April 26, 2018

Cepheid
Jim Kelly
Executive Director, Regulatory Affairs
904 Caribbean Drive
Sunnyvale, California 94089

Re: K173398
Trade/Device Name: Xpert Xpress Strep A
Regulation Number: 21 CFR 866.2680
Regulation Name: Streptococcus spp. nucleic acid-based assay
Regulatory Class: Class II
Product Code: PGX, OOI
Dated: October 28, 2017
Received: October 31, 2017

Dear Jim Kelly:

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. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR

Part 820); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/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
For
Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K173398

Device Name

Xpert Xpress Strep A

Indications for Use *(Describe)*

The Xpert Xpress Strep A test, performed on the GeneXpert Xpress System, is a rapid, qualitative in vitro diagnostic test for the detection of Streptococcus pyogenes (Group A β-hemolytic Streptococcus, Strep A) in throat swab specimens from patients with signs and symptoms of pharyngitis. The Xpert Xpress Strep A test can be used as an aid in the diagnosis of Group A Streptococcal pharyngitis. The assay is not intended to monitor treatment for Group A Streptococcus infections.

The Xpert Xpress Strep A test utilizes an automated real-time polymerase chain reaction (PCR) to detect Streptococcus pyogenes DNA.

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

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (847) 228-3299 Fax number: (847) 890-6589
Contact:	Jim Kelly, Ph.D.
Date of Preparation:	April 23, 2018
Device:	
Trade name:	Xpert® Xpress Strep A
Common name:	Xpert Xpress Strep A
Type of Test:	Real-time PCR assay for qualitative detection of Group A *Streptococcus* DNA in throat swab specimens.
Regulation number, Classification name, Product code:	21 CFR 866.2690, *Streptococcus* spp. nucleic acid based assay, PGX 21 CFR 862.2570, Instrumentation for clinical multiplex test systems, OOI
Classification Advisory Panel	Microbiology (83)
Prescription Use	Yes
Predicate Device Assay:	IQuum Roche Liat™ Strep A Assay [510(k) #K141338]

Device Description:

The Xpert Xpress Strep A test is an automated real-time polymerase chain reaction (PCR) *in vitro* diagnostic test for qualitative detection of *Streptococcus pyogenes* from throat swab specimens from patients with signs and symptoms of pharyngitis.

The Xpert Xpress Strep A test is performed on the Cepheid GeneXpert® Xpress System. The GeneXpert Xpress System platform automates sample preparation, amplification and real-time detection.

The GeneXpert Xpress System requires the use of single-use, disposable cartridges (the Xpert Xpress Strep A 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.

The Xpress Strep A test includes primers and probes for the detection of a targeted sequence of the *S. pyogenes* genome allowing detection of Strep A directly from throat swab specimens collected from patients with signs and symptoms of pharyngitis. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are internal controls utilized by the GeneXpert Xpress System platform. The SPC is present to control for adequate processing of the target bacteria and to monitor for the presence of inhibitor(s) in the PCR assay to avoid false-negative results. The Probe Check Control verifies reagent rehydration, real-time 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 genomic DNA *S. pyogenes* in ~24 minutes or less. The GeneXpert Xpress System, comprised of the GeneXpert Xpress II and GeneXpert Xpress IV, is 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.

Throat swab specimens are collected using the ESwab collection device and transported to the GeneXpert area and prepared according to package insert instructions. After mixing the specimen, the liquid sample is transferred to the Xpert Xpress Strep A cartridge. The user initiates a test from the system user interface and places the cartridge into the GeneXpert Xpress instrument platform, which performs hands-off real-time, multiplex PCR for detection of DNA. The results are automatically generated at the end of the process in a report that can be viewed and printed.

Device Intended Use:

The Xpert® Xpress Strep A test, performed on the GeneXpert Xpress System, is a rapid, qualitative *in vitro* diagnostic test for the detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcu*s, Strep A) in throat swab specimens from patients with signs and symptoms of pharyngitis. The Xpert Xpress Strep A test can be used as an aid in the diagnosis of Group A Streptococcal pharyngitis. The assay is not intended to monitor treatment for Group A *Streptococcus* infections.

The Xpert Xpress Strep A test utilizes an automated real-time polymerase chain reaction (PCR) to detect *Streptococcus pyogenes* DNA.

