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

A. 510(k) Number:

K183366

B. Purpose for Submission:

To obtain a Substantial Equivalence Determination for the GenePOC Strep A assay

C. Measurand:

Conserved regions of the *Streptococcus pyogenes* bacterial genome

D. Type of Test:

Qualitative real-time Polymerase Chain Reaction (PCR)

E. Applicant:

GenePOC Inc.

F. Proprietary and Established Names:

GenePOC Strep A

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.2680: *Streptococcus* spp. nucleic acid-based assay

2. Classification:

   Class II

3. Product code:

   PGX: Groups A, C and G β-Hemolytic *Streptococcus* Nucleic Acid Amplification System

   OOI: Real time nucleic acid amplification system

4. Panel:

   83-Microbiology

H. Intended Use:

1. Intended use(s):

   The GenePOC Strep A assay, performed on the revogene instrument, is an automated, qualitative *in vitro* diagnostic test that utilizes real-time polymerase chain reaction (PCR) for the direct detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcus*) nucleic acids from throat swab specimens obtained from patients with signs and symptoms of pharyngitis. The GenePOC Strep A assay is intended for use as an aid in the diagnosis of Group A *Streptococcus* infection.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   For prescription use only.

   (Limitation) Additional follow-up testing by culture is required if the GenePOC Strep A assay result is negative and clinical symptoms persist, or in the event of an outbreak of acute rheumatic fever (ARF).

4. Special instrument requirements:

   The GenePOC Strep A assay is indicated for use with the revogene instrument.

I. Device Description:

The GenePOC Strep A assay is a single-use test for qualitative detection of *Streptococcus pyogenes* (group A *Streptococcus*-GAS) nucleic acids from throat swab specimens obtained from patients with signs and symptoms of pharyngitis. The GenePOC Strep A assay kit is comprised of the disposable microfluidic cartridge (PIE) with Strep A reagents, Sample Buffer Tube (SBT), and Disposable Transfer Tool (DTT). These components are used to suspend the sample, extract, amplify, and detect *Streptococcus pyogenes (S. pyogenes)* nucleic acid.

A Process Control (PrC) is also incorporated into each PIE to verify sample processing and amplification steps. The PrC allows for the verification of potential inhibitor substances as well as microfluidic, instrument, or reagent failures. The GenePOC Strep A assay is designed to be used on the revogene instrument, which automates sample homogenization, sample dilution, cell lysis, DNA amplification, and detection of the amplified PCR products.

Each GenePOC Strep A assay kit provides components for twenty-four (24) tests. User intervention is required for sample preparation, transferring throat swab specimen into the SBT, using the DTT to transfer the sample into the PIE, and loading/unloading the PIE into the revogene carousel. Each PIE is a completely integrated closed device in which a sample is dispensed and processed through different microfluidic chambers and channels that allow for the sample processing and subsequent real-time PCR steps.

Upon completion of a run, the results are computed by the revogene instrument from measured fluorescent signals and embedded calculation algorithms. The possible output results are: positive, negative, indeterminate, or unresolved results. The user removes the used cartridges and disposes of them in normal biological waste. Results may be viewed, printed, transferred, and/or stored by the user.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Xpert Xpress Strep A

2. Predicate 510(k) number(s):

   K172126

3. Comparison with predicate:

Similarities		
Item	**Device (K183366)**	**Predicate (K172126)**
	GenePOC Strep A assay	**Xpert Xpress Strep A Assay**
Regulation	21 CFR 866.2680	Same
Product Code	PGX	Same
Device Class	Class II	Same
Intended Use	The GenePOC Strep A assay, performed on the revogene instrument, is an automated, qualitative *in vitro* diagnostic test that utilizes real-time polymerase chain reaction (PCR) for the direct detection of *Streptococcus pyogenes* (Group A β-hemolytic *Streptococcus*) nucleic acids from throat swab specimens obtained from patients with signs and symptoms of pharyngitis. The GenePOC Strep A assay is intended for use as an aid in the diagnosis of Group A *Streptococcus* infection.	The Xpert Xpress Strep A Assay, performed on the GeneXpert Instrument Systems, 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 Assay utilizes an automated real-time polymerase chain reaction (PCR) to detect *Streptococcus pyogenes* DNA.
Analyte	Group A *Streptococcus*	Same
Measurand	Conserved region of the *S. pyogenes* genome	Same
Specimen Type	Throat swab in Liquid Stuart or Liquid Amies Transport Medium	Throat swab in liquid Amies medium
Assay Format	Single-use; Automated DNA extraction, amplification and detection	Same
External Controls	Materials available commercially	Same
Result	Qualitative, Automated	Same

Differences		
Item	**Device (K183366)**	**Predicate (K172126)**
	GenePOC Strep A assay	**Xpert Xpress Strep A Assay**
Instrument System	revogene	GeneXpert Dx, GeneXpert Infinity-48s or GeneXpert Infinity-80 instrument systems.

