510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K222638

B Applicant

Cepheid

C Proprietary and Established Names

Xpert Xpress GBS, GeneXpert Dx System, GeneXpert Infinity Systems

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NJR	Class I	21 CFR 866.3740 - Streptococcus Spp. Serological Reagents	MI - Microbiology
OOI	Class II	21 CFR 862.2570 - Instrumentation for clinical multiplex test systems	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

To obtain substantial equivalence determination for the Xpert Xpress GBS test for intrapartum testing.

B Measurand:

Two conserved chromosomal regions within *Streptococcus agalactiae* (Group B *Streptococcus* genome):

- Coding region for a member of the glycosyl transferase gene family
- Coding region for a LysR family transcriptional regulator

C Type of Test:

Real Time Polymerase Chain Reaction (PCR)

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Xpert Xpress GBS test, performed on the GeneXpert Instrument Systems, is an automated, real-time PCR test for the qualitative detection of Group B Streptococcus (GBS) DNA from vaginal/rectal swab specimens collected from pregnant patients for intrapartum testing at term (e.g., >37 weeks) who have unknown or unavailable antepartum GBS screening test results and no additional risk factors that would warrant empiric antibiotic prophylaxis. The Xpert Xpress GBS test performed during intrapartum is intended to aid in the detection of GBS colonization in patients presenting in labor who may be 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.

This test is conducted using direct specimen without enrichment (enrichment is recommended to enhance detection of GBS colonization). In contrast to a positive test result, which can indicate colonization, a presumptive negative result cannot exclude the possibility of GBS colonization. A false negative test result at intrapartum carries a potential harm to the infant if it is used in making decisions regarding empiric antibiotic prophylaxis. Providers must use caution and default to known patient risk factors and clinical guidance regarding a role for intrapartum prophylaxis.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

GeneXpert Instrument Systems
- GeneXpert Dx
- GeneXpert Infinity-48s
- GeneXpert Infinity-80

IV Device/System Characteristics:

A Device Description:

The Xpert Xpress GBS test is an automated *in vitro* diagnostic test for the qualitative detection of Group B *Streptococcus* (GBS) DNA from vaginal/rectal swab specimens collected from pregnant patients at intrapartum. The test is performed on the GeneXpert Instrument System

which automates and integrates sample preparation, nucleic acid amplification, and real-time detection of target sequences. The system consists of an instrument, computer, and preloaded software for running tests and viewing the results.

The sample collection device allows dual vaginal/rectal swab specimens from patients to be collected and transported to laboratory prior to analysis with the Xpert Xpress GBS test. The Xpert Xpress GBS has an Early Assay Termination (EAT) feature that enables early result reporting. EAT is activated when the pre-determined threshold for a positive test result is reached before the full number of PCR cycles have been completed.

B Principle of Operation:

Depending on the instrument, the GeneXpert Instrument Systems can have from 1-80 randomly accessible modules, each capable of performing separate sample preparation and real-time PCR tests. Each module contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells or spores, and a proprietary I-CORE thermocycler for performing real-time PCR as well as detection. The systems require the use of single-use disposable cartridges that hold the PCR reagents and host sample purification, nucleic acid amplification, and detection of the target sequences. Because the cartridges are self- contained, cross-contamination between cartridges during the testing process is minimized.

The Xpert Xpress GBS test includes reagents for the simultaneous detection of target GBS DNA from vaginal/rectal swab specimens, where primers and probes in the Xpert test are designed to amplify and detect unique sequence in two conserved chromosomal targets in *S. agalactiae*: 1) a member of the glycosyl transferase gene family, and 2) a *LysR* transcriptional regulator. A Sample Adequacy Control (SAC), Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge utilized by the GeneXpert instrument. The SAC is a non-target sequence naturally present in the specimen, which is amplified along with the assay target to ensure that the sample is properly collected and contains adequate human cells from the vaginal/rectal flora. 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 PCC verifies reagent rehydration, PCR tube filling, and confirms that all reaction components are present in the cartridge including monitoring for probe integrity and dye stability.

C Instrument Description Information:

1. Instrument Name:
   The Xpert Xpress GBS test can be run on the following GeneXpert Instruments:
   - GeneXpert Dx (software version 5.3 or higher)
   - GeneXpert Infinity-48s (software version Xpertise 6.8 or higher)
   - GeneXpert Infinity-80 (software version Xpertise 6.8 or higher)

2. Specimen Identification:
   To perform a test, the user selects the ‘Create Test’ icon, enters or scans the sample ID barcode, scans the cartridge barcode, selects the assay that has been ordered, and loads the

cartridge in into the module to start the test. The GeneXpert System software controls the operation of the sample processing and the I-CORE module that collect, analyze and interpret the acquired optical data.