Substantial Equivalence:

The Xpert Xpress Strep A test is substantially equivalent to the Roche Liat Strep A Assay [510(k) # K141338]. The performance of the Xpert Xpress Strep A test was evaluated in a multi-site clinical study in which the performance of Xpert Xpress Strep A was determined relative to culture. The results of the study demonstrated that the performance of Xpert Xpress Strep A is substantially equivalent to the predicate device.

Table 8-1 shows the similarities and differences between Xpert Xpress Strep A and the predicate device.

Table 8-1: Comparison of Similarities and Differences of Xpert Xpress Strep A with the Predicate Device

Similarities		
Item	**Device**	**Predicate Device**
	Cepheid Xpert Xpress Strep A	**IQuum Inc. (Roche) Liat Strep A Assay**
510(k) Number	To be assigned	K141338
Regulation	Same	866.2680
Product Code	Same	PGX
Device Class	Same	II
Intended Use	The Xpert® Xpress Strep A test, performed on the GeneXpert Xpress System, is a rapid, qualitative *in vitro* diagnostic test for the detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcus*, Strep A) in throat swab specimens from patients with signs and symptoms of pharyngitis. The Xpert Xpress Strep A test can be used as an aid in the diagnosis of Group A Streptococcal pharyngitis. The assay is not intended to monitor treatment for Group A *Streptococcus* infections. The Xpert Xpress Strep A test utilizes an automated real-time polymerase chain reaction (PCR) to detect *Streptococcus pyogenes* DNA.	The Liat™ Strep A Assay, performed on the Liat™ Analyzer, is a qualitative *in vitro* diagnostic test for the detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcus*) in throat swab specimens from patients with signs and symptoms of pharyngitis. The Liat™ Strep A Assay utilizes nucleic acid purification and polymerase chain reaction (PCR) technology to detect *Streptococcus pyogenes* by targeting a segment of the *Streptococcus pyogenes* genome.
Assay Target	Same	*Streptococcus* A

Similarities		
Item	**Device**	**Predicate Device**
	Cepheid Xpert Xpress Strep A	**IQuum Inc. (Roche) Liat Strep A Assay**
Specimen Type	Same	Throat swab
Assay Controls	Yes	Yes
Strep A Target	Same	Conserved sequence within the genome of *S. pyogenes*
Assay Method	Same	PCR for detecting the presence / absence of bacterial DNA in clinical specimens
Extraction Method	Same	Automated nucleic acid extraction and purification
Detection Technique	Same	Different reporter dyes for target and Internal Control
Assay Result	Same	Qualitative
Differences		
	New Device	**Predicate Device**
Item	**Cepheid Xpert Xpress Strep A**	**IQuum Inc. (Roche) Liat Strep A Assay**
Equipment Required	Cepheid GeneXpert® Dx, GeneXpert Infinity-48s, GeneXpert Infinity-80, and GeneXpert Xpress System	Liat™ Analyzer
Early assay termination function	Yes (for positive samples)	No
Time-to-result	~24 minutes without early assay termination; ~18 minutes with early assay termination for positive samples	~15 minutes

The Xpert Xpress Strep A test has the same general intended use as the predicate device and has the same technological characteristics as the predicate device. The differences between Xpert Xpress Strep A and the predicate device do not raise different questions of safety and effectiveness. The clinical study demonstrates that the Xpert Xpress Strep A test is acceptable for its intended use with inexperienced lab users and is substantially equivalent to the predicate device described above.

Non-Clinical Studies:

Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical sensitivity or Limit of Detection (LoD) of the Xpert Xpress Strep A using the ESwab collection kit. The limit of detection is the lowest concentration of sample (reported as CFU/mL in ESwab transport medium or CFU/test) that can be reproducibly distinguished from negative samples 95% of the time, or the lowest concentration of organisms at which 19 of 20 replicates were positive. This study determined the lowest concentration of *Streptococcus pyogenes* cells diluted into pooled clinical throat swab matrix that can be detected using the Xpert Xpress Strep A.

The analytical sensitivity of the Xpert Xpress Strep A was performed using two lots of reagents tested across three testing days with two *Streptococcus pyogenes* strains: ATCC BAA-946 and ATCC 19615.

The claimed LoD for each Strep A strain tested is summarized in Table 8-2.