K. Standard/Guidance Document Referenced (if applicable):

- CLSI Guideline EP25-A, *Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline*. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

- CLSI Guideline EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition.*Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
- CLSI Guideline EP17-A2, *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*; Approved Guideline. Second Edition. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.

L. Test Principle:

The revogene automates and integrates nucleic acid extraction, amplification, and detection of the target sequence in complex samples using real-time PCR. A throat swab specimen is collected using a rayon tipped swab. The specimen is transferred into the SBT containing 1.5 ml of sample buffer, and the swab stem is broken. After a 15-second vortex step at maximal speed, the inoculated sample buffer is transferred into the GenePOC Strep A PIE using the DTT. The loaded GenePOC Strep A PIE is placed into the revogene for further sample processing. No operator intervention is necessary once the PIE is loaded onto the revogene instrument.

Each GenePOC Strep A PIE is a completely integrated and self-contained device. Each sample is sequentially transferred by centrifugation from one microfluidic chamber to the next and all reagents specific for the PCR reaction are incorporated and dried within the PCR wells. The stepwise process includes sample homogenization, lysis of cells, sample dilution, and DNA extraction followed by the subsequent real-time PCR steps within one PCR well in the cartridge. An internal PrC is contained in the homogenization chamber and is therefore present in every test to verify critical steps of the analytical process as well as system or reagent failures. The amplified products are detected in real-time from measured fluorescent signals and embedded calculation algorithms. Results may be viewed, printed, transferred, and/or stored by the user using target-specific TaqMan chemistry-based probes. An Early Positive Result Outcome (E-PRO) feature provides positive results if the signal from the target reaches a predetermined threshold before the full PCR cycles have been completed. The results are computed by the system. Results may be viewed, printed, transferred, and/or stored by the user.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Site-to-Site Reproducibility

   The reproducibility of the GenePOC Strep A assay between sites was evaluated in a study performed by two operators at each of three sites over a period of five days. Each operator tested a blinded panel of *S. pyogenes* positive (two different levels based on multiples of the LoD) and negative samples using the same lot of reagents. Ninety (90) data points were collected for each positive panel member, and (120) data points were collected for the negative panel member. The panels were prepared in Sample Buffer

(SB) using *S. pyogenes*-negative throat swab matrix and two *S. pyogenes* strains (ATCC 12344 and ATCC 19615). No differences in reproducibility between sites or operators were observed for the panel members.

The results of the study demonstrated acceptable reproducibility from site-to-site at target levels close to the limit of detection (LoD) of the assay (**Table 1**). No unresolved results were observed in this study. Across the Reproducibility Study (site-to-site and within site studies), eight samples were indeterminate (IND) for a rate of 1.6% (8/500). The samples were repeated and yielded a reportable result after repeat for a final IND rate of 0%. Each Positive External Control and Negative External Control tested during the Reproducibility Study yielded the expected results.

Table 1. Summary of Results from the GenePOC Strep A Assay Site-to-Site Reproducibility Study, Stratified by Site and Panel Member.

Level	Positive/Number (%)			
	Site 1	**Site 2**	**Site 3**	**Overall**
Moderate Positive 3X LoD [1]	30/30 (100%)	30/30 (100%)	30/30 (100%)	90/90 (100%)
Low Positive 1-2X LoD[2]	30/30 (100%)	30/30 (100%)	30/30 (100%)	90/90 (100%)
Negative	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/120 (0.0%)

[1] LoD: Limit of Detection for *S. pyogenes* strain ATCC 19615
3X LoD = 3.0 x 10^3 CFU/ml of SB; 1X LoD = 1.0 x 10^3 CFU/ml of SB

[2] LoD: Limit of Detection for *S. pyogenes* strain ATCC 12344
1-2X LoD= 650 CFU/ml of SB; 1X LoD= 333 CFU/ml of SB

Within Laboratory Precision/Repeatability

Within laboratory precision/repeatability of the GenePOC Strep A assay was evaluated by two operators who tested a panel of samples on a single revogene instrument over a period of 20 days. Eighty (80) replicates were tested for each panel member. The panel members were the same as those used in the Site-to-Site Reproducibility Study, above. The results of the study demonstrated acceptable repeatability and precision from day-to-day with target levels even close to the LoD of the assay (**Table 2**). One unresolved (UNR) was observed. This sample was repeated for a valid result.

