imported into the software.

This section lists the basic steps for running the test. For detailed instructions, see the *GeneXpert Infinity System Operator Manual*.

Note The steps you follow can be different if the system administrator changed the default workflow of the system.

1. Power up the instrument. The Xpertise software will launch automatically. If it does not, double-click the Xpertise software shortcut icon on the Windows® desktop.
2. Log on to the computer, then log on to the GeneXpert Xpertise software using your user name and password.
3. In the **Xpertise Software Home** workspace, click **Orders** and in the **Orders** workspace, click **Order Test**.
   The **Order Test - Patient ID** workspace displays.
4. Scan or type in the Patient ID. If typing the Patient ID, make sure the Patient ID is typed correctly.
   The Patient ID is associated with the test results and displays in the **View Results** window and all the reports.
5. Enter any additional information required by your institution and click the **CONTINUE** button.
   The **Order Test - Sample ID** workspace displays.
6. Scan or type in the Sample ID. If typing the Sample ID, make sure the Sample ID is typed correctly.
   The Sample ID is associated with the test results and displays in the **View Results** window and all the reports.
7. Click the **CONTINUE** button.
   The **Order Test - Assay** workspace displays.
8. Scan the barcode on the 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.

Note If the barcode on the cartridge does not scan, then repeat the test with a new cartridge. If you have scanned the cartridge barcode in the software and the assay definition file is not available, a screen displays indicating the assay definition file is not loaded on the system. If this screen displays, contact Cepheid Technical Support.

After the cartridge is scanned, the **Order Test - Test Information** workspace displays.

9. Verify that the information is correct and click **Submit**. In the dialog box that displays, type your password, if required.
10. Place the cartridge on the conveyor belt.
    The cartridge automatically loads, the test runs, and the used cartridge are placed into the waste container.

14.2.2 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 Infinity System Operator Manual*.

1. In the **Xpertise Software Home** workspace, click the **RESULTS** icon. The Results menu displays.
2. In the Results menu, select the **VIEW RESULTS** button. The **View Results** workspace displays showing the test results.
3. Click the **REPORT** button to view and/or generate a PDF report file.

15 Quality Control

15.1 Internal Controls

Each test includes a Sample Processing Control (SPC), Sample Adequacy Control (SAC) and a Probe check control (PPC).

- **Sample Adequacy Control (SAC)**: Detects the presence of a single copy human gene present in one copy per cell and monitors whether the sample contains human DNA. The SAC controls for adequate sample collection and sample stability to minimize risk of false negative. The SAC should PASS (*i.e.*, generate a valid cycle threshold (Ct) in a negative sample) and may not amplify in a high positive sample. The SAC passes if it meets the assigned acceptance criteria and is required for a **GBS NEGATIVE** result.
- **Sample Processing Control (SPC)**: Ensures the sample was processed correctly. The SPC verifies that sample processing is adequate. Additionally, this control detects sample-associated inhibition of the real-time PCR assay, ensures the PCR reaction conditions (temperature and time) are appropriate for the amplification reaction, and that the PCR reagents are functional. The SPC should PASS (*i.e.*, 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.
- **Probe Check Control (PCC)**: 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 External Controls meets the assigned acceptance criteria.

15.2 External Controls

External controls should be used in accordance with local, state, and federal accrediting organizations as applicable.

16 Interpretation of Results

The results are determined 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 Xpress GBS Assay results are provided in Figure 4, Figure 5, Figure 6, Figure 7, and Figure 8.

Table 1. GBS Results and Interpretation

Result	Interpretation
GBS — POSITIVE[a] See Figure 4.	GBS target DNA is detected – presumed for GBS colonization. • GBS — POSITIVE • SPC — NA (not applicable). The SPC is ignored because GBS target amplification can compete with this control • Probe Check Controls — PASS • SAC — NA (not applicable)
GBS — NEGATIVE See Figure 5.	GBS target DNA is not detected - presumed not colonized for GBS. • GBS — NEGATIVE • SPC — PASS • Probe Check Controls — PASS • SAC — PASS
INVALID See Figure 6.	Presence or absence of the GBS target DNA cannot be determined. SAC and/ or SPC failed and does not meet acceptance criteria. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. • GBS — INVALID • SPC — FAIL[b] • Probe Check Controls — PASS • SAC — FAIL[b]
ERROR See Figure 7.	Presence or absence of GBS target DNA cannot be determined. A system component failed, the maximum pressure was reached, or the probe check failed. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. • GBS — NO RESULT • SPC — NO RESULT • Probe Check Controls — FAIL[c] • SAC — NO RESULT
NO RESULT See Figure 8.	Insufficient data was collected. Presence or absence of GBS target DNA cannot be determined. 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 during the test. Repeat test according to the Retest Procedure in Section 17.2 of the IFU. • GBS — NO RESULT • SPC — NO RESULT • Probe Check Controls — NA (not applicable) • SAC — NO RESULT

[a] The Xpert Xpress GBS test includes an Early Assay Termination (EAT) function that will provide earlier time to results in high titer specimens if the signal from the GBS target reaches a predetermined threshold before the PCR cycles have been completed. When GBS titers are high enough to initiate the EAT function, the SPC and SAC amplification curves may not be seen, and their results may not be reported. EAT can reduce the test time for positive results to approximately ~30 minutes. With GBS negative samples, the test returns within ~42 minutes.

[b] The SPC and/or the SAC failed.

[c] If the probe check passed, the error is caused by a system component failure or by exceeding maximum allowable pressure.