Table 8-2: Strep A LoD

Strep A Strain	***emm* type**	**LoD (CFU/mL in ESwab transport medium)**	**LoD (CFU/test)**
ATCC BAA-946	6	9	3
ATCC 19615	80	18	6

Analytical Reactivity (Inclusivity)

Twenty-four *Streptococcus pyogenes* strains were tested at 3X LoD using the Xpert Xpress Strep A in replicates of three. The strains tested included representative isolates of *emm* types 1, 3, 4, 6, 11, 12, 18, 22, 25, 27, 38, 75, 77, 89, 94, 95. The list of strains tested in ESwab medium containing simulated throat swab matrix is shown in Table 8-3. All 24 strains were correctly reported as **Strep A DETECTED** with the Xpert Xpress Strep A.

Table 8-3: Analytical Reactivity (Inclusivity) of Xpert Xpress Strep A

Strep A Strain ID	***emm* type**	**Strain**
ATCC 12202	1	NCTC 8370
ATCC 12344	1	T1
ATCC 700294	1	SF370
ATCC 12383	3	D58X
ATCC 12384	3	C203
ATCC 12385	4	J17A4
ATCC 12203	6	NCTC 8709

Strep A Strain ID	*emm* type	Strain
ATCC 12352	11	T11
ATCC BAA-1065	12	MGAS 2096
ATCC BAA-1315	12	MGAS9429
ATCC 12357	18	J17C
ATCC 10403	22	T22
ATCC 12204	25	A25
ATCC 8135	27	T27
ATCC 12365	38	C107
ATCC 12370	38	C94
ATCC 700497	75	CDC-SS-1147
ATCC 700499	77	CDC-SS-1149
ATCC 700949	89	CDC-SS-1397
ATCC BAA-355	94	N/A
ATCC BAA-356	95	N/A
ATCC 14289	M protein-deficient *S. pyogenes*	C203 S
ATCC 49399	*emm* type not available	QC A62
ATCC 51339	*emm* type not available	1805

Analytical Specificity (Exclusivity)

The analytical specificity of the Xpert Xpress Strep A was evaluated by testing a panel of 70 potentially cross-reactive microorganisms, including species that are phylogenetically related to *Streptococcus pyogenes* and members of the throat commensal microflora (e.g., other bacteria, viruses, and yeast). The 70 organisms tested were identified as either Gram-positive (27), Gram-negative (33), or Gram-indeterminate (3), yeast (1), and viruses (6). *Streptococcus* Group B, *Streptococcus* Group C, and *Streptococcus* Group G strains were also included in this study. All strains were tested in triplicate in ESwab transport medium containing simulated throat swab matrix at $\geq 10^6$ CFU/mL for bacteria and yeast and $\geq 10^5$ $TCID_{50}$/mL for viruses. All three replicates of all 70 organisms were reported as **Strep A NOT DETECTED** by the Xpert Xpress Strep A (Table 8-4). The analytical specificity of the Xpert Xpress Strep A was 100%.

Table 8-4: Analytical Specificity of Xpert Xpress Strep A

Organism	Results
Acinetobacter baumannii	Strep A NOT DETECTED
Arcanobacterium haemolyticum	Strep A NOT DETECTED
Adenovirus, Type 1	Strep A NOT DETECTED
Adenovirus, Type 7	Strep A NOT DETECTED
Bacillus cereus	Strep A NOT DETECTED
Bordetella bronchiseptica	Strep A NOT DETECTED
Bordetella parapertussis	Strep A NOT DETECTED
Bordetella pertussis	Strep A NOT DETECTED