Table 2. Summary of Results from the Within Laboratory Precision/ Repeatability Study for the GenePOC Strep A Assay

Level	Positive/Tested (%)
Moderate Positive 3X LoD [1]	80/80 (100%)
Low Positive 1-2X LoD[2]	80/80 (100%)
Negative	2/80 (2.5%)

[1] LoD: Limit of Detection for *S. pyogenes* strain ATCC 19615
3X LoD: 3.0 x 10^3 CFU/ml of SB; 1X LoD: 1.0 x 10^3 CFU/ml of SB
[2] LoD: Limit of Detection for *S. pyogenes* strain ATCC12344
1-2X LoD: 650 CFU/ml of SB

Lot-to-Lot Reproducibility

The lot-to-lot reproducibility of the GenePOC Strep A assay was evaluated by testing a panel of *S. pyogenes* positive and negative samples in negative throat matrix and SB with each of three lots of reagents over a period of five days. Ninety (90) replicates per positive panel member were tested, and a total of 120 replicates were tested for the negative panel member. All the panel members were the same as those used in the Reproducibility and Precision/Repeatability Studies above. The results are summarized in **Table 3** and show acceptable performance with each lot of reagents.

Table 3. Summary of Results from the GenePOC Strep A assay Lot-to-Lot Reproducibility Study, Stratified by Reagent Lot and Panel Member

Level	Positive/Tested (%)			
	Lot 1	Lot 2	Lot 3	Overall
Moderate Positive 3X LoD [1]	30/30 (100%)	30/30 (100%)	30/30 (100%)	90/90 (100%)
Low Positive 1-2X LoD[2]	30/30 (100%)	29/30 (96.7%)	29/30 (96.7%)	88/90 (97.8%)
Negative	0/40 (0.0%)	0/40 (0.0%)	0/40 (0.0%)	0/120 (0.0%)

[1] LoD: Limit of Detection for *S. pyogenes* strain ATCC 19615
3X LoD: 3.0 x 10^3 CFU/ml of SB; 1X LoD: 1.0 x 10^3 CFU/ml of SB
[2] LoD: Limit of Detection for *S. pyogenes* strain ATCC 12344
1-2X LoD: 650 CFU/ml of SB

b. Linearity/assay reportable range:

Not Applicable.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Internal process control (PrC):

Each PIE contains a PrC that controls for amplification inhibition, assay reagents, and sample processing effectiveness.

A sample in which there is an amplification/detection failure of the PrC and the GAS target DNA is reported as "Unresolved" (UNR) and must be re-tested.

External Controls

Two External Controls are to be prepared by the end user. GenePOC recommends using a 0.5 ± 0.05 McFarland suspension of a *S. pyogenes* commercially available strain (e.g., ATCC 12344) diluted 1/100 in saline as a Positive External Control and a 0.5 ± 0.05 McFarland suspension of a *Streptococcus salivarius* commercially available strain (e.g., ATCC 13419) as a Negative External Control. These are recommended, but not required, to allow the user to select the most appropriate for their laboratory quality control program.

Sample Stability in PIE

The GenePOC Strep A assay PIE (microfluidic cartridge) stability study was validated using positive samples comprised of the *S. pyogenes* (GAS) strain ATCC 12344 (at 3X LoD) and negative samples in presence of *S. pyogenes*-negative throat matrix. The study was conducted using three (3) GenePOC Strep A kit lots, three (3) replicates of *S. pyogenes* and negative samples (one replicate per kit lot), and five (5) revogene instruments. Samples were tested across four (4) time points: 0 minutes (T0), 60 minutes (T60), 120 minutes (T120), and 180 minutes (T180) to validate the PIE stability study at 25°C after opening the PIE pouch. No unresolved (UNR) samples were recorded in the PIE stability study. One IND was observed for an initial IND rate of 2.8%; however, this sample was repeated and yielded reportable results for a final 0% IND rate. The results of the study support the recommended maximum interval of one hour from the opening of the PIE pouch and sample addition into the GenePOC Strep A assay PIE to the processing on the revogene instrument.

