Cepheid
Robert Resnick
Principal Regulatory Affairs Specialist
904 Caribbean Drive
Sunnyvale, California 94089

May 9, 2022

Re: K203429
Trade/Device Name: Xpert GBS LB XC, GeneXpert Dx System, GeneXpert Infinity System
Regulation Number: 21 CFR 866.3740
Regulation Name: Streptococcus Spp. Serological Reagents
Regulatory Class: Class I
Product Code: NJR, OOI
Dated: November 18, 2020
Received: November 20, 2020

Dear Robert Resnick:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for

Ribhi Shawar, Ph.D. (ABMM)
Branch Chief, General Bacteriology and Antimicrobial Susceptibility Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K203429

Device Name
Xpert GBS LB XC

Indications for Use *(Describe)*
The Xpert GBS LB XC test, performed on the GeneXpert® Instrument Systems, is an automated qualitative in vitro diagnostic test for the detection of Group B *Streptococcus* (GBS) DNA from enriched vaginal/rectal swab specimens, using real- time polymerase chain reaction (PCR).

Xpert GBS LB XC testing is indicated as an aid in determining the GBS colonization status of antepartum women.

• The Xpert GBS LB XC test is intended for antepartum testing on enriched Lim broth cultures of vaginal/rectal swabs after 18–24 hours of incubation
• The Xpert GBS LB XC test does not provide antimicrobial susceptibility test results. Culture is necessary to obtain isolates to perform susceptibility testing as recommended for penicillin-allergic women

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

As required by 21 CFR Section 807.92(c).

I. SUBMITTER

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (408) 541-4191 Fax number: (408) 541-4192
Contact:	Robert Resnick. M.S.
Date of Preparation:	December 06, 2021

II. DEVICE

Trade name:	Xpert® GBS LB XC
Common name:	Xpert® GBS LB XC
Type of Test:	Qualitative real-time polymerase chain reaction (PCR) and detection test
Regulation number, Classification name, Product code: Definition	21 CFR 866.3740, Streptococcus spp. serological reagents. NJR; Definition: A nucleic acid amplification assay system (including probes, other reagents, and instrumentation) is an aid in the identification of group b *streptococci* from pre-partum and intra-partum women to establish colonization status. 21 CFR 862.2570, Instrumentation for clinical multiplex test systems, OOI; Definition: The system is a clinical multiplex instrument intended to measure and sort multiple signals generated my multiple probes, intercalating dyes, or other ligands in an assay from a clinical sample. Signals may be generated by fluorescence or other phenomena and may be measured using filters on a photodiode or other detector. It may integrate sample and/or reagent handling, amplification, dedicated instrument control, data acquisition software, raw data storage mechanisms and other essential hardware components along with the signal reader unit. The system is used with specific assays to comprise an assay test system.
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes

III. PREDICATE DEVICE

Predicate Device Assay:	Xpert GBS LB (K121539)

IV. DEVICE DESCRIPTION

The Xpert GBS LB XC test is an automated *in vitro* diagnostic test for qualitative detection of DNA from Group B *Streptococcus* (GBS) from vaginal-rectal swab specimens obtained from pregnant women that are transported to the laboratory following enrichment in Lim broth.
The primers and probes in the Xpert GBS LB XC test are designed to simultaneously amplify and detect two unique GBS chromosomal targets: the first is a target within a coding region for a glycosyl transferase family protein and the second is within a coding region for a *LysR* family transcriptional regulator of *Streptococcus agalactiae* DNA.

The Xpert GBS LB XC test includes reagents for the detection of DNA from GBS in Lim broth-enriched vaginal/rectal swabs. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate extraction and processing of the target sequences and to monitor for the presence of inhibitors in the PCR reaction. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The single-use, multi-chambered fluidic cartridges are designed to complete sample preparation and real-time PCR for the detection of GBS genomic DNA in as little as 27 minutes with high titer specimens; GBS negative specimens generate results in approximated 43 minutes. The GeneXpert Instrument Systems, comprised of the GeneXpert Dx Systems and the GeneXpert Infinity Systems, have 1 to 80 randomly accessible modules, depending upon the instrument, that are each capable of performing separate sample preparation and real-time PCR and RT-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 and RT-PCR and detection.