Organism	Results
Burkholderia cepacia	Strep A NOT DETECTED
Campylobacter rectus	Strep A NOT DETECTED
Candida albicans	Strep A NOT DETECTED
Corynebacterium diphtheriae	Strep A NOT DETECTED
Corynebacterium	Strep A NOT DETECTED
Cytomegalovirus AD-169	Strep A NOT DETECTED
Enterococcus faecalis	Strep A NOT DETECTED
Enterococcus faecium	Strep A NOT DETECTED
Epstein-Barr Virus 4	Strep A NOT DETECTED
Escherichia coli	Strep A NOT DETECTED
Fusobacterium necrophorum	Strep A NOT DETECTED
Haemophilus influenzae type A	Strep A NOT DETECTED
Haemophilus parahaemolyticus	Strep A NOT DETECTED
Haemophilus parainfluenzae	Strep A NOT DETECTED
Hepatitis B Virus	Strep A NOT DETECTED
Herpes Simplex Virus	Strep A NOT DETECTED
Klebsiella pneumoniae	Strep A NOT DETECTED
Lactobacillus acidophilus	Strep A NOT DETECTED
Lactococcus lactis subsp. *lactis*	Strep A NOT DETECTED
Legionella jordanis	Strep A NOT DETECTED
Legionella micdadei	Strep A NOT DETECTED
Legionella pneumophila	Strep A NOT DETECTED
Listeria monocytogenes	Strep A NOT DETECTED
Moraxella catarrhalis (two strains)	Strep A NOT DETECTED
Moraxella lacunata	Strep A NOT DETECTED
Mycoplasma pneumoniae	Strep A NOT DETECTED
Neisseria gonorrhoeae	Strep A NOT DETECTED
Neisseria lactamica	Strep A NOT DETECTED
Neisseria meningitidis	Strep A NOT DETECTED
Neisseria mucosa	Strep A NOT DETECTED
Neisseria sicca	Strep A NOT DETECTED
Neisseria subflava	Strep A NOT DETECTED
Peptostreptococcus micros	Strep A NOT DETECTED
Prevotella (Bacteroides) oralis	Strep A NOT DETECTED
Proteus mirabilis	Strep A NOT DETECTED
Proteus vulgaris	Strep A NOT DETECTED
Pseudomonas aeruginosa	Strep A NOT DETECTED
Pseudomonas fluorescens	Strep A NOT DETECTED
Serratia marcescens	Strep A NOT DETECTED
Staphylococcus aureus	Strep A NOT DETECTED
Staphylococcus epidermidis	Strep A NOT DETECTED

Organism	Results
Staphylococcus haemolyticus	Strep A NOT DETECTED
Stenotrophomonas maltophilia	Strep A NOT DETECTED
Streptococcus agalactiae	Strep A NOT DETECTED
Streptococcus anginosus	Strep A NOT DETECTED
Streptococcus bovis	Strep A NOT DETECTED
Streptococcus canis	Strep A NOT DETECTED
Streptococcus constellatus	Strep A NOT DETECTED
Streptococcus dysgalactiae	Strep A NOT DETECTED
Streptococcus equi	Strep A NOT DETECTED
Streptococcus gallolyticus	Strep A NOT DETECTED
Streptococcus intermedius	Strep A NOT DETECTED
Streptococcus mitis	Strep A NOT DETECTED
Streptococcus mutans	Strep A NOT DETECTED
Streptococcus oralis	Strep A NOT DETECTED
Streptococcus pneumoniae	Strep A NOT DETECTED
Streptococcus salivarius	Strep A NOT DETECTED
Streptococcus sanguinus	Strep A NOT DETECTED
Treponema denticola	Strep A NOT DETECTED
Veillonella parvula	Strep A NOT DETECTED
Yersinia enterocolitica	Strep A NOT DETECTED

Microbial Interference

An interfering microorganism study was performed to assess the inhibitory effects of commensal microorganisms in throat swab samples on the performance of the Xpert Xpress Strep A. Twenty-seven microorganisms were tested for potential interference with Strep A detection (Table 8-5). The microorganisms were tested at $\geq 10^6$ CFU/mL in the presence of Strep A at 3X LoD concentration in ESwab medium containing simulated throat swab matrix. The results showed that the presence of the tested microorganisms did not interfere with the detection of Strep A target DNA.

Table 8-5: Commensal Microorganisms Tested

Organism
Acinetobacter baumannii
Candida albicans
Enterococcus faecalis
Fusobacterium necrophorum
Haemophilus influenzae type A
Lactobacillus acidophilus
Neisseria lactamica[a]
Peptostreptococcus micros
Prevotella (Bacteroides) oralis

Staphylococcus epidermidis
Streptococcus agalactiae
Streptococcus anginosus
Streptococcus bovis
Streptococcus canis
Streptococcus constellatus
Streptococcus dysgalactiae
Streptococcus equi
Streptococcus gallolyticus
Streptococcus intermedius
Streptococcus mitis
Streptococcus mutans
Streptococcus oralis
Streptococcus pneumoniae
Streptococcus salivarius
Streptococcus sanguinus
Treponema denticola
Veillonella parvula

a. Although all samples were reported appropriately as positive, reduced fluorescent signal was observed for the *S. pyogenes* target in the presence of high concentrations of *N. lactamica.*