3. Specimen Sampling and Handling:
   Vaginal/rectal swabs are collected using the Cepheid Collection Device with Liquid Stuart Medium. The two swabs should be brushed together using a twirling motion for five seconds. The second swab is then returned to the transport tube. The swab for testing is held above the score mark using gauze or equivalent and inserted into the Xpert Xpress GBS cartridge sample chamber. The swab is broken by snapping the shaft to the right. After lid closure, the cartridge is loaded on the GeneXpert Instrument System platform for automated sample processing and real-time PCR for detection of targets.

4. Calibration:
   Routine calibration of the GeneXpert instrument systems is performed periodically by Cepheid Field Service Engineers.

5. Quality Control:
   Each test includes a SPC, SAC, and PPC. External controls should be used in accordance with local, state, and federal accrediting organizations as applicable.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Xpert GBS, Genexpert Dx System

B Predicate 510(k) Number(s):
K060540

C Comparison with Predicate(s):

Device & Predicate Device(s):	K222638	K060540
Device Trade Name	Cepheid Xpert Xpress GBS	Cepheid Xpert GBS
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Xpert Xpress GBS test, performed on the GeneXpert Instrument Systems, is an automated, real-time PCR test for the qualitative detection of Group B Streptococcus (GBS) DNA from vaginal/rectal swab specimens collected from pregnant patients for intrapartum testing at term (e.g., >37 weeks) who have unknown or unavailable antepartum GBS screening test results and no additional risk factors that would warrant empiric antibiotic	The Cepheid Xpert GBS performed on the GeneXpert Dx System is a qualitative in vitro diagnostic test designed to detect Group B Streptococcus (GBS) DNA from vaginal/rectal swab specimens, using fully automated real-time polymerase chain reaction (PCR) with fluorogenic detection of the amplified DNA. Xpert GBS Assay testing is indicated for rapid identification of antepartum

	prophylaxis. The Xpert Xpress GBS test performed during intrapartum is intended to aid in the detection of GBS colonization in patients presenting in labor who may be 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. This test is conducted using direct specimen without enrichment (enrichment is recommended to enhance detection of GBS colonization). In contrast to a positive test result, which can indicate colonization, a presumptive negative result cannot exclude the possibility of GBS colonization. A false negative test result at intrapartum carries a potential harm to the infant if it is used in making decisions regarding empiric antibiotic prophylaxis. Providers must use caution and default to known patient risk factors and clinical guidance regarding a role for intrapartum prophylaxis.	and intrapartum GBS colonization. • The use of the Xpert GBS for intrapartum screening should not preclude the use of other strategies (e.g., antepartum testing). Intrapartum Xpert GBS results are useful to identify candidates for intrapartum antibiotic prophylaxis when administration of intravenous antibiotics is not delayed pending results. • The Xpert GBS Assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.
Technology	Same	Real-Time PCR
Collection Device	Same	Cepheid Collection Device with Liquid Stuart Medium (Catalog Part 900-0370)
Specimen Type	Same	Direct from vaginal/rectal swab specimens
Single Use Cartridge	Same	Yes
Automated Nucleic Acid Extraction, Detection, and Results Interpretation	Same	Yes
Assay Results	Same	Qualitative
General Device Characteristic Differences		
Assay Targets	Dual target assay design against two conserved	3’ region adjacent to *cfb* gene CAMP-factor

	sequences in *S. agalactiae*: • a member of the glycosyl transferase gene family and • a *LysR* transcriptional regulator	hemolysin gene of *S. agalactiae*
Internal Controls	Sample Processing Control (SPC) Sample Adequacy Control (SAC) Probe Check Control (PCC)	Sample Processing Control (SPC) Internal Control (IC) Probe Check Control (PCC)
Instrument Systems	Cepheid GeneXpert Instrument Systems (Dx and Infinity)	Cepheid GeneXpert Dx Systems
Early Assay Termination (EAT) Feature	Yes EAT feature enables early result reporting	No
Time to Result	< 50 minutes	< 60 minutes

VI Standards/Guidance Documents Referenced:

- ISO 14971:2019 Medical devices -Application of risk management to medical devices
- CLSI EP12-A2 User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline - Second Edition.
- CLSI EPl7-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline
- CLSI EP25-A Evaluation of Stability of ln Vitro Diagnostic Reagents; Approved Guideline.
- CLSI EP05-A3 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline -Third Edition
- CLSI MM03-A3 Molecular Diagnostic Methods for Infectious Disease; Approved Guideline -Third Edition.
- CLSI EP07-A3 Interference Testing in Clinical Chemistry Approved Guideline - Third Edition
- CLSI MM13-A2 Collection, Transport, Preparation, and Storage of Specimens for Molecular Methods; Second Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The reproducibility 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 (see matrix equivalency section), as well as low positive (~1-1.5x LoD) and moderate positive (~3x LoD) samples prepared by spiking GBS strains 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 by two operators on six different days at three different sites (10 panel 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 operators and site is shown in **Table 1** below. 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 1. Summary of Reproducibility Results

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	~1xLoD	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	~1xLoD	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	~1xLoD	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	~3xLoD	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	~3xLoD	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	~3xLoD	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	~1.5xLoD	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	~3xLoD	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 Xpert Xpress GBS test was analyzed. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-lots, between-days, between-operators and within-assay for each panel member are shown in **Table 2**.

Table 2. 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 ~1xLoD	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 ~1xLoD	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 ~1xLoD	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 ~3xLoD	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 ~3xLoD	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 ~3xLoD	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 ~1.5xLoD	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 ~3xLoD	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*

2. Linearity:
N/A

3. Analytical Specificity/Interference:

Analytical Specificity
The analytical specificity and microbial interference of the Xpert Xpress GBS test were evaluated by testing a panel of 129 non-GBS organisms that can potentially cross-react and interfere with the detection of GBS both in the presence (microbial interference) and absence (cross-reactivity/exclusivity) of GBS. Challenge organisms tested included bacterial, viral, parasite, and yeast strains commonly found in vaginal/rectal flora or were considered phylogenetically related to GBS. On each day of testing, one positive and one negative control were also tested in parallel. Panel members are shown in **Table 3** below.

Pools were prepared by diluting each organism into GBS negative simulated sample matrix to produce final concentrations in replicates of 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 was tested either individually or in pools of 2 - 6 microorganisms in simulated sample matrix in presence of GBS (at 3x LoD) or absence of GBS. No cross-reactivity or microbial interference of GBS detection was observed with any of the clinically relevant pathogens tested in the study.

Table 3: Panel for Testing the 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]
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*

Organism		
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*
Citrobacterfreundii	*Pasteurellaaerogenes*	*Serratia liquefaciens*
Clostridiumdifficile	*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*
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*

Collectively, the results for the GBS positive samples demonstrated that none of the 129 microbial organisms included in this study interfered with the Xpert Xpress GBS test's ability to detect GBS and are not cross-reactants under these conditions.

Interference Study
Substances that may be present in vaginal/rectal specimens with the potential to interfere with the Xpert Xpress GBS test were evaluated. The inhibitory effects were assessed with 8 endogenous and 25 exogenous substances both in the presence and absence of GBS. Potentially interfering endogenous and exogenous substances included 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. 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 then liquid added directly to the swab. These substances are listed in **Table 4** below.

Negative samples consisting only of simulated matrix were tested in replicates of 6 in the presence of each substance to determine the effect on the performance of the SPC and SAC. Positive samples were prepared by spiking GBS serotype Ia into simulated matrix at 3x LoD then 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.

Among the 25 exogenous substances tested in this study, 5 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 along with their forms 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) are shown in **Table 4** below. Cord serum stock was contaminated with GBS and, therefore, the results were not valid for analysis of interference. These data were excluded from further evaluation. No interference was observed with any of the other endogenous substances tested in the study. The inhibitory effects of Aquasonic gel, Xyloproct, Multi-Gyn Floraplus, Pepto Bismol, and skin oil were included in the product labeling.

Of 879 tests (including external controls), 10 tests (1.1%) provided non-substance-related non-determinate test results—4 INVALID, 5 NO RESULT and 1 ERROR. In addition, 65 tests provided substance-related non-determinate GeneXpert results (63 INVALID, 1 NO RESULT and 1 ERROR). The samples were re-tested as allowed by the protocol and valid or non-determinate results were obtained for the re-test. Non-determinate results from re-tests were reported as such. Each of the positive and negative external controls run daily during the study produced the expected GeneXpert test results.