Specimen Stability

The stability of throat swab specimens collected with rayon swabs in Liquid Stuart transport media was evaluated analytically with the GenePOC Strep A assay. The time periods tested in this study were used to establish specimen stability between: i) throat swab specimen collection and SBT inoculation and ii) SBT inoculation and loading of the GenePOC Strep A PIE prior to initiation of the revogene run. The stability study was conducted by testing positive samples comprised of the *S. pyogenes* (GAS) strain ATCC 12344 (3X LoD) and negative samples in the presence of *S. pyogenes*-negative throat matrix. The cumulative shelf life stability (nested stability) corresponds to the period of time from swab specimen collection up to the initiation of the revogene assay run. The study included three (3) lots GenePOC Strep A assay kits. For each sample type (positive or negative), and for each time point, a total of twelve (12) swabs were inoculated. Study results support throat swab specimen storage at 25±2°C up to two (2) days or 2-8°C for up to seven (7) days. SBT inoculated with throat swab specimens may be stored up to three (3) days at 25±2°C or 2-8°C for up to seven (7) days prior testing with the GenePOC Strep A assay.

Swab Specimen Stability-Various Swabs

This study was designed to evaluate the cumulative stability of throat swabs specimens

when collected and conserved with Rayon Liquid Amies, Polyester Liquid Stuart, Polyester Liquid Amies and the inoculated SBT used with the GenePOC Strep A assay at defined temperature of 25 ± 2°C and 2-8°C. The study was executed by testing *S. pyogenes* strain ATCC 12344 at 3X LoD and negative samples in presence of *S. pyogenes*-negative throat matrix in SB. The study included three (3) to four (4) lots GenePOC Strep A assay kits for each type of swab. For each sample type (positive or negative), and for each time point, a total of twelve (12) swabs were inoculated. Study results support throat swab specimen stability for GenePOC Strep A assay at 25±2°C up to two (2) days or 2-8°C for up to seven (7) days; SBT inoculated with throat swab specimens may be stored up to three (3) days at 25±2°C or 2-8°C for up to seven (7) days prior testing with the GenePOC Strep A assay, as confirmed with the rayon swab in Liquid Amies transport media and Polyester swab in Liquid Stuart and Liquid Amies transport media.

Reagent Stability

The shelf life of the GenePOC Strep A assay reagents was evaluated in a real-time stability study performed on three lots of reagents that were stored under different conditions. GenePOC claims a shelf life of 2 months.

d. *Detection limit:*

Limit of Detection

The Limit of Detection (LoD) of the GenePOC Strep A assay was estimated for three strains of *S. pyogenes* by testing various dilutions of enumerated cell stocks in *S. pyogenes*-negative throat swab matrix. The LoD for each strain was then confirmed by testing a further 20 replicates at the lowest target level that produced 100% positive results. The LoD was defined as the lowest concentration tested at which ≥95% of assay replicates produced positive results. For ATCC 19615, ATCC 12344, and ATCC 700942, the LoD was determined to be 1.0×10^3 CFU/ml, 333 CFU/ml, and 1.3×10^3 CFU/ml, respectively. No unresolved (UNR) results were obtained during the study. Eighteen (18) out of 595 samples obtained IND results during the GenePOC Strep A assay LoD determination study for an initial IND rate of 3.0%. These samples were repeated and all yielded reportable results for a final IND rate of 0%.

Inclusivity (Analytical Reactivity)

The inclusivity of the GenePOC Strep A assay was evaluated by testing nine additional strains of *S. pyogenes* in negative throat matrix (**Table 4**). Eight of the nine strains produced 9/9 positive results at a concentration of 999 CFU/ml (3X the LoD for ATCC12344). Strain ATCC 49399 gave one false negative result at this target level but produced 9/9 positive results at 1.67×10^3 CFU/ml, equivalent to 5X LoD for ATCC 12344. These results are acceptable.