Potentially Interfering Substances Study

Ten potentially interfering substances that may be present in clinical throat specimens with the potential to interfere with the performance of the Xpert Xpress Strep A were evaluated. The potentially interfering substances included blood, mucus, human saliva, sugar-containing cold and flu remedies, cough medicine, antiseptic, salt-modifying remedies, pH-modifying remedies, antacids, and foods or drinks that increase salivary viscosity. The substances, active ingredients, and concentrations tested are listed in Table 8-6. Medically and/or physiologically relevant concentrations of potential interferents were tested in simulated throat swab matrix in the presence and absence of Strep A at 3X LoD.

There was no assay 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 Xpress Strep A.

Table 8-6: Potential Interfering Substances Tested

Substance/Class	Description/Active Ingredient	Concentration Tested
Saliva	100% Human Saliva	6.5% (v/v)
Mucin	Bound sialic acid, 0.5-1.5%	2.5% (w/v)
Blood	Whole human blood	5.0% (v/v)
Antiseptic	0.092% Eucalyptol, 0.042% menthol, 0.060% methyl salicylate, 0.064% thymol	6.5% (v/v)[a.]
Cough Medicine	Dextromethorphan HBr USP 10 mg, Guaifenesin USP 200 mg	5 mg/mL
Sugar-containing cold and flu remedies	Acetaminophen 650 mg, Dextromethorphan HBr 20 mg, Doxylamine Succinate 12.5 mg, Phenylephrine HCl 10 mg	6.5% (v/v)
Salt-modifying remedies	Sodium Chloride (0.65%)	6.5% (v/v)
Foods/drinks that increase salivary viscosity	Milk	6.5% (v/v)
pH Modifying Remedies	100% Orange juice	6.5% (v/v)
Antacids	Aluminum Hydroxide 400 mg (equivalent to dried gel, USP) – antacid, Magnesium Hydroxide 400 mg – antacid, Simethicone 40 mg – antigas	6.5% (v/v)

a. Although all samples were reported appropriately as positive or negative, reduced fluorescent signal for the *S. pyogenes* target was observed in the presence of antiseptic mouthwash at 6.5% v/v.

Carry-Over Contamination

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent specimen and amplicon carry-over contamination from very high titer positive samples (*S. pyogenes*) into successively run negative samples when processed in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately after processing a very high titer positive sample at a concentration $\geq 1 \times 10^6$ CFU/mL in ESwab transport medium containing simulated throat swab matrix. The testing scheme was repeated 40 times between 2 GeneXpert instruments (one module per instrument) for a total of 41 runs per instrument (20 high positive samples per instrument and 21 negative samples per instrument). There was no evidence of any carry-over contamination. All 42 negative samples were correctly

reported as **Strep A NOT DETECTED**. All 40 positive samples were correctly reported as **Strep A DETECTED**.

Linearity

Not applicable, the Xpert Xpress Strep A test is a qualitative assay.

Clinical Studies

Clinical Performance

A prospective, multi-center investigational study was conducted to evaluate the clinical performance of the Xpert Xpress Strep A. An initial throat swab was collected for the standard of care method and a second throat swab was collected from consented subjects for testing by the Xpert Xpress Strep A and reference method. The specimens were collected using ESwabs (flocked swab in Liquid Amies medium) from patients presenting with signs and symptoms of pharyngitis. The Xpert Xpress Strep A test was evaluated at nine clinical sites from geographically diverse regions within the United States between January 2017 and May 2017.

Six hundred sixty-six (666) specimens were initially enrolled in the study. Of these, 43 were excluded from the analysis due to failure to comply with the inclusion criteria (11), delay in shipment (27), reference method indeterminate (4) or incorrect specimen type (1).

Among the 623 specimens included in the analysis, 94.7% (590/623) were successful on the initial test and 99.2% (618/623) upon retest.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the Xpert Xpress Strep A were established relative to culture and latex agglutination for Strep A typing. The overall performance of the Xpert Xpress Strep A is presented in Table 8-7. Discordant results between Xpert Xpress Strep A and culture were investigated using an alternative PCR/bidirectional sequencing assay; the results of which are footnoted in Table 8-7.