Table 4: Potentially Interfering Substances

Substance	Substance Form	Highest Concentration on Swab Resulting in No Interference
Human Amniotic Fluid	Liquid	60% (v/v)
Human Urine	Liquid	60% (v/v)
Human Whole Blood – EDTA	Liquid	80% (v/v)
Human Whole Blood – Na Citrate	Liquid	80% (v/v)
Leukocytes, Buffy coat, $2x10^7$ WBCs/mL	Liquid	80% (v/v)
Meconium	Solid	100% [a]
Mucus – mucin from porcine stomach	Solid	30% (w/v)
Human Feces – Pool of 10 donors	Solid	100% [a]
Anti-Diarrheal Medication – Pepto Bismol	Liquid [b]	40% (v/v)
Anti-Diarrheal Medication – Dimor Comp [Dimeticone]	Tablet	0.03% loperamid + 1.7% dimetikon (w/v)
Lubricant – RFSU Klick Ultra Glide	Solid	100% [a]
Lubricant – Sense Me Aqua Glide	Solid	100% [a]
Lubricant – KY-Jelly	Solid	100% [a]
Body Oil – ACO Repairing Skin Oil	Liquid [c]	100% [a]
Dialon Baby – Dialon Baby Powder	Solid	100% [a]
Deodorant Powder – Vagisil Deodorant Powder	Solid	100% [a]
Deodorant Spray – LN Intimate Deo	Liquid	60% (v/v)
Deodorant Suppositories – Norforms Feminine Deodorant Suppositories	Tablet	46.4% (w/v)
Enema solution – Microlax mikrolavemang	Solid	100% [a]
Oral Laxative – Mylan	Solid	25% (w/v)
Oral Laxative – Phillips Milk of Magnesia	Liquid	60% (v/v)
Oral Laxative – Pursennid Ex-Lax	Tablet	0.64% (w/v)
Spermicidal Foam – Caya preventivgel	Solid	100% [a]
Stool Softener – Laktulos Meda	Liquid	60% (v/v)
Stool Softener – Movicol	Tablet	9% (w/v)
Topical Hemorrhoid Ointment – Xyloproct Rectal Ointment	Solid [d]	8% (v/v)
Topical Hemorrhoid Ointment – Scheriproct rektalsalva / Prednisolone Ointment	Solid	100% [a]
Ultrasound Transmission Gel – Aquasonic Gel	Solid [d]	20% (v/v)
Vaginal Antifungal Gel – Multi-Gyn Actigel	Solid	100% [a]
Vaginal Antifungal Gel – Multi-Gyn Floraplus	Solid [d]	75% (w/v)
Vaginal Anti-itch Cream – Ellen Probiotisk Utvärtes Intim Creme	Solid	100% [a]
Vaginal Antifungal Cream – Canesten	Solid	100% [a]
Vaginal Antifungal Cream – Daktar	Solid	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 above the typical concentrations found in clinical specimens.*
b. *Pepto Bismol diluted to 40% in simulated background matrix and no interference observed.*
c. *Skin oil was tolerated when tested as a solid by dipping 2/3 of the swab head into the substance.*
d. *Substances were diluted into a simulated background matrix prior to testing: Xyloproct Rectal Ointment was tested at 8%, Aquasonic Gel was tested at 20%, and MultiGyn Floraplus was tested at 75%. No interference was detected after dilution.*

4. Assay Reportable Range:
N/A

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
Each test includes a Sample Processing Control (SPC), Sample Adequacy Control (SAC) and a Probe check control (PCC).

Internal Controls

- 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 PRESUMPTIVE 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 meets the assigned acceptance criteria.

External Controls

External controls were evaluated in a study with three lots of commercially available, single, ready-to-use, external controls (positive and negative) manufactured by Microbiologics (St. Cloud, MN, USA) for use with Xpert Xpress GBS test. These external controls were used as daily controls during design verification studies and clinical studies. The external positive control swab was comprised of a lyophilized isolate of *Streptococcus agalactiae*, whereas the negative external control swab included of a lyophilized mixture of *Lactobacillus acidophilus* and a recombinant *E. coli* strain carrying the SAC target. The test results for the positive control were considered valid if a "*GBS POSITIVE"* result was generated. The valid test result for the negative control was *"GBS PRESUMPTIVE NEGATIVE."* Twenty replicates for each of the 3 positive external control lots and 20 replicates for each of the 3 negative external control lots were evaluated using one lot of the Xpert Xpress GBS test (lot 10751) for a total of 120 replicates. All negative external control replicates (60/60) and positive external control replicates (60/60) were correctly reported. Of the 120 tests performed between negative and positive external controls, none (0%) provided non-determinate GeneXpert results.