Table 4. Strains of *S. pyogenes* used to Evaluate the Inclusivity of the GenePOC Strep A assay

Origin	Strain Number	Emm-Type[1]
USA	ATCC 12384	3
Unknown	ATCC 49399	N/A
Sweden	CCUG 33409	N/A
Sweden	CCUG 39158	N/A
Sweden	CCUG 53553	N/A
New Zealand	ATCC 700952	92
Unknown	ATCC 700294	1
England	ATCC 12357	18
Sweden	CCUG 65322	N/A

[1] *For the LoD Study, the Emm-type for ATCC 19615, ATCC 12344, and ATCC 700942 were reported as 80, 1, and 82.*

e. Analytical specificity:

Cross-reactivity Study

The analytical specificity of the GenePOC Strep A assay was evaluated by testing a 50-member panel [(42) bacteria, (1) yeast, (6) viruses, (1) human gDNA] with organisms that might be found in throat swab specimens (**Table 5**). Each panel member was tested in triplicate in SB with *S. pyogenes*-negative throat matrix. Bacteria and yeast were tested at $\geq 10^6$ CFU/ml while viral nucleic acid and human gDNA samples were tested at a concentration $\geq 10^5$ cp/ml. No cross-reactivity was observed. No UNR were observed. Three IND were produced for an initial IND rate of 1.9%; all repeats yielded valid results. These study results are acceptable.

Table 5. Organisms Tested for Potential Cross-Reaction in the GenePOC Strep A Assay

Name	Identification	Name	Identification
Bacteria and Yeasts			
Acinetobacter lwoffii	ATCC 15309	*Klebsiella pneumoniae*	ATCC 27736
Arcanobacterium haemolyticum	ATCC BAA-1784	*Lactococcus lactis*	ATCC 19435
Bacillus cereus	ATCC 14579	*Legionella jordanis*	ATCC 33623
Bordetella pertussis	ATCC 9797	*Legionella micdadei (Tatlockia micdadei)*	CCUG 31229
Burkholderia cepacia	ATCC 25416	*Legionella pneumophila*	ATCC 33152
Corynebacterium diphtheriae	ATCC 13812	*Moraxella catarrhalis*	ATCC 25238
Enterococcus faecalis	ATCC 19433	*Neisseria gonorrhoeae*	ATCC 43069
Escherichia coli	ATCC 11775	*Neisseria subflava*	ATCC 49275
Fusobacterium necrophorum	ATCC 25286	*Parvimonas micra*	ATCC 33270
Haemophilus influenza	ATCC 9006	*Pseudomonas aeruginosa*	ATCC 35554
Serratia marcescens	ATCC 13880	*Streptococcus dysgalactiae* subsp. *dysgalactiae*	ATCC 9926
Staphylococcus aureus	ATCC 33592	*Streptococcus dysgalactiae* subsp. *dysgalactiae*	ATCC 43078
Staphylococcus epidermidis	ATCC 14990	*Streptococcus gordonii*	ATCC 10558
Stenotrophomonas maltophilia	ATCC 13637	*Streptococcus intermedius*	ATCC 27335
Streptococcus agalactiae	ATCC 12403	*Streptococcus mitis*	NCIMB 13770
Streptococcus anginosus	ATCC 33397	*Streptococcus mutans*	ATCC 25175

Name	Identification	Name	Identification
Streptococcus anginosus subsp. *whileyi*	CCUG 39159	*Streptococcus oralis*	ATCC 6249
Streptococcus bovis	ATCC 33317	*Streptococcus pneumoniae*	ATCC 49619
Streptococcus canis	ATCC 43496	*Streptococcus salivarius*	ATCC 13419
Streptococcus constellatus subsp. *viborgensis*	CCUG 62387	*Streptococcus sanguinis*	ATCC 10556
Streptococcus suis	CCUG 7984	*Veillonella parvula*	ATCC 10790
		Candida albicans	ATCC 10231
Viruses and Human DNA			
Adenovirus Type 1	ATCC VR-1D	Influenza A/Aichi/2/68/H3N2	ATCC VR-1680D
Influenza B/Taiwan/2/62	ATCC VR-1735D	Parainfluenza virus 4b	ATCC VR-1377D
Rhinovirus Type 17	ATCC VR-1663D	Human DNA	N/A
Adenovirus type 11 (Slobitski)	ATCC VR-12D		

Bioinformatic Analysis

The *in silico* specificity of the GenePOC Strep A assay was validated through analysis of the assay's primers and probe sequences specific for the detection of *S. pyogenes*. The *in silico* study suggested that non-specific amplifications or detection will not occur with the primers and probe of the GenePOC Strep A assay used to target the *S. pyogenes* sequence. The primers and probes have been proven to be specific to their respective target following Basic Local Alignment Search Tool (BLAST) analysis. No target other than *S. pyogenes* was found to have a significant level of homology with the *S. pyogenes* primers and probe. In addition, it was concluded that the *S. pyogenes* target primers and probe will not interact with the PrC sequence. Further, the PrC primers did not demonstrate cross-reactivity with other organisms.