The Xpert GBS LB XC test is performed on the Cepheid GeneXpert® Instrument Systems (GeneXpert Dx, GeneXpert Infinity-48s, and GeneXpert Infinity-80 systems). The GeneXpert Instrument System platform automates sample preparation, amplification and real-time detection. The GeneXpert systems consist of an instrument, computer, and preloaded software for running tests and viewing the results.

The GeneXpert Instrument Systems require the use of single-use, disposable cartridges (the Xpert GBS LB XC cartridges) that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained and specimens never come into contact with working parts of the instrument modules, cross-contamination between samples is minimized.

V. DEVICE INTENDED USE:

The Xpert® GBS LB XC test, performed on the GeneXpert® Instrument Systems, is an automated qualitative *in vitro* diagnostic test for the detection of Group B *Streptococcus* (GBS) DNA from enriched vaginal/rectal swab specimens, using real-time polymerase chain reaction (PCR).

Xpert GBS LB XC testing is indicated as an aid in determining the GBS colonization status of antepartum women.

- The Xpert GBS LB XC test is intended for antepartum testing on enriched Lim broth cultures of vaginal/rectal swabs after 18–24 hours of incubation.
- The Xpert GBS LB XC test does not provide antimicrobial susceptibility test results. Culture is necessary to obtain isolates to perform susceptibility testing as recommended for penicillin-allergic women.

This device is intended for prescription use only.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Substantial Equivalence:

The Xpert GBS LB XC test is substantially equivalent to the Xpert GBS LB Assay [510(k) # K121539].

The performance of the Xpert GBS LB XC test was evaluated in a multi-site clinical study in which the performance of the Xpert GBS LB XC test was determined relative to a composite comparator reference method using both results from culture and a FDA cleared nucleic acid test. The results of the study demonstrated that the performance of the Xpert GBS LB XC is substantially equivalent to the predicate device.

The following tables compare Xpert® GBS LB XC test to Xpert® GBS LB Assay (K121539). Table 1 shows similarities between the new device and the predicate, while Table 2 shows the differences.

Table 1. Similarities between New Device and Predicate Device

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® GBS LB XC	**Xpert GBS LB (K121539)**
Regulation	Same	**21CFR 866.3740** *Streptococcus* spp. serological reagents
Product Code	Same	NJR Nucleic acid amplification assay system, group b *streptococcus*, direct specimen test
Device Class	Same	I (non-exempt)
Intended Use	The Xpert GBS LB XC test, performed on the GeneXpert® Instrument Systems, is an automated qualitative *in vitro* diagnostic test for the detection of Group B *Streptococcus* (GBS) DNA from enriched vaginal/rectal swab specimens, using real-time polymerase chain reaction (PCR). Xpert GBS LB XC testing is indicated as an aid in determining the GBS colonization status of antepartum women. • The Xpert GBS LB XC test is intended for antepartum testing on enriched Lim broth cultures of vaginal/rectal swabs after 18–24 hours of incubation	The Cepheid Xpert GBS LB Assay, performed on the GeneXpert® Instrument Systems, is a qualitative *in vitro* diagnostic test designed to detect Group B Streptococcus (GBS) DNA from enriched vaginal/rectal swab specimens, using fully automated real-time polymerase chain reaction (PCR) with fluorogenic detection of the amplified DNA. Xpert GBS LB Assay testing is indicated as an aid in determining GBS colonization status in antepartum women. • The Xpert GBS LB Assay is used for antepartum testing on enriched Lim broth cultures of vaginal/rectal swabs after 18–24 hours of incubation • The Xpert GBS LB Assay does not provide susceptibility results. Culture

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® GBS LB XC	**Xpert GBS LB (K121539)**
	• The Xpert GBS LB XC test does not provide antimicrobial susceptibility test results. Culture is necessary to obtain isolates to perform susceptibility testing as recommended for penicillin-allergic women,	isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.
Instrument Systems	Same	Cepheid GeneXpert Instrument Systems
Laboratory Users	Same	CLIA Moderate Complexity
Specimen Type	Same	Enriched Lim broth cultures prepared from vaginal/rectal swabs after 18–24 hours of incubation
Collection and Transport Media	Same	Cepheid Swab Collection Device or equivalent swab in non-nutritive transport medium
Assay Technology	Same	Real-Time PCR
Self-Contained System Assay	Same	Yes
Single Use	Same	Yes
Automated Extraction, detection and result interpretation	Same	Yes
Fluidics	Same	Self-contained
External Assay Controls	Same	Materials available but not required
Built in Lysis Control	Same	Yes
Assay Results	Same	Qualitative
Time to Result (after enrichment)	Same	<60 minutes

