September 27, 2023

Cepheid
Shilpa Kuttetira
Senior Regulatory Affairs Specialist
904 Caribbean Drive
Sunnyvale, California 94089

Re: K222638
Trade/Device Name: Xpert® Xpress GBS, GeneXpert® Dx System, GeneXpert® Infinity Systems
Regulation Number: 21 CFR 866.3740
Regulation Name: Streptococcus Spp. Serological Reagents
Regulatory Class: Class I
Product Code: NJR, OOI
Dated: August 31, 2022
Received: September 1, 2022

Dear Shilpa Kuttetira:

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,

Ribhi Shawar -S

Ribhi Shawar, Ph.D. (ABMM)
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K222638

Device Name
Xpert® Xpress GBS

Indications for Use *(Describe)*

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

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.

510(k) Summary
for
Xpert Xpress GBS

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5. 510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone Number: (408) 966-8860
Contact:	Shilpa Kuttetira
Date of Preparation:	September 18, 2023
Device Trade name: Common name:	 Xpert® Xpress GBS Xpert Xpress GBS
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; 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; 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
Predicate Device	Xpert® GBS (K060540)

5.1. 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 Xpert Xpress GBS test is performed on the Cepheid GeneXpert® Instrument Systems (GeneXpert Dx, GeneXpert Infinity-48s and GeneXpert Infinity-80 systems), which consist of an instrument, computer and preloaded software for running tests and viewing the results. The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification, and real-time detection. Depending on the instrument, the GeneXpert Instrument Systems can have from 1 and up to 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. The primers and probes in the Xpert Xpress GBS test are designed to amplify and detect unique sequence in two conserved chromosomal targets in *S. agalactiae*: a) a member of the glycosysl transferase gene family, and b) 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. In the Xpert Xpress GBS test, the SAC detects the presence of the human hydroxymethylbilane synthase (HMBS) gene 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.

The Xpert Xpress GBS test is designed for use with vaginal/rectal swab specimens collected from pregnant patients at intrapartum and placed into a collection device. The ancillary specimen collection kit validated for use with the Xpert Xpress GBS test is the Cepheid Collection Device (Catalog 900-0370). 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.

5.2. Device 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 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.

5.3. Substantial Equivalence

Table 5-1 shows the similarities and differences between Xpert Xpress GBS and the predicate device, Xpert GBS [K060540].

Table 5-1: Comparison of Similarities and Differences Between Xpert Xpress GBS and the Predicate Device

Attribute	Investigational Device	Predicate Device – K060540
	Cepheid Xpert® Xpress GBS	**Cepheid Xpert® GBS**
Regulation	Same	**21 CFR 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)
Technology/ Detection	Same	Real-Time PCR

Attribute	Investigational Device Cepheid Xpert® Xpress GBS	Predicate Device – K060540 Cepheid Xpert® GBS
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 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.	The Cepheid Xpert GBS performed on the GeneXpert Dx System is a qualitative in vitro diagnostic test designed to detect Group B Streptococcus (GBS) DNA from vaginal/rectal swab specimens, using fully automated real-time polymerase chain reaction (PCR) with fluorogenic detection of the amplified DNA. Xpert GBS Assay testing is indicated for rapid identification of antepartum and intrapartum GBS colonization. • The use of the Xpert GBS for intrapartum screening should not preclude the use of other strategies (e.g., antepartum testing). Intrapartum Xpert GBS results are useful to identify candidates for intrapartum antibiotic prophylaxis when administration of intravenous antibiotics is not delayed pending results. • The Xpert GBS Assay does not provide susceptibility results. Culture isolates are needed for performing susceptibility testing as recommended for penicillin-allergic women.
Assay Targets	Dual target assay design against two conserved sequences in *S. agalactiae*: • a member of the glycosyl transferase gene family and • a *LysR* transcriptional regulator	• 3' region adjacent to *cfb* gene CAMP-factor hemolysin gene of *S. agalactiae*
Specimen Type	Same	Direct from vaginal/rectal swab specimens
Collection Device	Same	Cepheid Collection Device with Liquid Stuart Medium (Catalog Part 900-0370)

