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

A. 510(k) Number:

K173653

B. Purpose for Submission:

To obtain a Substantial Equivalence determination for the Alere i Strep A 2 performed on the Alere i Analyzer for the detection of *Streptococcus pyogenes* (Group A *Streptococcus*).

C. Measurand:

Group A *Streptococcus* DNA

D. Type of Test:

Isothermal DNA amplification assay for the qualitative detection of Group A *Streptococcus* in throat swab specimens.

E. Applicant:

Alere Scarborough, Inc.

F. Proprietary and Established Names:

Alere i Strep A 2
Alere i Instrument
Alere i Strep A 2 Control Swab Kit

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.2680 *Streptococcus* spp. Nucleic Acid-Based Assay

2. Classification:

   Class II

3. Product codes:

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

OOI: Real-Time Nucleic Acid Amplification System

4. Panel:

   83: Microbiology

H. Intended Use:

1. Intended use(s):

   Alere i Strep A 2 is a rapid, instrument-based, molecular *in vitro* diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of *Streptococcus pyogenes*, Group A *Streptococcus* bacterial nucleic acid in throat swab specimens obtained from patients with signs and symptoms of pharyngitis. It is intended to aid in the rapid diagnosis of Group A *Streptococcus* bacterial infections.

2. Indication(s) for use:

   Same as Intended Use.

3. Special conditions for use statement(s):

   For prescription use only.

   Additional follow-up testing by culture is required if the Alere i Strep A 2 assay result is negative and clinical symptoms persist, or in the event of an outbreak of acute rheumatic fever (ARF).

   For optimal performance, use the specimen collection swabs provided in the test kit. Analytical studies have demonstrated that rayon swabs and the BBL CultureSwab Liquid Stuart Medium are not suitable for use with this assay and may produce false negative results.

4. Special instrument requirements:

   Alere i Instrument

I. Device Description:

Alere i Strep A 2 is a rapid, instrument-based isothermal assay for the qualitative detection of *Streptococcus pyogenes* (Group A *Streptococcus*) DNA in throat swab specimens from patients suspected of pharyngitis. Alere i Strep A 2 is performed on the Alere i Instrument and is comprised of the following single-use disposables:

- Sample Receiver
  - Containing Elution Buffer for swab expression

- Transfer Cartridge
    - For transfer of the eluted sample to the Test Base
- Test Base
    - Consisting of two sealed reaction tubes, each containing a lyophilized reagent pellet;
    - One tube is for detection the *S. pyogenes* target, the other for an oligonucleotide Internal Control

Alere i Strep A was originally cleared under K141757. Alere i Strep A 2 includes various modifications to the original Alere i Strep A assay chemistry to improve clinical sensitivity and alleviate the need for culture confirmation of negative test results, as well as to improve manufacturability of the reagents.

The reaction tubes in the Test Base contain the reagents required for enzymatic lysis of *S. pyogenes*, and the subsequent amplification of the target nucleic acid and an Internal Control. Alere i Strep A 2 uses a pair of templates (similar to primers) and a strand displacing DNA polymerase to amplify the *S. pyogenes* target DNA and Internal Control. Detection of the amplified products occurs through hybridization of fluorescently labeled Molecular Beacon probes. Alere i Strep A 2 is performed within the confinement of the Test Base, and no other part of the Alere i Instrument is in contact with the sample during the amplification process, thereby reducing the risk of instrument contamination and sample carry-over between measurements.

To perform the assay, the Sample Receiver and Test Base are inserted into the Alere i Instrument. A throat swab is expressed in the Elution Buffer contained within the Sample Receiver and a Transfer Cartridge is used to move the specified volume of swab eluate to the Test Base to dissolve the lyophilized reagent pellets that contain the reagents for bacterial lysis and target amplification. Heating of the reaction tubes, mixing of reagents, fluorescent detection of the amplification products and result interpretation are performed automatically by the instrument.

Inactivated bacterial Positive and Negative External Controls for use with Alere i Strep A 2 are provided within the assay kit and are also available separately. The controls consist of swabs that are coated with enumerated suspensions of inactivated bacteria and dried. The Positive Control is comprised of *S. pyogenes* while the Negative Control is comprised of Group C *Streptococcus*.