Table 2. Differences between New Device and Predicate

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® GBS LB XC	**Xpert GBS LB (K121539)**
Analyte Target	Dual target assay design: The test targets two conserved chromosomal sequences in *S. agalactiae*: 1) a member of the glycosysl transferase gene family and 2) a *LysR* transcriptional regulator.	Single target assay design: The test targets the 3' DNA region adjacent to the *cfb* CAMP-factor hemolysin gene of *S. agalactiae.*
Assay Internal Controls	Same except that the IPC was eliminated since SPC is a fully process control monitoring both sample processing and PCR inhibition (monitored by the IPC).	Integrated internal controls to monitor sample processing, reagent hydration and PCR inhibition. • Specimen Processing Control (SPC) • Internal Process Control (IPC) • Probe Check Control (PPC)

Comparison		
Attribute	**New Device**	**Predicate Device**
	Xpert® GBS LB XC	**Xpert GBS LB (K121539)**
Early Assay Termination (EAT) Feature	Yes Early Assay Termination can reduce the test time for positive results as early as 27 minutes. With GBS negative samples, the test returns results in approximately 43 minutes.	No

The Xpert GBS LB XC test has the same general intended use as the predicate device and has the same technological characteristics as the predicate device. The differences between the Xpert GBS LB XC test and the predicate device do not raise different questions of safety and effectiveness.

VII. PERFORMANCE DATA

Non-Clinical Studies:

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

The analytical reactivity and limit of detection (LoD) of the Xpert GBS LB XC test were determined for 12 different strains representing 12 known serotypes of GBS, of which 2 were characterized as non-hemolytic (Table 3). Serial dilutions of each serotype were prepared in a Lim broth negative clinical sample matrix or 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 with one reagent lot for a total of 24 replicates of each dilution level 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. The results for all serotypes except serotype V and VI were ≥95% (≥19/20) detected. The result for serotype V and VI was 85% (17/20) detected and the claimed LoD is based on the upper level of 95% confidence interval.

Table 3. GBS Limit of Detection (LoD)

Serotype	LoD (CFU/mL) Probit Result	95% CI Probit Result	Percent Detected	LoD (CFU/mL) Verified	LoD (CFU/swab) Verified
Ia	663	492-835	100%	663	50
Ib	40	32-49	95%	40	3
Ic[a]	301	231-370	100%	301	23
II[a]	173	132-213	100%	173	13
III	540	409-670	100%	540	41
IV	429	324-533	95%	429	32
V	618	384-618	85%	618[b]	46
VI	544	353-544	85%	544[b]	41
VII	620	512-728	100%	620	47
VIII	682	509-855	100%	682	51
IX	465	354-575	100%	465	35
X	677	525-829	95%	677	51

[a] Non-hemolytic strain
[b] Claimed LoD corresponds to upper 95% upper CI

Analytical Reactivity with GBS cfb Mutants

A study was performed to evaluate the analytical reactivity of Xpert GBS LB XC test using GBS strains containing deletions in or adjacent to the region of the chromosome that encodes the CAMP factor hemolysis gene *cfb*. Ten unique, well characterized GBS clinical isolates representing different *cfb* mutations were tested at 833 CFU/mL. All strains with *cfb* mutations were detected with a positivity rate of 100%.

Analytical Specificity (Exclusivity) and Microbial Interference

The analytical specificity of the Xpert GBS LB XC test was evaluated by testing a panel of 128 strains, representing bacterial, viral, parasite and yeast strains commonly found in vaginal/rectal flora or phylogenetically related to GBS (Table 4) in the Xpert GBS LB XC test in the absence (exclusivity) or presence (microbial interference) of GBS. Bacteria were tested at $\geq 1x10^6$ CFU/ml, except as noted, and viruses and parasites were tested at a level of $\geq 1x10^5$ organisms, yeast, IU or copies/ml. Microorganisms with potential to grow to high titers in Lim broth during enrichment (*Candida albicans, Enterococcus faecalis, Enterococcus faecium, Enterococcus gallinarum, Streptococcus anginosus, Streptococcus parasanguinis, Corynebacterium accolens*) were tested at > $1x10^8$ CFU/ml. Of the 128 strains, 121 were tested in Lim broth clinical sample matrix or in simulated sample matrix, both in presence of GBS at 3x LoD and in absence of GBS.