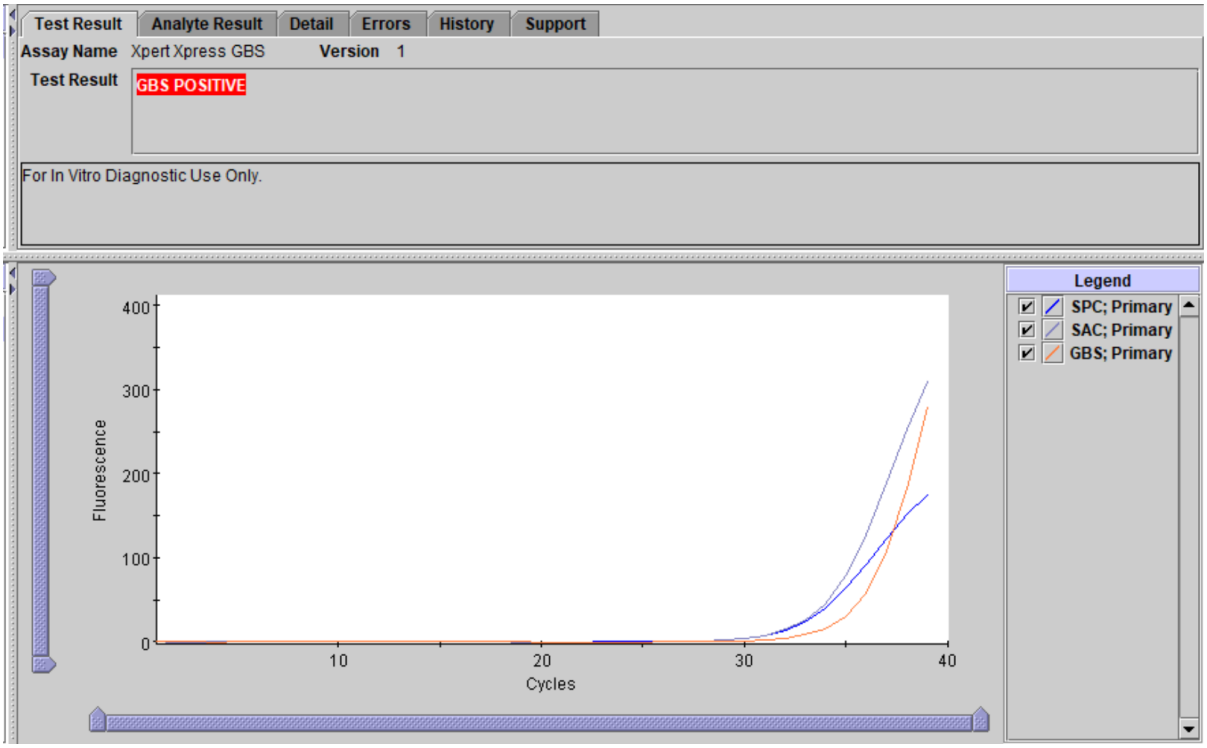

Figure 4. An Example of a GBS POSITIVE Result

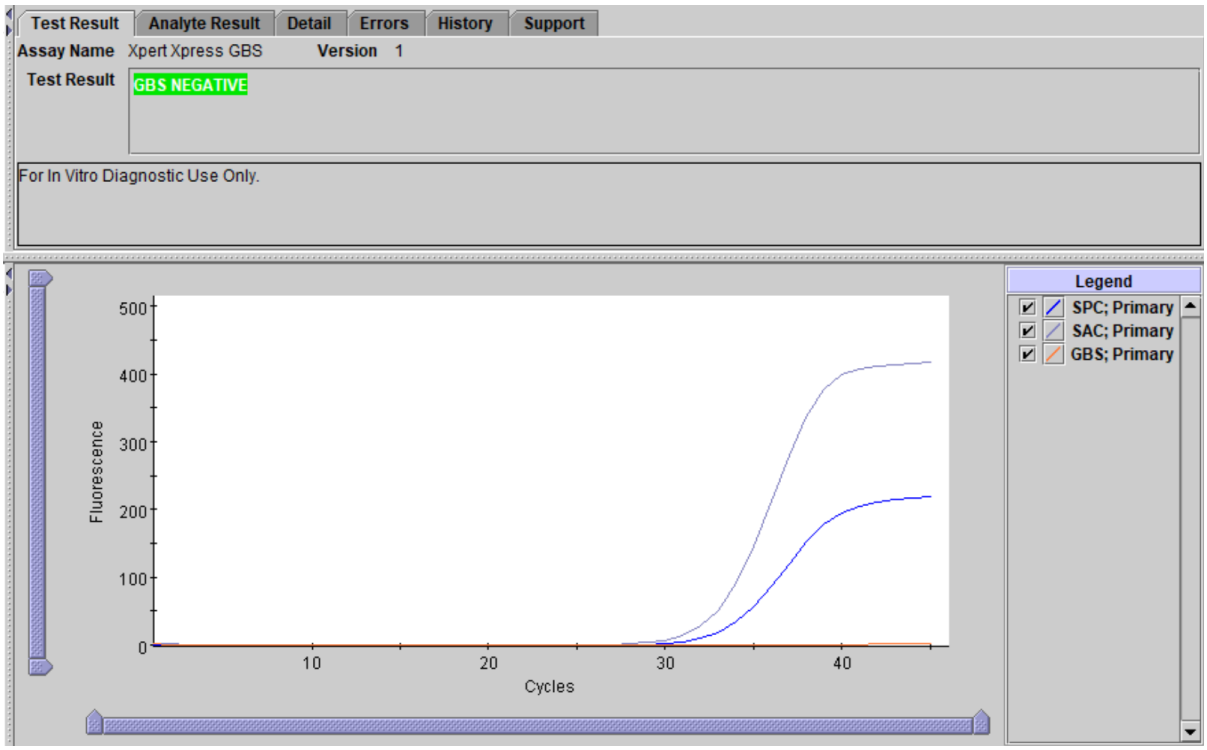

Figure 5. An Example of a GBS NEGATIVE Result

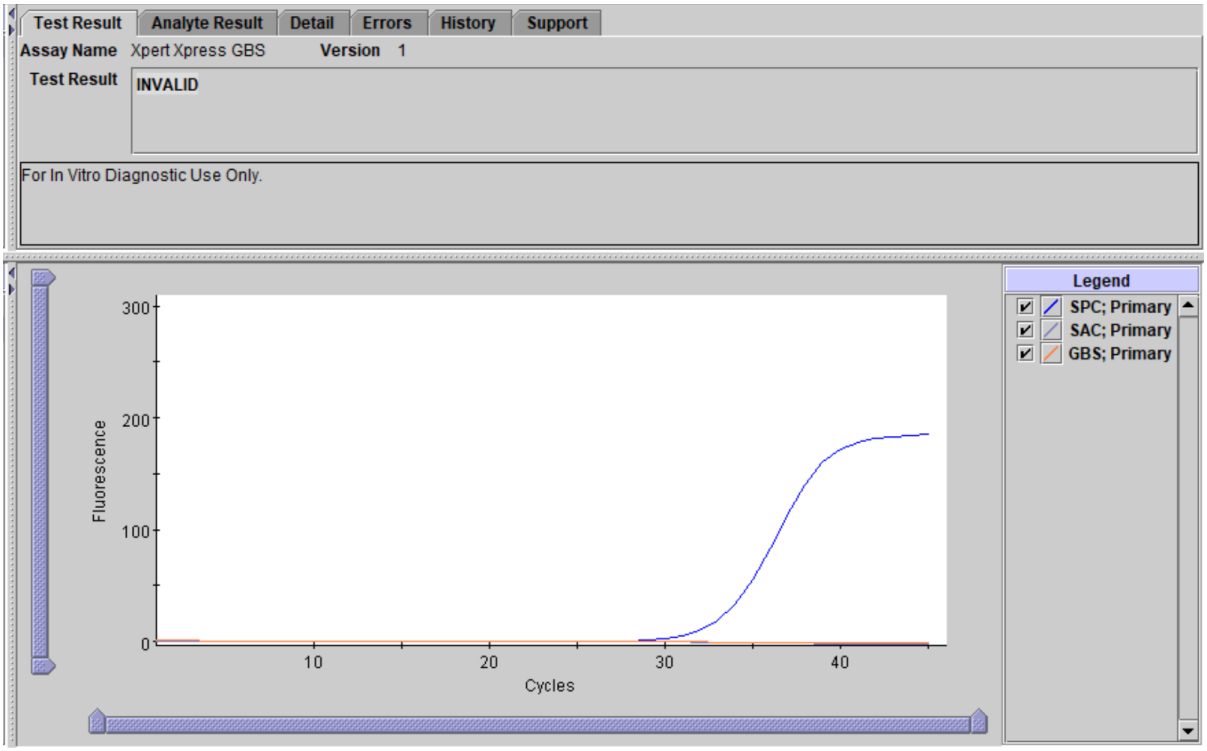

Figure 6. An Example of an Invalid Result

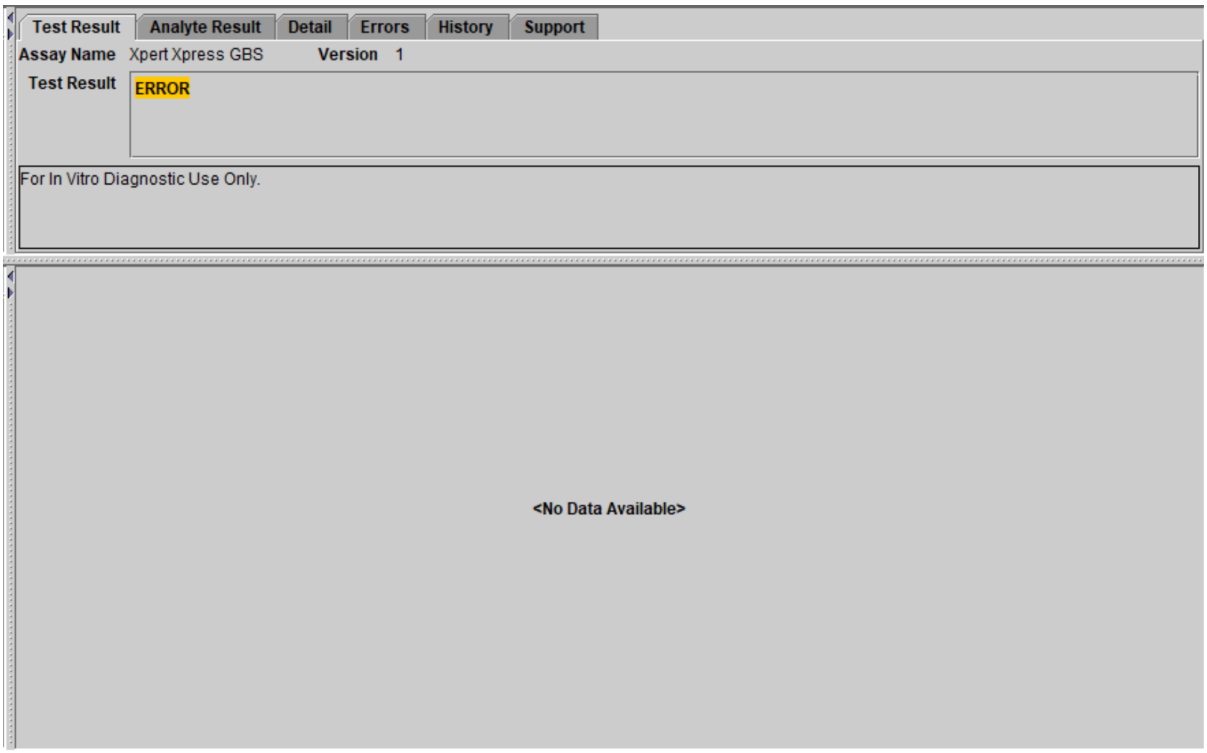

Figure 7. An Example of an ERROR Result

Figure 8. An Example of NO RESULT

17 Retesting

17.1 Reasons to Repeat Testing

If any of the test results mentioned below occur, repeat the test according to the instructions in Section 17.2.

- An **INVALID** result indicates GBS is not detected and the control SPC and/or SAC failed in one or more of the following causes:
  - The specimen was not properly collected or processed.
  - The specimen was not added to the cartridge.
  - 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; system component failure 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.

17.2 Retest Procedure

For retest of a **NO RESULT**, **INVALID**, or **ERROR** result, use a new cartridge (do not re-use the cartridge). Use the remaining specimen swab for retesting.

1. Remove the cartridge from the package. Open the cartridge by lifting the cartridge lid.
2. Remove the remaining swab from the collection transport tube.
3. Insert swab into the sample chamber of a new Xpert Xpress GBS cartridge.
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. Ensure the swab is properly positioned in the cartridge and the swab end is not in the notch of the sample chamber opening and does not prevent lid closure. If the swab is stuck in the notch, use a lint free wipe/gauze or the remaining end of the swab to release it from the notch to minimize the risk of contamination.

7. Close the cartridge lid.
8. Follow the procedure for starting a test.
    - For the *GeneXpert Dx System*, see Section 14.1.
    - For the *GeneXpert Infinity System*, see Section 14.2.