Sample Stability

The objective of this study was to determine the specimen stability to support the transport and storage claims for the following specimen types and transport media to be used with the Xpert Xpress GBS test:

- Dual rayon swab for vaginal/rectal specimen
- Copan, Liquid Stuart Medium (polyurethane sponge)

Specimen stability studies were conducted in simulated and clinical sample matrices to establish specimen transport and storage claims in the Cepheid collection device. For the specimen stability study with simulated matrix, samples were evaluated with negative and positive samples spiked onto swabs. The positive sample was one strain of GBS serotype Ia (ATCC 12386) spiked at 1989 CFU/ml (3xLoD) into simulated sample matrix. The assay performance using each specimen type was established by storing each sample under room temperature (25 ± 3°C) for up to 30 hours and at refrigerated (2-8°C) temperatures for up to seven days. The data support a specimen stability claim for dual vaginal/rectal swabs using the Cepheid collection device at room temperature (25±3 °C) up to 24 hours and at refrigerated temperatures (2-8 °C) for up to six days. For the clinical sample evaluation, 26 GBS positive specimens were available for analysis. All 26 specimens were stored at 2-8°C from the time of swab collection until time of Xpert Xpress GBS testing (3.3 days to 16.2 days). Even though the assay is qualitative, the mean GBS Ct values observed for samples stored at various times were used to assess specimen stability. It was observed that the mean GBS Ct values of specimens collected at intrapartum that were stored at 2-8°C for ≤7 days (N=8; mean 31.8; SD 5.9) had similar ranges to the GBS Ct values of specimens that were stored for >7 Days (N=18; mean 30.8; SD 4.4). All samples remained positive.

Labeling will state that specimens can be stored up to 24 hours at 2-25°C (if repeat testing is needed). Cepheid indicated that additional stability information will be made available upon request.

Reagent Stability
The shelf-life of the Xpert Xpress GBS test was determined in stability studies using real-time stability data from three lots of the final product configuration. Each kit lot used in the stability study was functionally tested with five samples—four of which were positive for GBS, and one which was negative for GBS. For all 3 lots used in the real-time and shipping stability study, functional testing is ongoing for up to 37 months. Currently, the stability testing data on three lots (10451, 10651 and 10751) support a shelf-life claim of 24 months at the temperature range of 2°-28°C.

6. Detection Limit:

The objective of this study was to determine the analytical sensitivity or Limit of Detection (LoD) of Xpert Xpress GBS with known GBS serotypes (serotype Ia, Ib, Ic, II-X). The analytical reactivity (inclusivity) of the Xpert Xpress GBS test was determined for 12 different strains representing 12 known serotypes of GBS, including both hemolytic and non-hemolytic GBS strains. This study was conducted in 2 parts: (1) LoD estimation and (2) LoD verification. The LoD was defined as the lowest concentration of GBS (reported as CFU/mL or CFU/swab) that could be reproducibly distinguished from negative samples with 95% confidence using Probit analysis (**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

estimated LoD values were verified by testing 20 replicates of each serotype diluted in simulated sample matrix with one reagent lot across three days. Serotype Ia, III and V were also verified in clinical matrix. The result for serotypes V and VI was 85% (17/20) detected and the claimed LoD was based on the upper limit of 95% confidence interval. The verified LoD values for the GBS serotypes tested are provided in **Table 5**. All serotypes (Ia, Ib, Ic, II, III, IV, V, VI, VII, VIII, IX and X) were detected by the Xpert Xpress GBS test.

Table 5. Xpert Xpress GBS Limit of Detection

Serotype	Source	LoD (CFU/mL)	LoD (CFU/Swab)
Ia	ATCC 12386/ CCUG 4209	663	50
Ib	ATCC 12401/ CCUG 29780	40	3
Ic[a]	ATCC 13813/ CCUG 4208	301	23
II[a]	ATCC 12973	173	13
III	ATCC 12403/ CCUG 29782	540	41
IV	ATCC 49446/ CCUG 29783	429	32
V	ATCC BAA-23	618[b]	46
VI	Cepheid (CDC ID: 2010228816)	544[b]	41
VII	Cepheid (CDC ID: 4832-06)	620	47
VIII	Cepheid (CDC ID: 5030-08)	682	51
IX	ATCC BAA-2668	465	35
X	ATCC 49449	677	51

a. Non-hemolytic strain
b. Claimed LoD corresponds to the upper limit of 95% CI

Analytical Inclusivity of Cfb Mutants
An additional 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%. Of the 208 tests (including external controls), 2 tests (1.0%) provided non-determinate GeneXpert results (2 NO RESULT). All non-determinate runs were successfully repeated. Each of the positive and negative external controls run daily during the study produced the expected GeneXpert test results. Therefore, the Xpert Xpress GBS test detected GBS strains with mutations in the cfb gene.