Seven of 128 strains (*Finegoldia magna, Mobiluncus curtisii subsp. curtisii, Peptoniphilus asaccharolyticus, Fusobacterium nucleatum, Peptostreptococcus anaerobius, Anaerococcus tetradius* and *Anaerococcus prevotii*) were not available for *in vitro* testing and were evaluated by *in silico* analysis using the Xpert GBS LB XC primer and probe sequences as queries for organism- specific BLAST (Basic Local Alignment Search Tool) analysis of the NCBI (National Center for Biotechnology Information) Nucleotide collection (nr/nt) database.

No cross-reactivity or microbial interference of GBS detection was observed, both *in silico* and *in vitro*, with any clinically relevant pathogens.

Table 4. Analytical Specificity of the Xpert GBS LB XC Test

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*[c]
Acinetobacter lwoffii	Human immunodeficiency virus	*Staphylococcus epidermidis*
Actinobacillus pleuropneumoniae	Human Papillomavirus 18[b]	*Staphylococcus haemolyticus*

Organism		
Aeromonas hydrophila	*Klebsiella (Enterobacter) aerogenes*	*Staphylococcus intermedius*
Alcaligenes faecalis	*Klebsiella oxytoca*	*Staphylococcus lugdunensis*
Anaerococcus lactolyticus	*Klebsiella pneumoniae*	*Staphylococcus saprophyticus*
Anaerococcus prevotii[a]	*Lactobacillus acidophilus*	*Staphylococcus simulans*
Anaerococcus tetradius[a]	*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*[a]	*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*	*Streptococcus mutans*
Clostridium difficile	*Peptoniphilus asaccharolyticus*[a]	*Streptococcus oralis*
Cytomegalovirus	*Peptostreptococcus anaerobius*[a]	*Streptococcus parasanguinis*
Corynebacterium accolens	*Porphyromonas asaccharolytica*	*Streptococcus pneumoniae*
Corynebacterium sp. (genitalium)	*Prevotella bivia*	*Streptococcus pseudoporcinus*
Corynebacterium urealyticum	*Prevotella melaninogenica*	*Streptococcus pyogenes*[b]
Cryptococcus neoformans	*Prevotella oralis*	*Streptococcus ratti*
Enterobacter cloacae	*Propionibacterium acnes*	*Streptococcus salivarius*

Organism		
Enterococcus durans	*Proteus mirabilis*	*Streptococcus sanguinis*
Enterococcus faecalis	*Proteus vulgaris*	*Streptococcus sobrinus*
Enterococcus faecium	*Providencia stuartii*[b]	*Streptococcus suis*
Enterococcus gallinarum	*Pseudomonas aeruginosa*	*Streptococcus uberis*
Epstein-Barr virus	*Pseudomonas fluorescens*	*Streptococcus vestibularis*
Escherichia coli	*Rhodococcus equi*	*Toxoplasma gondii*
Finegoldia magna[a]	Rubella virus	*Trichomonas vaginalis*
Fusobacterium nucleatum[a]	*Salmonella enterica subsp. enterica ser. Dublin (group D)*	*Vibrio cholerae*
Gardnerella vaginalis	*Salmonella enterica subp. typhimurium*	*Yersinia enterocolitica*
Giardia lamblia[b]	*Serratia liquefaciens*	

a Evaluated in silico
b Evaluated with DNA
c Tested < 1x106 (2x105 CFU/ml)

Interfering Substances Study

Substances that may be present in vaginal/rectal specimens with the potential to interfere with the Xpert GBS LB XC 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 5. All liquid substances were tested by adding 100% of the substance to the swab, solid substances by covering swab head to 75% and tablets were dissolved to their highest soluble concentration in simulate sample matrix and added to the swab. Five exogenous substances (Aquasonic® gel, Floraplus, Pepto Bismol®, Skin oil and Xyloproct) were tested at lower concentration to determine the highest tolerated amount on swab (Table 5). The interferents were tested in the absence of GBS or in the presence of GBS at 3x LoD.

There was no interference in the presence of the substances at the concentrations tested in this study. All positive and negative samples were correctly identified using the Xpert GBS LB XC test.