Contamination Study

The potential for false-positive results with the GenePOC Strep A assay due to within-run or between-run cross contamination was evaluated by testing an alternating series of *S. pyogenes* "high positive" and negative samples in successive instrument runs. The high positive samples contained *S. pyogenes* at a concentration of 10^6 CFU/ml in the presence of *S. pyogenes*-negative throat matrix. Negative samples comprised *S. pyogenes*-negative throat matrix without GAS. The expected results were obtained for all *S. pyogenes* positive and negative samples (40/40 each). No false positive results were detected in the within-run cross-contamination study (n=80) or in the between-run carry-over study (n=80). No UNR or IND results were obtained throughout the cross-contamination and carry-over study. These results are acceptable.

f. Assay cut-off:

Thresholds and cut-offs for the GenePOC Strep A assay are embedded within the Assay Definition File that also encodes the instrument settings required to perform the test. Both native (throat swab specimens) and contrived samples were used to set the thresholds of positivity and negativity of the GenePOC Strep A assay. The assay cut-off was determined by testing n=509 native and contrived samples.

g. Assay interference:

Potentially Interfering Substances

The potential for interference with the GenePOC Strep A assay was evaluated with (19) endogenous and exogenous substances that may be present in throat swab specimens (**Table 6**). Two (2) strains of *S. pyogenes* (ATCC 12344 and ATCC 19615) were tested at a moderate load (3X LoD, 999 CFU/ml and 3000 CFU/ml of SB, respectively) in the presence of potentially interfering substances and *S. pyogenes*-negative throat matrix. Negative samples were also tested in the presence of potentially interfering substances to evaluate the impact on the PrC. The potentially interfering substances were tested at the highest concentration that may be encountered in a throat swab specimen. Results demonstrated that Analgesic/Antipyretic (Tylenol), Nonsteroidal anti-inflammatory drug (Aspirin, Advil), Bronchodilator (Albuterol sulfate), Whole Blood, and Mucin had a potentially inhibitory effect on the detection of PrC or *S. pyogenes* when any of these substances was present in SBT at a concentration of 4.3% (w/v or v/v). At 0.4% (w/v), Tylenol, Advil, Albuterol sulfate and Mucin showed no reportable interference with the GenePOC Strep A assay. When tested at for at 0.1%, no interference was observed with Aspirin (w/v) and Whole Blood (v/v). The potential for certain substances to interfere with the GenePOC Strep A assay is noted in the device labeling.

Table 6. Substances Evaluated for Potential Interference with the GenePOC Strep A Assay

Substance	Test Concentration (in SBT)
Endogenous Substances	
Human Saliva	4.3% (v/v)
Whole Blood	4.3% (v/v)
Mucin	4.3% (v/v)
Exogenous Substances	
Tylenol	4.3% (w/v)
Aspirin	4.3% (w/v)
Advil	4.3% (w/v)
Albuterol sulfate	4.3% (w/v)
Zicam	4.3% (w/v)
Hall Mentho-Lyptus	4.3% (w/v)
Cepacol Extra Strength (Cough lozenge)	4.3% (w/v)
Sucrets Complete (Cough lozenge)	4.3% (w/v)
Crest Pro-Health Advanced (toothpaste)	0.56% (w/v)
Crest Scope Classic (Mouthwash)	4.3% (v/v)
Listerine Ultraclean (Mouthwash)	4.3% (v/v)
NyQuil Complete	4.3% (v/v)
Dimetapp (Cough Syrup)	4.3% (v/v)
Robitussin Cough Control Extra Strength	4.3% (v/v)
Robitussin Total Cough, Cold & Flu Extra Strength Nighttime	4.3% (v/v)
Benadryl Allergy Elixir (Antihistamines)	4.3% (v/v)