When performing intrapartum testing, repeat testing may not be feasible and will depend on practices and policies within each facility. Coordination between clinicians and the testing laboratory is important to not delay administration of antibiotics while results are pending.

18 Limitations

- Erroneous test results might occur from improper specimen collection, handling or storage, technical error, or sample mix-up. Careful compliance to the instructions in this insert is important to avoid erroneous results.
- The performance of the Xpert Xpress GBS test was validated using the procedures provided in these Instructions for Use only. Modifications to these procedures may alter the performance of the test.
- The Xpert Xpress GBS test has only been validated with the vaginal/rectal swab specimen using the Cepheid Collection device (listed in Section 8).
- A negative result does not exclude the possibility of GBS colonization. False negative results may occur if the organism is present at levels below the analytical limit of detection.
- The Xpert Xpress GBS test does not provide antibiotic susceptibility results. Culture isolates are needed to perform susceptibility testing as recommended for penicillin-allergic patients.
- Test results may be affected by concurrent antibiotic therapy. GBS DNA may continue to be detected following antimicrobial therapy.
- The effect of interfering substances has only been evaluated for those listed within the labeling. Interference by substances other than those described can lead to erroneous results.
- A positive result does not necessarily indicate the presence of viable organisms.
- Mutations in primer or probe binding regions may affect detection of new or unknown variants and may result in a false negative result.
- This test was validated on vaginal/rectal swab specimens collected at antepartum or intrapartum from antibiotic naïve pregnant patients. The use of this test has not been validated in pregnant patients having received antibiotics within 14 days prior to sample collection.
- Clinical data includes antibiotic naïve pregnant study participants of 14 years of age or older. The 14–17 age group for antibiotic naïve pregnant participants includes two intrapartum vaginal/rectal specimens and zero antepartum vaginal/rectal specimens.

19 Expected Values

The Xpert Xpress GBS clinical study included vaginal/rectal specimens collected from antibiotic naïve pregnant female participants. The number and percentage of specimens positive for GBS as determined by the Xpert Xpress GBS test are presented in Table 2, per specimen collection type.

Table 2. Positivity Rates by the Xpert Xpress GBS Test in Participants at Antepartum and Intrapartum

Specimen Collection Type	Number of Specimens	Number of Positives	Positivity
Antepartum vaginal/rectal	661	128	19.4%
Intrapartum vaginal/rectal	899	109	12.1%

20 Clinical Performance

Performance characteristics of the Xpert Xpress GBS test were evaluated in a multi-site observational, method comparison study using vaginal/rectal swab specimens collected from pregnant patients. The study was conducted at thirteen (13) sites across the United States (10 enrollment and Xpert testing sites; 1 enrollment only site; 1 reference laboratory site that

conducted Xpert testing and comparator method testing; 1 reference laboratory that conducted discrepant testing with an FDA cleared NAAT). Three of the eleven Xpert testing sites were near patient testing (NPT) settings (i.e., in the Labor & Delivery unit, outside a laboratory environment).

The clinical performance of the Xpert Xpress GBS test was compared to enriched bacterial culture with species identification via MALDI-TOF MS. Eligible participants provided two sets of dual vaginal/rectal swabs. The first set of swabs was divided – one swab was used for Xpert Xpress GBS testing; the other was used for culture, if the Xpert Xpress GBS test gave a valid result. If the Xpert Xpress GBS test resulted in a non-determinate result, the second set of marked swabs was divided – one swab was used for repeat Xpert Xpress GBS testing; the other was used for culture testing. The study included testing vaginal/rectal swab specimens collected from antibiotic naïve pregnant study participants at antepartum and intrapartum.

Discordant results between the Xpert Xpress GBS test and the comparator method were investigated using an FDA-cleared nucleic acid amplification test (NAAT); the results of which are footnoted in Table 4, for informational purposes only.

Performance of the Xpert Xpress GBS Test vs. Enriched Culture + MALDI-TOF MS

One thousand five-hundred seventy-nine (1579) vaginal/rectal swab specimens were enrolled from eligible participants. Age distribution of vaginal/rectal specimens collected at intrapartum and antepartum are represented in Table 3.

Table 3. Age Distribution of Specimens Included

Age Group	Antepartum Vaginal/ Rectal (ABX-) N (%)	Intrapartum Vaginal/ Rectal (ABX-) N (%)
14-17	0 (0.0%)	2 (0.2%)
18-24	153 (22.9%)	285 (31.3%)
25-34	403 (60.4%)	507 (55.6%)
≥ 35	111 (16.6%)	118 (12.9%)
Total	667 (100.0%)	912 (100.0%)

Of the 1579 eligible specimens, 667 were collected at antepartum and 912 were collected at intrapartum. Six specimens collected at antepartum were excluded from analyses due to retests not being performed or retests resulting in non-determinate Xpert Xpress GBS results. A total of 661 antepartum vaginal/rectal specimens were included in the analyses. Thirteen specimens collected at intrapartum were excluded from analyses due to non-determinate Xpert Xpress results upon retest or no culture results. A total of 899 intrapartum vaginal/rectal specimens were included in the analyses. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the Xpert Xpress GBS test as compared to enriched culture with species identification via MALDI-TOF MS are presented in Table 4. Clinical performance characteristics such as likelihood ratio and threshold values in normal and affected populations were not performed as Xpert Xpress GBS is intended to aid in the detection of GBS DNA and is not intended to be used as a diagnostic test.

The sensitivity and specificity of the Xpert Xpress GBS test compared to the comparator method were 88.1% and 95.6% in vaginal/rectal swab specimens collected at antepartum and 93.5% and 95.5% in vaginal/rectal swab specimens collected at intrapartum, respectively. The PPV and NPV of the Xpert Xpress GBS test compared to the comparator method were 81.3% and 97.4% in vaginal/rectal swab specimens collected at antepartum and 66.1% and 99.4% in vaginal/rectal swab specimens collected at intrapartum, respectively. The Xpert Xpress GBS test met the sensitivity and specificity performance criteria in antibiotic naïve pregnant study participants at antepartum and intrapartum.