7. Assay Cut-Off:
   The Xpert Xpress GBS test uses channels to detect the GBS target, SPC, and SAC. The Ct cut-offs are included as automatic calculations in the assay definition file (ADF) of the Xpert Xpress GBS test.

   The Xpert Xpress GBS has an EAT feature that enables early result reporting. EAT is activated when the pre-determined threshold for a positive test result is reached before the full number of PCR cycles have been completed.

8. Accuracy (Instrument):
   N/A

9. Carry-Over:

   A study was conducted to demonstrate that Xpert Xpress GBS single-use, self-contained cartridges prevent specimen and amplicon carry-over contamination into negative samples when following the testing of high positive samples 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, a high GBS positive sample was processed in the same GeneXpert module. This process 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 results yielded expected results based on sample type.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   N/A

2. Matrix Comparison:
   Two separate studies were conducted to support the use of simulated sample matrix.

   Study #1
   The objective of this study was to demonstrate equivalent performance of a simulated sample matrix and clinical matrix when used for sample preparation in the Xpert Xpress GBS test. The simulated sample matrix was qualified by comparing analytical performance of the Xpert Xpress GBS when using the simulated sample matrix and a clinical sample matrix for the dilution of samples. Both clinical sample matrices from antepartum and intrapartum collection were included in the comparison. Matrices were spiked with GBS at three different levels: 5x LoD, 2x LoD, 0.5x LoD. Matrices without GBS were used as negatives. The simulated sample matrix composition is provided in **Table 6** below.

Table 6. Simulated Matrix Composition

Component	Rationale
3.0 g/L Porcine Mucin (0.3%)	Mimics viscosity in vaginal fluids due to mucin glycoproteins.
200 ml/L Blood (20%)	20% WB provides human gDNA that gives a SAC Ct representative of that observed with clinical samples.
10 ml/L Urine (1%)	Information provided with clinical samples acquired for feasibility studies report *"trace amounts"* consistent with the literature.
10 g/L Stool (1%)	Clinical samples rarely exhibit visible soiling by stool and information provided with clinical samples acquired for feasibility studies report "*trace amounts",* consistent with the literature. Stool component contributes to non-target biomass DNA likely present on swabs.
Phosphate Buffered Saline (PBS)	To mimic a plasma exudate.

GBS negative clinical matrices (by Xpert Xpress testing) were acquired by first testing swabs obtained from GBS negative subjects in the Xpert Xpress GBS test (29 antepartum and 35 intrapartum clinical swabs). After testing, the left-over eluted sample in cartridge chamber 3 (approximately 1 mL) was collected and pooled into one antepartum and one intrapartum pool (clinical sample matrices). Both clinical matrix and the simulated matrix were then spiked with GBS strain ATCC 12973 (serotype II) at concentrations representing 5x LoD, 2x LoD and 0.5x LoD. Since this study was performed prior to establishing the final LoD, a preliminary LoD of 103 CFU/mL (7.7 CFU/swab) estimated by Probit analysis was used instead of the final LoD (173 CFU/mL or 13 CFU/swab). A negative control consisting of the respective matrix without GBS was also included. **Table 7** shows the results of testing for Study #1.

Table 7. Study #1—Overall Results Simulated vs Clinical Matrix Equivalency Study

Matrix	GBS Level (Multiple of LOD) CFU/ml	Expected Results (% Positive)	Number of Valid Replicates	Number of Replicates with Positive Results	% Positive (Positivity Rate)
Simulated Sample Matrix	5x	100	10	10	100
	2x	≥95	30	30	100
	0.5x	10-90	20	15	75
	Negative	0	10	0	0
Clinical Sample Matrix Antepartum	5x	100	10	10	100
	2x	≥95	30	30	100
	0.5x	10-90	20	18	90
	Negative	0	10	0	0
Clinical Sample Matrix – Intrapartum	5x	100	10	10	100
	2x	≥95	30	30	100
	0.5x	10-90	20	18	90
	Negative	0	10	0	0

Of the 224 tests (including external controls), 8 tests (3.6%) provided non-determinate GeneXpert results (6 NO RESULT and 2 ERROR). All non-determinate runs were successfully repeated. One of negative external control initially yielded an ERROR result and was successfully repeated. Positive and negative external controls generated expected results on each of the testing day. The acceptance criteria were met for all three matrices (clinical

antepartum matrix, clinical intrapartum matrix and simulated matrix); thus, the simulated sample matrix was qualified to be used in analytical performance studies and the preparation of reproducibility/precision panels.