Microbial Interference

The potential for interference with the GenePOC Strep A assay was investigated using (30) non-targeted microorganisms genetically close to the assay analytes, flora potentially

found in the mouth/throat/respiratory tract, and the most frequent throat and upper respiratory tract infection causative agents. Two (2) *S. pyogenes* strains, ATCC 12344 and ATCC 19615, were tested at 3X LoD (999 CFU/ml and 3000 CFU/ml of SB, respectively) in triplicate in the presence of potentially interfering non-targeted microorganisms and *S. pyogenes*-negative throat matrix. Negative samples were also tested in the presence of potentially interfering non-targeted microorganisms to evaluate the impact on the PrC. None of the thirty (30) organisms present at 10^6 CFU/ml of SB for bacteria and yeast and 10^5 copies/ml of SB for viruses interfered with the detection of PrC or with *S. pyogenes* strain ATCC 19615. A combinatory effect of *Streptococcus mutans*, *Streptococcus oralis*, *Streptococcus salivarius* and *Moraxella catarrhalis* at $\geq 10^6$ CFU/ml of SB (pool), or the presence of *Streptococcus dysgalactiae* subsp. *dysgalactiae* at $\geq 10^6$ CFU/ml of SB, may have an inhibitory effect on the detection of *S. pyogenes* ATCC 12344. When each bacterium from the pool (*Streptococcus mutans*, *Streptococcus oralis*, *Streptococcus salivarius* and *Moraxella catarrhalis*) was tested individually at the same load (1×10^6 CFU/ml of SB) in presence of *S. pyogenes* ATCC 12344, none interfered with the detection of *S. pyogenes*. After additional testing, *S. dysgalactiae* subsp. *dysgalactiae* strain ATCC 43078 no longer showed interference with *S. pyogenes* ATCC 12344 at a load of 1×10^5 CFU/ml of SB. These results are noted in the device labeling, where appropriate.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Not Applicable.

   b. *Matrix comparison:*

      Not Applicable.

3. Clinical studies:

   a. *Clinical Sensitivity:*

      The performance of the GenePOC Strep A assay was evaluated in a prospective multicenter study that was conducted at geographically diverse clinical trial sites. These included: (7) collection/testing sites [(5) US sites and (2) Canadian sites] and (1) dedicated reference method center (across the US and Canada). Throat swab specimens were collected from patients with signs and symptoms of pharyngitis. Samples were tested with both the Reference Method (culture) and the GenePOC Strep A assay.

      The reference culture procedure was performed within 48 hours of specimen collection and comprised inoculation of BAP with one swab of a dual throat swab set and incubation of plates under anaerobic conditions for up to 48 hours. Culture plates that did not exhibit β-hemolytic colonies after 48 hours were recorded as negative for Group A *Streptococcus*. Colonies morphologically resembling *S. pyogenes* were isolated on a new

BAP and identified by catalase, gram-stain, Latex agglutination, and Matrix-Assisted Laser Desorption/Ionization Time-Of-Flight Mass Spectrometry (MALDI-TOF).

Seven hundred and sixty-seven (767) specimens were initially enrolled in the study. Of these, 163 were excluded from the analysis of performance due to: failure to comply with the revogene testing procedures—delay in pouch opening or transfer to SBT (3), exceeded the delay in shipment (13), did not meet inclusion criteria (23), did not have complete testing results (27), and failure to comply with the reference culture protocol (97). A total of 604 specimens were used to evaluate performance of the assay (**Table 7**). For UNR samples, there was an initial UNR rate of 0.5% (3/610) with a final UNR rate of 0.2% (1/610) after re-testing. For IND samples, there was an initial IND rate of 1.1% (7/610) with a final rate of 0.8% (5/610) after re-testing.

Table 7. GenePOC Strep A Clinical Performance vs Reference Culture

		Reference Culture		
		Positive	**Negative**	**Total**
GenePOC Strep A assay	**Positive**	151	24 [1]	**175**
	Negative	3[2]	426	**429**
	Total	**154**	**450**	**604**
Sensitivity		151/154 = 98.1% (95% CI: 94.4-99.3%)		
Specificity		426/450 = 94.7% (95% CI: 92.2-96.4%)		
Positive Predictive Value		151/175 = 86.3% (95% CI: 80.4-90.6%)		
Negative Predictive Value		426/429 = 99.3% (95% CI: 98.0-99.8%)		

95% CI: Two-sided 95% score confidence interval

[1] 17/24 specimens were positive by an alternative PCR/bi-directional sequencing assay; 1/24 samples was inconclusive.