Table 5. Potentially Interfering Substances Tested

Substance (Source)	Substance Form	Concentration on Swab
Human Amniotic Fluid (Lee Biosolutions Inc.)	Liquid	60% (v/v)
Human Urine (Novakemi)	Liquid	60% (v/v)
Human Whole Blood - EDTA (BioChemed)	Liquid	80%(v/v)
Human Whole Blood - Na Citrate (BioChemed)	Liquid	80% (v/v)
Leukocytes, Buffy coat, $2x10^7$ WBCs/ml (Karolinska University Hospital)	Liquid	80% (v/v)
Meconium (Lee Biosolutions)	Solid	100% (w/v)
Mucus (Sigma-Aldrich/Merck)	Solid	30% (w/v)
Human Feces - Pool of 10 donors	Solid	100 % (w/v)
Anti-Diarrheal Medication (Pepto Bismol)	Liquid[a]	40 % (v/v)
Anti-Diarrheal Medication (Dimor Comp [Dimeticone] from Nordic Drugs)	Tablet	0.03% loperamid + 2% dimetkon (w/v)
Lubricant (RFSU Klick Ultra Glide)	Solid	100% (w/v)
Lubricant (Sense Me Aqua Glide)	Solid	100% (w/v)
Lubricant (KY-Jelly)	Solid	100% (w/v)
Body Oil (ACO Repairing Skin Oil)	Liquid[b]	100% (w/v)
Dialon Baby (Dialon Baby powder)	Solid	100% (w/v)
Deodorant Powder (Vagisil® Deodorant Powder)	Solid	100% (w/v)
Deodorant Spray (LN Intimate Deo)	Liquid	60% (v/v)
Deodorant Suppositories (Norforms Feminine Deodorant Suppositories)	Solid	28.5% (w/v)
Enema solution (Microlax mikrolavemang – McNeil)	Solid	100% (w/v)
Oral Laxative (Inolaxol – Mylan)	Solid	25% (w/v)
Oral Laxative (Phillips Milk of Magensia – Bayer)	Liquid	60% (w/v)
Oral Laxative (Pursennid Ex-Lax – GSK)	Tablet	0.64% (w/v)
Spermicidal Foam (Caya preventivgel)	Solid	100% (v/v)
Stool Softener (Laktulos - Meda	Liquid	60% (v/v)
Stool Softener (Movicol – Norgine)	Solid	11% (w/v)
Topical Hemorrhoid Ointment (Xyloproct Rectal Ointment - Aspen)	Solid[c]	10% (w/v)
Topical Hemorrhoid Ointment (Scheriproct rektalsalva / Prednisolone Ointment– Bayer)	Solid	100% (v/v)
Ultrasound Transmission Gel (Aquasonic Gel – Parker)	Solidc	25% /w/v)
Vaginal Antifungal Gel (Multi-Gyn Actigel)	Solid	100% (v/v)
Vaginal Antifungal Gel (Multi-Gyn Floraplus)	Solidc	75% (w/v)
Vaginal Anti-itch Cream (Ellen Probiotisk Utvärtes Intim Creme)	Solid	100% (v/v)
Vaginal Antifungal Cream (Canesten - Bayer)	Solid	100% (v/v)
Vaginal Antifungal Cream (Daktar – McNeil)	Solid	100% (v/v)

a Pepto Bismol® diluted to 50% in background simulated background matrix and no interference observed.
b Skin oil tolerated when 67% of swab head covered (tested as solid substance).
c Substances were diluted into a simulated background matrix prior to testing: Xyloproct Rectal Ointment was tested at 10%, Aquasonic Gel was tested at 25% and MultiGyn Floraplus was tested at 75%. No interference was detection after dilution.

Carry-Over Contamination

A study was conducted to demonstrate that no carry-over contamination occurs when testing these single-use, self-contained GeneXpert cartridges in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately following a high GBS positive sample. Twenty-one runs alternating high titer GBS positive and GBS negative samples were performed consecutively on two GeneXpert modules, thus a total of 42 runs were executed for the study. All 20 positive samples were correctly reported as **GBS POSITIVE**. All 22 negative samples were correctly reported as **GBS NEGATIVE**.