Non-Determinate Rate

Of the 1579 Xpert Xpress GBS tests performed in the clinical study, 78 resulted in non-determinate (**Error**, **Invalid**, **No Result**, **Instrument Error** or **No Result-Repeat Test**) results on first attempt. Of these 78 specimens, 76 were retested per protocol. Upon retest, 18 specimens remained non-determinate. The initial non-determinate rate was 4.9% (78/1579) overall. Upon retest, the final non-determinate rate was 1.1% (18/1579) overall.

The initial non-determinate rate for antepartum specimens was 3.4% (23/667) and the final non-determinate rate was 0.9% (6/667). The initial non-determinate rate for intrapartum specimens was 6.0% (55/912) and the final non-determinate rate was 1.3% (12/912).

Table 4. Xpert Xpress GBS Results and Estimated Performance by Specimen Collection Type

Specimen Collection Type	Results	Culture Positive	Culture Negative	Total	Sensitivity (95% Confidence Interval)	Specificity (95% Confidence Interval)	PPV (95% Confidence Interval)	NPV (95% Confidence Interval)
Antepartum vaginal/ rectal	Xpert Xpress GBS Positive	104	24[a]	128	88.1% (81.1–92.8)	95.6% (93.5–97.0)	81.3% (73.6–87.1)	97.4% (95.6–98.4)
	Xpert Xpress GBS Negative	14[b]	519	533				
	Total	118	543	661				
Intrapartum vaginal/ rectal	Xpert Xpress GBS Positive	72	37[c]	109	93.5% (85.7–97.2)	95.5% (93.9–96.7)	66.1% (56.8–74.3)	99.4% (98.5–99.7)
	Xpert Xpress GBS Negative	5[d]	785	790				
	Total	77	822	899				

[a] Discrepant test results based on an FDA cleared NAAT: 14/24 GBS positive; 7/24 GBS negative; 3/24 no valid result

[b] Discrepant test results based on an FDA cleared NAAT: 11/14 GBS positive; 3/14 no valid result

[c] Discrepant test results based on an FDA cleared NAAT: 13/37 GBS positive; 15/37 GBS negative; 9/37 no valid result

[d] Discrepant test results based on an FDA cleared NAAT: 4/5 GBS positive; 1/5 GBS negative

21 Analytical Performance

21.1 Analytical Sensitivity (Limit of Detection) and Analytical Reactivity (Inclusivity)

The analytical limit of detection (LoD) and analytical reactivity (inclusivity) of the Xpert Xpress GBS test were determined for 12 different strains representing 12 known serotypes of GBS, 2 of which were characterized as non-hemolytic (Table 5). Serial dilutions of each serotype were prepared in a simulated sample matrix. Serotypes Ia, III and V were tested with 24 replicates per dilution level for each of two reagent lots across three days. Serotypes Ib, Ic, II, IV and VI-X were tested in replicates of 24 for each dilution level using one reagent lot across three days. The LoD was established for each serotype and reagent lot by probit logistic regression analysis. The LoD for each serotype was verified by testing 20 replicates at the 95% confidence interval upper limit with one reagent lot across three days, in a simulated sample matrix. Serotype Ia, III and V was also verified in clinical matrix. The results for all serotypes except serotype V and VI were ≥95% (≥19/20) percent detected. The result for serotype V and VI was 85% (17/20) percent detected and the claimed LoD is based on the upper level of 95% confidence interval, as shown in Table 5.

Table 5. GBS Limit of Detection (LoD)

Serotype	LoD (CFU/mL) Probitresult	95% CI	LoD (CFU/mL) Claimed LoD	LoD (CFU/swab) Claimed LoD
Ia	663	492-835	663	50
Ib	40	32-49	40	3

Serotype	LoD (CFU/mL) Probitresult	95% CI	LoD (CFU/mL) Claimed LoD	LoD (CFU/swab) Claimed LoD
Ic[a]	301	231-370	301	23
II[a]	173	132-213	173	13
III	540	409-670	540	41
IV	429	324-533	429	32
V	618[b]	384-618	618[b]	46
VI	544[b]	353-544	544[b]	41
VII	620	512-728	620	47
VIII	682	509-855	682	51
IX	465	354-575	465	35
X	677	525-829	677	51

[a] Non-hemolytic strain

[b] Claimed LoD corresponds to 95% upper CI

21.2 Analytical Reactivity with GBS cfb Mutants

A study was performed to evaluate the analytical reactivity (inclusivity) of Xpert Xpress GBS for strains containing different deletions ranging from 181 bp to 49 kb in or adjacent to the region of the chromosome that encodes the CAMP factor hemolysis gene *cfb*. Ten (10) unique, well characterized GBS clinical specimens representing different *cfb* mutations were diluted in simulated sample matrix to a concentration of 855 CFU/mL (~ 1x the highest observed LoD) and tested in the Xpert Xpress GBS test. The study was conducted over 3 days testing either 6 or 7 replicates on each day for a total of 20 replicates. All strains with *cfb* mutations were detected with a positivity rate of 100%.

21.3 Analytical Specificity (Exclusivity) and Microbial Interference

The analytical specificity and microbial interference of the Xpert Xpress GBS test were evaluated by testing a panel of 129 non-target challenge (non-GBS) organisms that can potentially cross-react or interfere with the detection of GBS both in the presence (microbial interference) and absence (exclusivity) of GBS. Challenge organisms tested included bacterial, viral, parasite and yeast strains commonly found in vaginal/rectal flora or phylogenetically related to GBS and are shown in Table 6.

Bacteria and yeast were tested at concentrations of $\geq 1x10^6$ CFU/mL, except for *Staphylococcus aureus* which was tested at $2x10^5$ CFU/mL. Viruses and parasites were tested at concentrations of $> 1x10^5$ units/mL (tachyzoites, IU or copies/mL). Genomic DNA was tested at $> 1x10^6$ copies/mL. The panel of 129 organisms were tested either individually or in pools of 2 - 6 microorganisms in simulated sample matrix, both in presence of GBS at 3x LoD and in absence of GBS. Each pool was tested in replicates of six (6). No cross-reactivity or microbial interference of GBS detection was observed with any of the clinically relevant pathogens tested in the study.