Table 8-7: Performance of Xpert Xpress Strep A vs. Reference Method

		Reference Method		
Xpert Xpress Strep A		**Pos**	**Neg**	**Total**
	Pos	157	27[a]	184
	Neg	1[b]	433	434
	Total	158	460	618[c]
			Sensitivity	99.4% (95%CI: 96.5-99.9)
			Specificity	94.1% (95%CI: 91.6-95.9)
			PPV	85.3% (95%CI: 79.5-89.7)
			NPV	99.8% (95%CI: 98.7-100.0)
			Accuracy	95.5% (95%CI: 93.5-96.8)
			Prevalence	25.6% (95%CI: 22.3-29.1)

a. Results from alternative PCR with bidirectional sequencing: 10 of 27 were Strep A Positive; 13 of 27 were Strep A Negative; 4 of 27 were inconclusive.

b. Results from alternative PCR with bidirectional sequencing: 1 of 1 was Strep A Negative.

c. On initial testing, 33/623 specimens (5.3%) produced indeterminate results; 31/33 were retested, of which 28 produced valid results that were included in the analysis of performance for a final indeterminate rate of 5/623 (0.8%).

Reproducibility Study

A four member reproducibility panel with varying concentrations of *Streptococcus pyogenes* was tested two times per day on five different days by three different operators at three sites (4 specimens x 2 times/day x 5 days x 3 operators x 3 sites). Three lots of Xpert Xpress Strep A cartridges were used. The samples were prepared in simulated throat swab matrix at the different concentration levels and are presented in Table 8-8. Results of the reproducibility study are summarized in Table 8-9 by study site/operator.

Table 8-8: Reproducibility Panel

Strain	Panel Member
Not applicable	Negative
ATCC BAA-946 (*Streptococcus pyogenes*)	High Negative (~0.05X LoD)
ATCC BAA-946 (*Streptococcus pyogenes*)	Low Positive (~1X LoD)
ATCC BAA-946 (*Streptococcus pyogenes*)	Moderate Positive (~3X LoD)

Table 8-9: Summary of Reproducibility Results: % Agreement by Study Site/Operator

Sample	Site 1				Site 2				Site 3				% Total Agreement by Sample[a,b]
	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	
Neg	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (90/90)
Strep A High Neg	70% (7/10)	100% (10/10)	100% (10/10)	90% (27/30)	80% (8/10)	100% (10/10)	100% (10/10)	93% (28/30)	90% (9/10)	100% (10/10)	80% (8/10)	90% (27/30)	91% (82/90)
Strep A Low Pos	100% (10/10)	100% (10/10)	90% (9/10)	97% (29/30)	100% (10/10)	90% (9/10)	100% (10/10)	97% (29/30)	100% (10/10)	100% (10/10)	90% (9/10)	97% (29/30)	97% (87/90)
Strep A Mod Pos	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (90/90)

a. Agreement based on expected result: Neg and High Neg=expected negative; Low Pos and Mod Pos=expected positive
b. Thirteen (13) indeterminate results were obtained over the course of the study for an initial indeterminate rate of 3.6% (13/360). In all cases, the expected results were obtained upon retesting.

The reproducibility of the Xpert Xpress Strep A was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. 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 8-10.

Table 8-10: Summary of Reproducibility Data

Sample	Assay Channel (Analyte)	N[a]	Mean Ct	Between-Site		Between-Lot		Between-Day		Between-Operator		Within-Assay		Total	
				SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
Neg	SPC	90	33.5	0.3	0.9	1.0	3.0	0.3	0.9	0	0	1.5	4.5	1.9	5.5
Strep A High Neg	SPC	82	33.6	0.4	1.2	1.1	3.2	0	0	0	0	1.3	3.9	1.7	5.2
Strep A Low Pos	SA[b]	87	38.6	0	0	0.4	0.9	0	0	0	0	1.3	3.4	1.3	3.5
Strep A Mod Pos	SA[b]	90	37.2	0	0	0.1	0.3	0.2	0.5	0.2	0.5	0.9	2.4	1.0	2.6

a. Results with non-zero Ct values out of 90.
b. SA = Strep A

Conclusions

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the Xpert Xpress Strep A test is substantially equivalent to the predicate device.