Reproducibility Study

A panel of ten samples with varying concentrations of four different GBS strains were tested by two operators each in triplicate on six different days at three sites using 3 different lots of Xpert GBS LB XC (2 operators × 3 replicates/day × 6 days × 3 sites) including negative panel members. Three lots of Xpert GBS LB XC were used at each of the three testing sites. The source of the three strains (serotype Ia, III, IV) representing a hemolytic phenotype and one strain (serotype Ic) representing a non-hemolytic phenotype is presented in Table 6. The three levels were ~3 × LOD and ~1 × LOD and negative.

Table 6. Reproducibility Panel

Strain	Phenotype	Panel Member
Not applicable	Not applicable	Negative
GBS Serotype Ia - ATCC12386	Hemolytic	Low Positive (~1X LoD)
		Moderate Positive (~3X LoD)
GBS Serotype Ic -ATCC13813	Non-emolytic	Low Positive (~1X LoD)
		Moderate Positive (~3X LoD)
GBS Serotype III - ATCC12403	Hemolytic	Low Positive (~1X LoD)
		Moderate Positive (~3X LoD)
GBS Serotype IV -ATCC49446	Hemolytic	Low Positive (~1X LoD)
		Moderate Positive (~3X LoD)

Xpert GBS LB XC testing was performed on the GeneXpert Instrument Systems according to the Xpert GBS LB XC test procedure.

The percent agreement of the qualitative results for GBS detection for each sample calculated for each of the six operators and for each site is shown in Table 7. In addition, the overall percent agreement for each sample (total agreement) and the 95% two-sided Wilson Score confidence interval are shown in the last column.

Table 7: Summary of Reproducibility and Precision Results

	Sample	Site 1			Site 2			Site 3			Total Agreement by Sample with 95% CI
		OP 1	OP 2	Subtotal	OP 1	OP 2	Subtotal	OP 1	OP 2	Subtotal	
01	Negative 1[a]	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
02	Negative 2[a]	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
03	GBS serotype Ia~1xLoD	100.0% (18/18)	94.4% (17/18)	97.2% (35/36)	100.0% (18/18)	94.4% (17/18)	97.2% (35/36)	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	98.1% (106/108) 93.5-99.5
04	GBS serotype Ic[b]~1xLoD	100% (18/18)	100% (18/18)	100% (36/36)	100% (18/18)	100% (18/18)	100% (36/36)	100% (18/18)	100% (18/18)	100% (36/36)	100.0% (108/108) 96.6-100.0
05	GBS serotype III~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) 96.6-100.0
06	GBS serotype IV ~1xLoD	100.0% (18/18)	100.0% (18/18)	100.0% (36/36)	94.0% (17/18)	94.0% (17/18)	94.0% (34/36)	100.0% (18/18)	94.0% (17/18)	97.0% (35/36)	97.2% (105/108) 92.1-99.4
07	GBS serotype Ia ~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
08	GBS serotype Ic[b]~3xLoD	100.0% (17/17)	100.0% (18/18)	100.0% (35/35)	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% (107/107) 96.5-100.0
09	GBS serotype III ~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
10	GBS serotype IV~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

a. Testing with Serotype Ic was performed separately from testing by the other panel members. Negative panel members were included in both rounds of testing and are represented separately in the performance table above.
b. Serotype Ic is characterized as non-hemolytic.

No statistically significant difference in performance (p-value of <0.01) was observed between the study sites, operators, or the lots used; p-values ranged from 0.7715 to 1.

ANOVA Analysis

The study also enabled evaluation of repeatability (within-run variance/assay precision) as well as the within-laboratory precision of the underlying quantitative result (Ct values) obtained from the Xpert test, on which the qualitative reportable results are based.

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 presented in Table 8.