Table 6. Analytical Specificity of Xpert Xpress GBS

Organism		
Arcanobacterium (Trueperella) pyogenes	Haemophilus influenzae	Serratia marcescens
Atopobium (Fannyhessea) vaginae	Hafnia alvei	Shigella flexneri
Abiotrophia defectiva	Hepatitis B virus	Shigella sonnei
Acinetobacter baumannii	Hepatitis C virus	Staphylococcus aureus[a]

Organism		
Acinetobacter lwoffii	Human immunodeficiency virus	Staphylococcus epidermidis
Actinobacillus pleuropneumoniae	Human Papillomavirus 18[b]	Staphylococcus haemolyticus
Aeromonas hydrophila	Klebsiella (Enterobacter) aerogenes	Staphylococcus intermedius
Alcaligenes faecalis	Klebsiella oxytoca	Staphylococcus lugdunensis
Anaerococcus lactolyticus	Klebsiella pneumoniae	Staphylococcus saprophyticus
Anaerococcus prevotii[b]	Lactobacillus acidophilus	Staphylococcus simulans
Anaerococcus tetradius	Lactobacillus casei	Stenotrophomonas maltophilia
Bacillus cereus	Lactobacillus delbrueckii lactis	Streptococcus acidominimus
Bacillus coagulans	Lactobacillus gasseri	Streptococcus anginosus
Bacteroides fragilis	Lactobacillus plantarum	Streptococcus bovis
Bifidobacterium adolescentis Reuter	Lactobacillus reuteri	Streptococcus canis
Bifidobacterium brevis	Listeria monocytogenes	Streptococcus constellatus
BK virus	Micrococcus luteus	Streptococcus criceti
Blastocystis hominis[b]	Mobiluncus curtisii subsp. Curtisii[b]	Streptococcus cristatus
Bordetella pertussis	Moraxella atlantae	Streptococcus downei
Burkholderia cepacia	Moraxella catarrhalis	Streptococcus dysgalactiae subsp. dysgalactiae
Campylobacter jejuni	Morganella morganii	Streptococcus dysgalactiae subsp. equisimilis
Candida albicans	Mycoplasma genitalium[b]	Streptococcus equi subsp. equi
Candida glabrata	Neisseria gonorrhoeae	Streptococcus gordonii
Candida tropicalis	Norovirus	Streptococcus intermedius
Chlamydia trachomatis	Pantoea agglomerans	Streptococcus mitis
Citrobacter freundii	Pasteurella aerogenes	Serratia liquefaciens
Clostridium difficile	Peptoniphilus asaccharolyticus	Streptococcus mutans
Cytomegalovirus	Peptostreptococcus anaerobius	Streptococcus oralis
Corynebacterium accolens	Porphyromonas asaccharolytica	Streptococcus parasanguinis
Corynebacterium sp. (genitalium)	Prevotella bivia	Streptococcus pneumoniae
Corynebacterium urealyticum	Prevotella melaninogenica	Streptococcus pseudoporcinus
Cryptococcus neoformans	Prevotella oralis	Streptococcus pyogenes[b]
Enterobacter cloacae	Propionibacterium acnes	Streptococcus ratti
Enterococcus durans	Proteus mirabilis	Streptococcus salivarius
Enterococcus faecalis	Proteus vulgaris	Streptococcus sanguinis
Enterococcus faecium	Providencia stuartii [b]	Streptococcus sobrinus
Enterococcus gallinarum	Providencia sp.	Streptococcus suis

Organism		
Epstein-Barr virus	Pseudomonas aeruginosa	Streptococcus uberis
Escherichia coli	Pseudomonas fluorescens	Streptococcus vestibularis
Finegoldia magna	Rhodococcus equi	Toxoplasma gondii
Fusobacterium nucleatum	Rubella virus	Trichomonas vaginalis
Gardnerella vaginalis	Salmonella enterica subsp. enterica ser. Dublin (group D)	Vibrio cholerae
Giardia lamblia[b]	Salmonella enterica subp. typhimurium	Yersinia enterocolitica subsp. palearctica

[a] Tested < $1x10^6$ ($2x10^5$ CFU/mL)

[b] Evaluated with DNA

21.4 Potentially Interfering Substances Study

Substances that may be present in vaginal/rectal specimens with the potential to interfere with the Xpert Xpress GBS test were evaluated. Potentially interfering endogenous and exogenous substances include human amniotic fluid, meconium, 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. These substances are listed in Table 7.

Potentially interfering substances were tested according to a liquid, solid or tablet workflow. Liquid substances were added directly to the swab. Solid substances were added to the swab by dipping three fourths (3/4) of the swab head into the substance. Tablets were first dissolved in simulated sample matrix and the liquid added directly to the swab.

Negative samples consisting of simulated matrix only were tested in replicates of 6 in the presence of each substance to determine the effect on the performance of the sample processing control (SPC) and Sample Adequacy Control (SAC). Positive samples were prepared using GBS serotype Ia in simulated matrix at 3x LoD and were tested in replicates of 6 per substance. The negative and positive controls were prepared in the absence of potentially interfering substances and consisted of simulated sample matrix only and GBS spiked at 3x LoD into simulated sample matrix, respectively.

For substances that resulted in an **INVALID** test result, the concentration of the substance was reduced by dilution in simulated sample matrix and re-tested. Five exogenous substances (Aquasonic® gel, Floraplus, Pepto Bismol®, Body oil and Xyloproct) showed interference at the concentration initially tested and were subsequently tested at a lower concentration to determine the highest concentration at which no interference was observed. A list of the endogenous and exogenous substances and the highest concentrations at which all GBS positive and negative samples were correctly identified by the Xpert Xpress GBS test (*i.e.,* no observed interference) is shown in Table 7.