[2] 1/3 specimens were positive by an alternative PCR/bi-directional sequencing assay; 2/3 samples were inconclusive.

The performance of the GenePOC Strep A assay at each clinical site in comparison to the reference culture method is shown in **Table 8**. The GenePOC Strep A assay sensitivity and specificity for the six hundred and four (604) prospective specimens were 98.1% (151/154) and 94.7% (426/450) respectively. Overall, performance was determined to be acceptable.

Table 8. Performance of the GenePOC Strep A Assay in Comparison to the Reference Culture Method, Stratified by Clinical Site

(Site)	**Culture Positive (%)**	**Sensitivity % (95% CI)**	**Specificity % (95% CI)**
1	16/69 (23.2%)	16/16 = 100% (95% CI: 80.6% - 100%)	52/53 = 98.1% (95% CI: 90.1% - 99.7%)
2	18/67 (26.9%)	18/18 = 100% (95% CI: 82.4% - 100%)	44/49 = 89.8% (95% CI: 78.2% - 95.6%)
3	2/42 (4.8%)	2/2 = 100% (95% CI: 34.2% - 100%)	39/40 = 97.5% (95% CI: 87.1% - 99.6%)

4	59/123 (48.0%)	58/59 = 98.3% (95% CI: 91.0% - 99.7%)	58/64 = 90.6% (95% CI: 81.0% - 95.6%)
5	30/178 (16.9%)	28/30=93.3% (95% CI: 78.7%-98.2%]	146/148=98.6% (95% CI: 95.2%-99.6%)
6	13/49 (26.5%)	13/13=100% (95% CI: 77.2%-100%)	32/36=88.9% (95% CI: 74.7%-95.6%)
7	16/76 (21.1%)	16/16=100% (95% CI: 80.6%-100%)	55/60=91.7% (95% CI: 81.9%-96.4%)

*b. Clinical specificity**:***

Refer to Section M(3)(a), above.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off**:**

Not applicable.

5. Expected values/Reference range:

The performance of the GenePOC Strep A assay was evaluated in a prospective clinical study. Collection/testing for *S. pyogenes* with the GenePOC Strep A assay was performed at (7) geographically diverse clinical sites. A separate site was used as a dedicated Reference Method Center. The overall prevalence of *S. pyogenes* (Group A *Streptococcus*) in throat swab specimens was 28.9% (175/604) as determined by the GenePOC Strep A assay and 25.5% (154/604) as determined by culture. The prevalence of *S. pyogenes*, as determined by the GenePOC Strep A assay (**Table 9)** and the Reference Method (**Table 10**), is shown below stratified by the age of the subjects.

Table 9. Prevalence of *S. pyogenes* Positive Subjects by Age (GenePOC Strep A Assay)

Age	Number	GenePOC Strep A Assay Positive	% Prevalence
Age Class			
>24 months-12 years	278	106	38.1%
13-21 years	80	15	18.8%
22-64 years	235	51	21.7%
≥65 years	11	3	27.3%
Total	**604**	**175**	**29.0%**

Table 10. Prevalence of *S. pyogenes* Positive Subjects by Age (Reference Method)

Age	Number	Reference Method Positive	% Prevalence
Age Class			
>24 months-12 years	278	94	33.8%
13-21 years	80	14	17.5%
22-64 years	235	44	18.7%
≥65 years	11	2	18.2%
Total	**604**	**154**	**25.5%**

N. Instrument Name:

revogene

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X___ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X___

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X___ or No _____

3. Specimen Identification:

   Barcodes are used to identify patient specimens. The GenePOC Strep A assay's SBT and PIE are both pre-labeled with a unique barcode to identify both specimen and assay. The instrument has two barcode readers to identify reagents and patient specimens. It provides traceability of the sample ID to the PIE ID, SBT ID, and assay ID.

4. Specimen Sampling and Handling:

   User intervention is required for discharging the patient sample into the SBT, transferring the sample into the microfluidic cartridge using the DTT, and for loading the microfluidic cartridge into the revogene. All further specimen handling is automated.

5. Calibration:

   The system is factory calibrated by the manufacturer. The calibration is verified annually. Upon the verification, maintenance is performed if required.

6. Quality Control:

   Refer to Section M(1)(c).

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable.

Q. Proposed Labeling:

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

R. Conclusion:

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