J. Substantial Equivalence Information:

1. Predicate device name(s):

    Alere i Strep A

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

    K141757

3. Comparison with predicate:

Similarities		
Item	**Device** **Alere i Strep A 2 (K173653)**	**Predicate** **Alere i Strep A (K141757)**
Intended Use	Alere i Strep A 2 is a rapid, instrument-based, molecular *in vitro* diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of *Streptococcus pyogenes*, Group A *Streptococcus* bacterial nucleic acid in throat swab specimens obtained from patients with signs and symptoms of pharyngitis. It is intended to aid in the rapid diagnosis of Group A *Streptococcus* bacterial infections.	Alere i Strep A is a rapid, instrument-based, molecular *in vitro* diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of *Streptococcus pyogenes*, Group A *Streptococcus* bacterial nucleic acid in throat swab specimens obtained from patients with signs and symptoms of pharyngitis. It is intended to aid in the rapid diagnosis of Group A *Streptococcus* bacterial infections. All negative test results should be confirmed by bacterial culture because negative results do not preclude infection with Group A *Streptococcus* and should not be used as the sole basis for treatment.
Regulation	21 CFR 866.2680	Same
Product Codes	PGX, OOI	Same
Sample Type	Throat swab	Same
Assay Method	Isothermal nucleic acid amplification and real-time fluorescent detection	Same
Extraction Method	None (assay performed on crude lysate)	Same
Detection Technique	Fluorescent DNA probe	Same
Internal Control	Yes	Same
Assay Result	Qualitative	Same

Differences		
Item	**Device**	**Predicate**
	Alere i Strep A 2 (K173653)	**Alere i Strep A (K141757)**
Amplification Primers (templates)	Modified to enhance performance	Targeted towards conserved regions of the *S. pyogenes* genome
Amplification Reaction Mixtures	Formulation optimized to enhance performance and manufacturability	Separate reaction mixtures for target nucleic acid and Internal Control
Internal Control	Sequence modified and concentration increased to improve tolerance to clinical matrix	Present
Mixing of Amplification Reactions	Magnetic mixing added to enhance performance	None
Sample Receiver Warm Up	Eliminated to reduce time-to-result	2 min incubation required prior to addition of sample
Time to Result	<6 minutes	<8 minutes

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

Not applicable.

L. Test Principle:

Alere i Strep A 2 uses isothermal nucleic acid amplification for qualitative detection of *Streptococcus pyogenes* (Group A *Streptococcus*) DNA from throat swab specimens from patients with signs and symptoms of pharyngitis. Alere i Strep A 2 for use on the Alere i Instrument consists of the following components:

a) Sample Receiver: containing Elution Buffer;
b) Transfer Cartridge: for transfer of an aliquot of the eluted sample to the Test Base;
c) Test Base: comprised of two sealed reaction tubes, each containing a lyophilized reagent pellet; one tube is for detection of the *S. pyogenes* target (if present), the other tube is for detection of the Internal Control.

The reaction tubes in the Test Base contain the reagents required for enzymatic lysis of *S. pyogenes* bacteria and amplification of the target nucleic acid and Internal Control. Isothermal amplification takes place using specific templates (similar to primers) that target a conserved region of the *S. pyogenes* genome. The same template primers are also used to amplify the oligonucleotide Internal Control. Detection of amplified products occurs through hybridization of fluorescently labeled Molecular Beacons that are specific to the intervening

regions between the template primers on the Internal Control and *S. pyogenes* amplicons. Result interpretation is based upon the gradient and amplitude of the fluorescence curves for the *S. pyogenes* and Internal Control targets in their respective optical channels and comparison to the appropriate threshold values.