Table 7. Potentially Interfering Substances Tested

Substance	Highest Concentration on Swab resulting in No Interference
Human Amniotic Fluid	60% (v/v)
Human Urine	60% (v/v)
Human Whole Blood - EDTA	80% (v/v)
Human Whole Blood - Na Citrate	80% (v/v)
Leukocytes, Buffy coat, $2x10^7$ WBCs/mL	80% (v/v)
Meconium	100%[a]
Mucus – mucin from porcine stomach	30% (w/v)
Human Feces - Pool of 10 donors	100%
Anti-Diarrheal Medication – Pepto Bismol	40% (v/v)

Substance	Highest Concentration on Swab resulting in No Interference
Anti-Diarrheal Medication – Dimor Comp [Dimeticone]	0.03% loperamid +1.7% dimetikon (w/v)
Lubricant– RFSU Klick Ultra Glide	100%[a]
Lubricant– Sense Me Aqua Glide	100%[a]
Lubricant– KY-Jelly	100%[a]
Body Oil – ACO Repairing Skin Oil	100%[a, b]
Dialon Baby – Dialon Baby powder	100%[a]
Deodorant Powder – Vagisil® Deodorant Powder	100%[a]
Deodorant Spray – LN Intimate Deo	60% (v/v)
Deodorant Suppositories – Norforms Feminine Deodorant Suppositories	46.4% (w/w)
Enema solution – Microlax mikrolavemang	100%
Oral Laxative – Mylan	25% (w/v)
Oral Laxative – Phillips Milk of Magensia	60% (v/v)
Oral Laxative – Pursennid Ex-Lax	0.64% (w/v)
Spermicidal Foam – Caya preventivgel	100%
Stool Softener – Laktulos - Meda	60% (v/v)
Stool Softener – Movicol	9% (w/v)
Topical Hemorrhoid Ointment – Xyloproct Rectal Ointment	8% (v/v)
Topical Hemorrhoid Ointment – Scheriproct rektalsalva / Prednisolone Ointment	100%[a]
Ultrasound Transmission Gel – Aquasonic Gel	20% (v/v)
Vaginal Antifungal Gel – Multi-Gyn Actigel	100%[a]
Vaginal Antifungal Gel – Multi-Gyn Floraplus	75% (w/v)
Vaginal Anti-itch Cream – Ellen Probiotisk Utvärtes Intim Creme	100%[a]
Vaginal Antifungal Cream – Canesten	100%[a]
Vaginal Antifungal Cream – Daktar	100% [a]

[a] 100% represents undiluted solid substances used directly by dipping the upper 3/4 of the swab head into the substance. The amount tested was regarded as well above the typical concentrations found in clinical specimens.

[b] Skin oil was tolerated when tested as a solid by dipping 2/3 of the swab head into the substance.

21.5 Carry-over Contamination Study

A study was conducted to assess whether the single-use, self-contained Xpert Xpress GBS cartridge prevents specimen and amplicon carryover by testing a negative sample immediately after testing a very high positive sample in the same GeneXpert module. The negative sample used in this study consisted of simulated vaginal/rectal matrix and the positive sample consisted of high GBS serotype Ia positive sample spiked at 1.00E+07 CFU/mL (7.50E+05 CFU/swab) into simulated vaginal/rectal matrix. The negative sample was tested in a GeneXpert module at the start of the study. Following the initial testing of the negative sample, the high GBS positive sample was processed in the same GeneXpert module immediately followed by another negative sample. This was repeated 10 times in the same modules, resulting in 10 positives

and 11 negatives for the module. The study was repeated using a second GeneXpert module for a total of 20 positive and 22 negative samples. All 20 positive samples were correctly reported as **GBS POSITIVE**. All 22 negative samples were correctly reported as **GBS NEGATIVE**.

22 Reproducibility and Precision

The reproducibility and precision of the Xpert Xpress GBS test was evaluated in a multi-center, blinded study using two panels totaling ten members that consisted of simulated vaginal/rectal matrix as negative sample as well as low positive (~1 – 1.5xLoD) and moderate positive (~3x LoD) samples prepared by spiking GBS strain into simulated vaginal/rectal matrix at the respective target levels. Three strains of GBS representing hemolytic phenotypes (serotypes Ia, III, IV) and one strain (Serotype Ic) representing a non-hemolytic phenotype were used in the study. Testing was performed at three sites (one internal, two external) using the GeneXpert Instrument Systems. Each panel member was tested in triplicate each day (one run/day) by two operators on six different days at three different sites (10 members x 2 operators x 3 replicates/day x 6 days x 3 sites). Three lots of the Xpert Xpress GBS cartridges were used, with each lot tested on two days.

The percent agreement of the qualitative results for GBS detection for each panel member analyzed by each of the six operators and by each site is shown in Table 8. In addition, the overall percent agreement for each sample (total agreement) and the 95% two-sided Wilson Score confidence interval are presented in the last column.

Table 8. Summary of Reproducibility and Precision Results – Percent Agreement

Panel Member	Sample	Level	Site 1			Site 2			Site 3			Total Agreement (95% CI)
			Op 1	Op 2	Site	Op 1	Op 2	Site	Op 1	Op 2	Site	
1	Negative	Negative	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	94.1% (16/17)	100.0% (18/18)	97.1% (34/35)	99.1% (106/107) (94.9% - 100.0%)
2	GBS serotype Ia Low Pos	~1x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (108/108) (96.6% - 100.00%)
3	GBS serotype III Low Pos	~1x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	83.3% (15/18)	100.0% (17/17)	91.4% (32/35)	97.2% (104/107) (92.1% - 99.0%)
4	GBS serotype IV Low Pos	~1x LoD	94.4% (17/18)	88.9% (16/18)	91.7% (33/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	88.9% (16/18)	94.4% (34/36)	95.4% (103/108) (89.6% - 98.0%)
5	GBS serotype Ia Mod Pos	~3x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (108/108) (96.6% - 100.0%)
6	GBS serotype III Mod Pos	~3x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100% (108/108) (96.6% - 100.0%)
7	GBS serotype IV Mod Pos	~3x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100% (108/108) (96.6% - 100.0%)
8	Negative 2	Negative	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (108/108) (96.6% - 100.0%)
9	GBS Serotype Ic Low Pos	~1.5x LoD	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (108/108) (96.6% - 100.0%)
10	GBS Serotype Ic Mod Pos	~3x LoD	94.4% (17/18)	100.0% (18/18)	97.2% (35/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	99.1% (107/108) (94.9% - 100.0%)

Evaluation of repeatability and the within-laboratory precision of the underlying Ct values obtained in the Xpress GBS test was analyzed. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-lots, between-days, and between-operators and within-assay for each panel member Table 9.