Table 8. ANOVA Summary of Reproducibility Data

Panel Member	N	Mean CT	Variance Source											
			Site		Operator		Lot		Day		Within-Run		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	CV(%)
Mod Pos GBS serotype Ia ~3xLoD	108	32.7	0.1	0.6	0	0	0.3	11.0	0	0	0.9	88.4	0.9	2.9
Mod Pos GBS serotype III ~3xLoD	108	33.9	0	0	0.2	5.6	0.3	10.7	0	0	0.9	83.6	0.9	2.8
Mod Pos GBS serotype IV ~3xLoD	108	33.3	0	0	0.2	4.1	0.4	21.0	0.1	1.0	0.8	73.9	1.0	2.9
Low Pos GBS serotype Ia ~1xLoD	106[a]	34.6	0.6	16.0	0	0	0.7	23.2	0	0	1.1	60.8	1.5	4.3
Low Pos GBS serotype III ~1xLoD	108	35.0	0.3	4.0	0	0	0.2	2.6	0.5	14.9	1.1	78.5	1.3	3.6
Low Pos GBS serotype IV ~1xLoD	105[b]	34.9	0	0	0.5	19.1	0.2	3.1	0.2	3.9	1.1	73.9	1.2	3.6
Negative 1[c]	108	32.1	0.1	0.7	0	0	0.3	18.2	0.2	10.7	0.6	70.4	0.7	2.2
Mod Pos GBS serotype Ic ~3xLoD	107[d]	33.5	0	0	0	0	0.3	11.0	0.5	34.9	0.6	54.1	0.8	2.4
Low Pos GBS serotype Ic ~1xLoD	108	35.2	0	0	0.2	2.7	0	0	0.6	21.5	1.0	75.8	1.2	3.4
Negative 2[c]	108	31.9	0	0	0	0	0.4	26.8	0.2	5.6	0.6	67.6	0.7	2.1

a. Two panel members with GBS negative results were excluded from ANOVA analysis.
b. Three panel members with GBS negative results were excluded from ANOVA analysis.
c. ANOVA calculations are based on the SPC Ct values for the negative panel members.
d. One sample with a GBS negative result was excluded from ANOVA analysis.

The total SDs ranged from 0.7 to 1.5. The SDs did not exceed 50% of the total SD for the following factors: Site-to-Site, Operator-to-Operator, Lot-to-Lot and Day-to-Day. The majority of the total variance came from within-assay random variance (assay noise), and not from the other evaluated factors.

Clinical Studies

Clinical Performance

Clinical performance of the Xpert GBS LB XC test was evaluated in a multisite study conducted in the United States using the GeneXpert Dx instrument system. Vaginal/rectal swab specimens were collected at three (3) geographically diverse sites from pregnant females for GBS testing as a part of routine care. Specimens were inoculated in Lim broth per institutional policy. For eligible specimens, aliquots of leftover Lim broth samples were obtained for testing with the Xpert GBS LB XC test. The results of the Xpert GBS LB XC test were compared to a composite comparator method. The composite comparator method comprised of enriched bacterial culture with species identification via Matrix Assisted Laser Desorption Ionization - Time of Flight Mass Spectroscopy (MALDI-TOF MS) and an FDA cleared NAAT. For the composite comparator, a specimen was considered positive if either enriched bacterial culture or the FDA cleared NAAT was positive and negative when both enriched bacterial culture and the FDA cleared NAAT were negative. Additionally, the Xpert GBS LB XC test was compared directly to the FDA cleared NAAT test.

Performance of Xpert GBS LB XC v Composite Comparator

A total of 621 specimens with results from enriched bacterial culture and the FDA cleared NAAT were included in the analyses of Xpert GBS LB XC versus the composite comparator method. The results are shown in the table below.

Table 9. Xpert GBS LB XC Performance vs. Composite Comparator

		Composite Comparator		
		Positive	**Negative**	**Total**
Xpert GBS LB XC	**Positive**	142	6	148
	Negative	1	472	473
	Total	143	478	621
	Sensitivity	99.3% (95%CI: 96.1-99.9)		
	Specificity	98.7% (95%CI: 97.3-99.4)		
	PPV	95.9% (95%CI: 91.4-98.1)		
	NPV	99.8% (95%CI: 98.8-100.0)		
	Prevalence	23.0% (95%CI: 19.9-26.5)		

As shown in Table 9, the sensitivity and specificity of the Xpert GBS LB XC test compared to the composite comparator method were 99.3% and 98.7%, respectively.

Performance of the Xpert GBS LB XC Test vs. FDA Cleared NAAT

A direct comparison of the Xpert GBS LB XC test to the FDA cleared NAAT was also performed. The results are shown in the table below.

Of 622 samples tested with the Xpert GBS LB XC test during this study, nine yielded non-determinate results on the initial test. These nine samples were retested and eight returned valid results. The initial non-determinate rate was 1.4% (9/622) and the final non-determinate rate was 0.2% (1/622).

VIII. CONCLUSIONS

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the Xpert GBS LB XC test is substantially equivalent to the predicate device.