To perform the assay, the Sample Receiver and Test Base are inserted into the Alere i Instrument. A throat swab is then expressed in the Elution Buffer. The operator uses the Transfer Cartridge to transfer a portion of the expressed sample to the Test Base to dissolve the lyophilized reagent pellets and initiate cell lysis and DNA amplification. Heating, mixing and fluorescent detection are conducted automatically by the instrument. Results are displayed on the instrument screen and archived on-board together with the sample identification number and date and time of testing. Results may also be printed.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   A study to evaluate the reproducibility of Alere i Strep A 2 was conducted at three sites, over a period of five days, with three operators per site. Swab samples for testing were prepared with throat swab matrix that was seeded with different levels of *S. pyogenes* strain ATCC 19615. The target levels tested included a true negative (no target), Low Positive (2X Limit of Detection (LoD) and Moderate Positive (3X LoD). On each day of testing, each operator tested a blinded panel consisting of two replicates of each target level, for a total of 90 data points per target level (5 days x 3 sites x 3 operators x 2 replicates = 90 replicates per target level). In total, 11 Alere i Instruments were included in the study, together with two lots each of the assay components (Sample Receiver, Test Base and Test Cartridge). All results were as expected (**Table 1**). The reproducibility of Alere i Strep A 2 was therefore considered acceptable.

Table 1. Results from the Alere i Strep A 2 Reproducibility Study by site and overall

Target Level	Number (%)							
	Site 1		Site 2		Site 3		Overall	
	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
Negative	0	30 (100)	0	30 (100)	0	30 (100)	0	90 (100)
Low Positive (2X LoD)	30 (100)	0	30 (100)	0	30 (100)	0	90 (100)	0
Moderate Positive (3X LoD)	30 (100)	0	30 (100)	0	30 (100)	0	90 (100)	0

b. *Linearity/assay reportable range:*

Not applicable.

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

Internal Control
Alere i Strep A 2 contains an oligonucleotide Internal Control that is designed to monitor the amplification/detection process and reagent function. The Internal Control is lyophilized in one of the two reaction tubes in the Test Base and is amplified and detected separately from the *S. pyogenes* target (if present) using a different optical channel of the Alere i Instrument. The Internal Control must be amplified and detected for a negative assay result to be reported. For *S. pyogenes* positive samples in which target amplification occurs, the amplification of the Internal Control is ignored. If *S. pyogenes* DNA is not detected and the Internal Control fails to amplify the test result is reported as "Invalid".

Positive and Negative Control Swabs
The Alere i Strep A 2 kit contains swabs for use as Positive and Negative Controls that should be tested when the assay is performed on an instrument for the first time, with each new shipment of reagents and by each new operator. Additional controls are available as a separate kit and may be tested as necessary to comply with Quality Control requirements. The Positive Control Swab is coated with inactivated Group A *Streptococcus*. The Negative Control Swab is coated with inactivated Group C *Streptococcus*.

During the prospective Clinical Study described in **Section M(3)(a)**, Positive and Negative Control Swabs were run on each Alere i instrument on each day that clinical specimens were tested. The expected results were obtained from 730/749 (97.5%) Positive Control Swabs and 729/742 (98.2%) Negative Control Swabs.

Reagent Stability
Alere i Strep A 2 reagents and controls should be stored at 2-30°C until the expiration date shown on the outer packaging.

Specimen Stability
During the Clinical Study that was conducted to establish the performance of Alere i Strep A 2 (**Section M(3)(a)**), the majority of throat swab specimens (898/981, 91.5%) were tested within 1 hour of collection. Those specimens not tested within 2 hours of collection were refrigerated at 2-8°C and tested within 24 hours.

Specimen stability was demonstrated analytically using alternative types of collection swab that were seeded with throat swab matrix either with or without *S. pyogenes*, and stored for different durations prior to testing. Ten *S. pyogenes* positive (~3X LoD) and 10 *S. pyogenes* negative samples were tested at each time point after

storage at either 2-8°C or 22°C. The sample storage conditions that were validated for each swab type are summarized in **Table 2**.

Table 2. Acceptable transport and storage conditions demonstrated analytically with alternative specimen collection devices

Collection & Transport Device	Maximum Storage Time	
	2-8°C	22 °C
Puritan Foam Swab	72 hours	72 hours
Puritan Polyester Swab	72 hours	72 hours
Puritan Hydraflock Swab	72 hours	72 hours
Copan Nylon Flocked Swab	72 hours	72 hours
BBL CultureSwab Liquid Amies	6 hours	6 hours

The analytical Specimen Stability Study also showed that rayon swabs and the BBL CultureSwab Liquid Stuart specimen collection and transport system are not compatible with Alere i Strep A 2 and should not be used. This is noted as a Limitation in the device labeling.

d. *Detection limit:*

Limit of Detection
The Limit of Detection (LoD) of Alere i Strep A 2 was estimated for two strains of *S. pyogenes* by testing various dilutions of enumerated cell stocks in 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.