Study #2
The objective of this study was to demonstrate comparable performance among antepartum clinical matrix, intrapartum clinical matrix, and simulated matrix by testing two additional GBS serotypes. The simulated sample matrix composition was identical to that shown in **Table 6** of Study #1 above. All matrices were spiked with GBS to three concentrations relative to the LOD (5x LoD, 1-2x LoD and <1x LoD). Matrices without GBS were used as negative samples.

GBS negative clinical matrix was acquired by pooling leftover sample from 56 clinical GBS negative antepartum or 132 clinical GBS negative intrapartum samples. Prior to use, both clinical sample pools were tested and confirmed as GBS negative. Each matrix was spiked with GBS strain ATCC 12386 (serotype Ia) or GBS strain 12403 (serotype III). **Table 8** and **Table 9** show results of testing with GBS Serotype Ia and GBS Serotype III, respectively.

Table 8. Study #2—Matrix Equivalency Results for ATCC12386 (GBS Serotype Ia)

Matrix	GBS Level (Multiple of LOD) CFU/ml	Expected Results (% Positive)	Number of Valid Replicates	Number of Replicates with Positive Results	% Positive (Positivity Rate)
Simulated Sample Matrix	5x	100	10	10	100
	2x	≥95	30	30	100
	0.2x	10-90	20[a]	7	35
	Negative	0	10	0	0
Clinical Sample Matrix – antepartum	5x	100	10	10	100
	2x	≥95	30	30	100
	0.2x	10-90	20[b]	12	60
	Negative	0	10	0	0
Clinical Sample Matrix – intrapartum	5x	100	10	10	100
	2x	≥95	30[a]	30	100
	0.2x	10-90	20	10	50
	Negative	0	10[c]	0	0

a. One of 20 replicates reported NO RESULT due to the use of an incorrect ADF. The run was repeated with the correct ADF and produced a valid GeneXpert result.
b. One of 20 replicates reported NO RESULT. The run was successfully repeated to yield 20 valid GeneXpert results.
c. One of 10 replicates reported ERROR. The run was successfully repeated to yield 10 valid GeneXpert results.

Table 9. Study #2—Matrix Equivalency Results for ATCC12403 (GBS Serotype III)

Matrix	GBS Level (Multiple of LOD) CFU/ml	Expected Results (% Positive)	Number of Valid Replicates	Number of Replicates with Positive Results	% Positive (Positivity Rate)
Simulated Sample Matrix	5x	100	10	10	100
	2x	≥95	30	30	100
	0.2x	10-90	20	13	65
	Negative	0	10	0	0
Clinical Sample Matrix – Antepartum	5x	100	10	10	100
	2x	≥95	30	30	100
	0.2x	10-90	20	16	80
	Negative	0	10[a]	0	0

Clinical Sample Matrix – Intrapartum	5x	100	10	10	100
	2x	≥95	30	30	100
	0.2x	10-90	20	15	75
	Negative	0	10	0	0

[a]One of 10 replicates reported ERROR. The run was successfully repeated to yield 10 valid GeneXpert results.

The overall positivity rates for GBS Serotype Ia and Serotype III were considered acceptable for each GBS level in each matrix. All replicates of the negative sample yielded the expected result. Of the 429 tests (including external controls), 5 tests (1.2%) provided non-determinate GeneXpert results (3 NO RESULT and 2 ERROR). All non-determinate runs were successfully repeated. Each of the positive and negative external controls run daily during the study reported the expected GeneXpert test results.

As in Study #1, the simulated sample matrix was shown to have comparable performance with clinical antepartum and clinical intrapartum matrix with the Xpert Xpress GBS.