Attribute	Investigational Device	Predicate Device – K060540
	Cepheid Xpert® Xpress GBS	**Cepheid Xpert® GBS**
Single Use Cartridge	Same	Yes
Automated Nucleic Acid Extraction, Detection and Results Interpretation	Same	Yes
Assay Results	Same	Qualitative
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 returns a high titer sample in ~ 30 minutes	No
Time to Result	< 50 minutes	< 60 minutes

The Xpert Xpress GBS test has the same general intended use and the same technological characteristics as the predicate device. The performance of the Xpert Xpress GBS test was evaluated in a multi-site clinical study. The differences between the Xpert Xpress GBS test and the predicate device do not raise different questions of safety and effectiveness.

The results from the clinical evaluation demonstrate that performance of the Xpert Xpress GBS test is acceptable for its intended use.

5.4. Performance Studies

5.4.1. Analytical Performance

Analytical Sensitivity (LoD) 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 5-2). 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 to the upper limit of the 95% confidence interval determined in the probit analysis 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 5-2.

Table 5-2. Xpert Xpress GBS Limit of Detection

Serotype	LoD (CFU/mL)	LoD (CFU/Swab)
Ia	663	50
Ib	40	3
Ic[a]	301	23
II[a]	173	13
III	540	41
IV	429	32
V	618[b]	46
VI	544[b]	41
VII	620	47
VIII	682	51
IX	465	35
X	677	51

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

Matrix Equivalency Studies were performed to support the use of simulated sample matrix for the analytical studies.

Analytical Inclusivity of 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%.

Analytical Specificity (Cross-Reactivity/Exclusivity) and Microbial Interference

The analytical specificity and microbial interference of the Xpert Xpress GBS test was 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 phylogenetically related to GBS and are shown in Table 5-3.

Bacteria and yeast were tested at concentrations of ≥ $1x10^6$ 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 6. No cross-reactivity or microbial interference of GBS detection was observed with any of the clinically relevant pathogens tested in the study.

Table 5-3: 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*
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*

Organism		
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

Potentially Interfering Substances

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 5-4.

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 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) is shown in Table 5-4.

Table 5-4: 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)

Substance	Substance Form	Highest Concentration on Swab Resulting in No Interference
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 well 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.

Carryover Contamination

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 PRESUMPTIVE NEGATIVE.**

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 5-5. 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 5-5. Summary of Reproducibility Results - % 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	~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 5-6.

Table 5-6. 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

5.4.2. Clinical Performance

Clinical 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 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 – 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.

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 5-8, for informational purposes only.

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

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 5-7.

Table 5-7: 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%)

Of the 912, 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 5-8. The Xpert Xpress GBS demonstrated a sensitivity of 93.5% and specificity of 95.5% in vaginal/rectal swab specimens collected at intrapartum, and a PPV of 66.1% and NPV of 99.4%, respectively.

Table 5-8. Xpert Xpress GBS Performance Results vs. Enriched Culture + MALDI-TOF MS – Intrapartum Specimens

Results	Culture Positive	Culture Negative	Total	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)
Xpert Xpress GBS Positive	72	37[a]	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 Presumptive Negative	5[b]	785	790				
Total	77	822	899				

a. Discrepant test results based on an FDA-cleared NAAT: 13/37 GBS positive; 15/37 GBS negative; 9/37 no valid result
b. Discrepant test results based on an FDA-cleared NAAT: 4/5 GBS positive; 1/5 GBS negative

Non-Determinate Rate

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 retest, 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).

5.5. Conclusion

The results of the non-clinical analytical and clinical performance studies summarized above demonstrated that the Xpert Xpress GBS test is substantially equivalent to the predicate device.