Table 9. ANOVA Summary of Reproducibility Data by the Coefficient of Variance

Panel Member	N[a]	Mean	Site		Op		Lot		Day		Within Assay		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Negative[b]	107[c]	32.4	0.1	0.2	0.0	0	0.5	1.5	0.2	0.7	0.8	2.4	1.0	2.9
Low Pos GBS serotype Ia ~1x LoD	108	34.7	0.0	0	0.0	0	0.3	0.9	0.2	0.5	1.2	3.3	1.2	3.5
Low Pos GBS serotype III ~1x LoD	104[d]	34.8	0.0	0	0.0	0	0.4	1.1	0.0	0	1.3	3.8	1.4	3.9
Low Pos GBS serotype IV ~1x LoD	103[e]	35.2	0.2	0.4	0.0	0	0.5	1.4	0.0	0	1.0	2.7	1.1	3.1
Mod Pos GBS serotype Ia ~3x LoD	108	33	0.3	1	0.0	0	0.0	0	0.0	0	1.0	3.1	1.1	3.3
Mod Pos GBS serotype III ~3x LoD	108	33.1	0.0	0	0.0	0	0.3	1	0.3	1	0.8	2.5	1.0	2.9
Mod Pos GBS serotype IV ~3x LoD	108	33.7	0.0	0	0.3	1	0.3	0.9	0.1	0.3	0.8	2.3	0.9	2.7
Negative 2[b]	108	32.5	0.2	0.5	0.0	0	0.5	1.4	0.2	0.7	0.6	2	0.8	2.6
Low Pos GBS serotype Ic ~1.5x LoD	108	34.7	0.1	0.3	0.0	0	0.2	0.6	0.5	1.3	1.1	3.2	1.2	3.5
Mod Pos GBS serotype Ic ~3x LoD	107[f]	33.8	0.0	0	0.2	0.5	0.1	0.3	0.4	1.2	0.7	2	0.8	2.4

[a] Results with valid non-zero Ct values of 108

[b] SPC Ct values were used to perform ANOVA analysis for Negative samples.

[c] One sample gave a non-determinate result

[d] Three samples with GBS Ct value = 0 and one non-determinate sample were excluded from ANOVA analysis

[e] Five samples with GBS Ct value = 0 were excluded from ANOVA analysis

[f] One sample with a GBS Ct value = 0 was excluded from ANOVA analysis

23 Summary of Safety and Performance

The Summary of Safety and Performance for the Xpert Xpress GBS test is available on the EUDAMED website: https://ec.europa.eu/tools/eudamed.

24 References

1. Di Renzo GC, Melin P, Berardi A, et al. Intrapartum GBS screening and antibiotic prophylaxis: a European consensus conference. J Matern Fetal Neonatal Med. 2015 May;28(7):766-82.
2. ACOG Committee Opinion. Prevention of Group B Streptococcal Early-Onset Disease in Newborns. Obstet Gynecol. 2020;135(2):e51-e72. doi:10.1097/AOG.0000000000003668.

3. Filkins, L, Hauser, J, Robinson-Dunn, B et al. Guidelines for the Detection and Identification of Group B *Streptococcus.* American Society for Microbiology, March 2020. https://asm.org/Guideline/Guidelines-for-the-Detection-and-Identification-of accessed Dec 1, 2021.
4. Young BC, et al. Evaluation of a rapid, real-time intrapartum group B streptococcus assay. Am J Obstet Gynecol. 2011 Oct;205(4):372.e1-6.
5. Zietek M, et al. Intrapartum PCR assay is a fast and efficient screening method for Group B Streptococcus detection in pregnancy. Ginekol Pol. 2020;91(9):549–53.
6. Zimmermann P and Curtus N. Effect of intrapartum antibiotics on the intestinal microbiota of infants: a systematic review. Arch Dis Child Fetal Neonatal Ed. 2020 Mar;105(2):201-208.
7. Melin P. Neonatal group B streptococcal disease: from pathogenesis to preventive strategies. Clin Microbiol Infect. 2011 Sep;17(9):1294-303.
8. Chemical hazards determined under REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 (on classification, labeling and packaging of substances and mixtures amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006) and the Occupational Safety and Health Standards, Hazard Communication, Toxic and Hazard Substances (March 26, 2012) (29 C.F.R., pt. 1910, subpt. Z), can be referenced on the Safety Data Sheet available at www.cepheid.com and www.cepheidinternational.com under the SUPPORT tab.
9. World Health Organization. Safe management of wastes from health-care activities. 2nd Edition. WHO, 2014. Accessed April 20, 2018 at http://www.who.int/water_sanitation_health/publications/wastemanag/en/.

25 Cepheid Headquarters Location

Corporate Headquarters

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www.cepheid.com

26 Technical Assistance

Before Contacting Us

Collect the following information before contacting Cepheid Technical Support:

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

Report serious incidents associated with the test to Cepheid and the competent authority of the member state in which the serious incident occurred.

United States Technical Support

Telephone: + 1 888 838 3222

Email: techsupport@cepheid.com

France Technical Support

Telephone: + 33 563 825 319

Email: support@cepheideurope.com

Contact information for all Cepheid Technical Support offices is available on our website: www.cepheid.com/en/support/contact-us.

27 Safety Reporting

Contact Information

Sweden

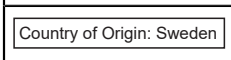
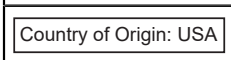
Telephone: + 1 888 838 3222
Email: techsupport@cepheid.com

Europe (France)

Telephone: + 33 563 825 319
Email: support@cepheideurope.com

Contact information for other Cepheid offices is available on our website at www.cepheid.com or www.cepheidinternational.com under the **SUPPORT** tab. Select the **Contact Us** option.

28 Table of Symbols

Symbol	Meaning
	Catalog number
	In vitro diagnostic medical device
	CE marking – European Conformity
	Do not reuse
	Batch code
	Consult instructions for use
	Manufacturer
	Country of manufacture
	Contains sufficient for n tests
	Expiration date
	Temperature limitation
	Biological risks
	Caution
	Warning
	Authorized Representative in Switzerland
	Importer
	Near patient testing
	Country of Origin: Sweden
	Country of Origin: United States of America

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CE 2797 IVD

29 Revision History

Description of Changes: 302-9599, Rev. A to Rev. B

Purpose: Initial release for commercialization. Aligns with the requirements of Regulation (EU) 2017/746.

Revision	Date of Issue	Description of Change
Rev B	August 2025	Include in the revision history the amendment from Revision A regarding the removal of European headquarters address in section 25. Initial release of IVDR IFU for commercialization.
Rev A	June 2025	Initial release