C Clinical Studies:

1. Clinical Sensitivity:

Clinical performance characteristics of the Xpert Xpress GBS test were evaluated in a multi-site, method comparison study using vaginal/rectal swab specimens collected from pregnant females at intrapartum. The study was conducted at twelve (12) clinical sites from geographically diverse regions within the United States between July 2020 and November 2021. 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, where one swab was used for Xpert Xpress GBS testing and the other was used for culture. 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. Discordant results between the Xpert Xpress GBS test and the comparator method were investigated using an FDA-cleared nucleic acid amplification test, which are footnoted in **Table 10.**

Of the 912 vaginal/rectal samples enrolled, 13 were excluded from the analysis of performance 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 performance 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 10**. The Xpert Xpress GBS demonstrated a sensitivity of 93.5% and specificity of 95.5% for vaginal/rectal swab specimens collected at intrapartum. A PPV of 66.1% and NPV of 99.4% were observed with these specimens.

Table 10. Xpert Xpress GBS Performance Results vs. Enriched Culture + MALDI-TOF MS – Intrapartum Specimens

Results	Culture[a] Positive	Culture Negative	Total	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)
Xpert Xpress GBS	72	37[a]	109	93.5%	95.5%	66.1%	99.4%

Positive				(85.7– 97.2)	(93.9 – 96.7)	(56.8 – 74.3)	(98.5 – 99.7)
Xpert Xpress GBS Presumptive Negative	5[b]	785	790				
Total	77	822	899				

a. Culture is "enriched" culture.

b. Discrepant test results based on an FDA-cleared NAAT: 13/37 GBS positive; 15/37 GBS negative; 9/37 no valid result

c. Discrepant test results based on an FDA-cleared NAAT: 4/5 GBS positive; 1/5 GBS negative

Of the 912 Xpert Xpress GBS tests performed in the clinical study, 55 resulted in non-determinate results (ERROR, INVALID or NO RESULT) on the first attempt. Upon re-test, 12 specimens remained non-determinate. The initial non-determinate rate was 6.0% (55/912). Upon retest, the final non-determinate rate was 1.3% (12/912).

Of the 734 external control samples tested, 88.6% (650/734) gave a valid result on the first test and 11.4% (84/734) were non-determinate. After re-testing 69, the final valid rate for the external control samples was 97.4% (715/734). Specimen testing did not proceed without valid external control results per protocol. Of the 715 samples that were valid in final testing, 99.9% (714/715) were in agreement with the expected results.

2. Clinical Specificity:

   See above.

3. Other Clinical Supportive Data (When 1. And 2. Are Not Applicable):

   N/A

D Clinical Cut-Off:

N/A

E Expected Values/Reference Range:

Nine hundred and twelve (912) vaginal/rectal swab specimens were enrolled from eligible participants. Age distribution of vaginal/rectal specimens collected at Intrapartum are represented in **Table 11**.

Table 11: Age Distribution of Specimens Included

Age Group	Intrapartum Vaginal/Rectal (ABX-) N (%)
14-17	2 (0.2%)
18-24	285 (31.3%)
25-34	507 (55.6%)
≥35	118 (12.9%)
Total	912 (100.0%)

F Other Supportive Instrument Performance Characteristics Data:

Prepared Cartridge Hold Time

A study was conducted to determine, under different conditions, the maximum elapsed time between sample addition and cartridge processing that will not alter the Xpert Xpress GBS performance. The positive sample consisted of GBS serotype Ia (ATCC 12386) seeded at 1989 CFU/ml (3x LoD) into simulated sample matrix The negative sample consisted of simulated sample matrix only. Swabs were spiked with 75µl of either the positive or negative sample, placed into the sample chamber of the cartridges, and held at four storage conditions:

- 25°C/35% relative humidity (RH)
- 15°C/35% RH
- 30°C/35% RH
- 30°C/95% RH

These storage conditions were monitored continuously. Subsequently, the prepared cartridges containing the positive and negative samples were processed at scheduled time intervals of T=0, 1, 3, 4.5 and 5 hours. Samples were tested in replicates of 8 for each storage condition using one lot of Xpert Xpress GBS test. One time point (at 15°C/35% RH) was not included due to a protocol deviation. All replicates of the negative sample that were tested at each storage condition and time point correctly reported the expected test results. All replicates of the positive sample that were tested at each storage condition and time point correctly reported *"GBS Positive."* Of the 254 tests (including external controls), 4 (1.6%) provided non-determinate GeneXpert results (3 INVALID and 1 ERROR). Samples with the non-determinate results were repeated such that the required number of valid test results were obtained. Each of the positive and negative external controls run daily during the study reported the expected GeneXpert test results.

The data support a claim of maximum elapsed time between sample addition and cartridge processing up to 4.5 hours, including a prepared cartridge hold time of 4 hours on the GeneXpert Infinity instrument.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.