Target levels were determined by measuring the optical density of stock suspensions of *S. pyogenes* at 630nm (OD_{630}) and using a quantitative laboratory-developed PCR assay to estimate genomic equivalents. [1] Chamber counts performed by microscopy showed that an OD_{630} of 0.1 was equivalent to 2 x 10^8 cells/mL. The results of the study are shown in **Table 3**. The higher of the two LoD values expressed in terms of genomic copies was used as the basis for testing the inclusivity of Alere i Strep A 2 (**Table 4**).

[1] Morozumi, M., *et al*. *J Clin Microbiol* 2006 44: 1440-1446

Table 3. Limit of detection (LoD) for Alere i Strep A 2

ATCC Strain	Limit of Detection (per mL of Elution Buffer)	
	Cells [1]	Genomic Copies [2]
12344	147	223
19615	25	512

ATCC: American Type Culture Collection
[1] As determined by OD_{630} and correlation with chamber counts
[2] As determined by quantitative PCR

Inclusivity
The inclusivity of Alere i Strep A 2 was evaluated by testing 14 strains of *S. pyogenes* in addition to those included in the LoD Study. Testing was performed in throat swab matrix and the lowest dilution of each strain at which each of 10 assay replicates produced a positive result is shown in **Table 4**.

Table 4. Reactivity titers of different strains of *S. pyogenes*

Source	Strain	Genomic copies Per mL Elution Buffer [1]	Multiple of LoD for ATCC 19615
ATCC	8135	1537	3
	12384	1537	3
	12202	1537	3
	12203	1537	3
	12204	1537	3
	12365	1537	3
	14289	1537	3
	49399	3074 [2]	6
	51339	1537	3
	700294	1537	3
	12357	2049 [2]	4
	12385 Type 4	1537	3
	12385 Loomis	1537	3
Zeptometrix	Z018	3074 [2]	6

ATCC: American Type Culture Collection; LoD: Limit of Detection
[1] Level at which 10/10 assay replicates produced positive results; the lowest level tested was 1537 genomic copies/mL, approximately 3X the LoD determined for strain ATCC 19615
[2] <10/10 positive results were obtained at lower target levels

Bioinformatic analysis:
The inclusivity of Alere i Strep A 2 assay was also assessed *in silico* by searching the National Center for Biotechnology Information (NCBI) Nucleotide database (https://www.ncbi.nlm.nih.gov/nuccore) using the Basic Local Alignment Search Tool (BLAST), with the *S. pyogenes* amplicon sequence as the query sequence. The region of the *S. pyogenes* genome targeted by the assay was shown to be well conserved, with no evidence of sequence heterogeneity that could lead to false

negative results. This analysis supports the ability of Alere i Strep A 2 to detect different strains of *S. pyogenes* and is acceptable.

e. *Analytical specificity:*

Cross-Reactivity
The analytical specificity of Alere i Strep A 2 was evaluated by testing a variety of commensal and pathogenic species of bacteria and yeast (**Table 5**). Suspensions of each organism were diluted in phosphate buffered saline and tested in triplicate at a final concentration ≥2 x 10^6 cells/mL of Elution Buffer. All results were as expected and no evidence of cross-reaction or assay interference was observed.

Table 5. Species tested for cross-reaction in Alere i Strep A

Bacteria	
Arcanobacterium haemolyticum	*Staphylococcus aureus*
Bacillus cereus	*Staphylococcus epidermidis*
Bordetella pertussis	*Streptococcus agalactiae*
Burkholderia cepacia	*Streptococcus anginosus*
Campylobacter rectus	*Streptococcus canis*
Corynebacterium diphtheriae	*Streptococcus constellatus* subsp. *pharyngis*
Enterococcus faecalis	*Streptococcus dysgalactiae* subsp. *equisimilis*
Escherichia coli	*Streptococcus gallolyticus*
Fusobacterium necrophorum	*Streptococcus intermedius*
Haemophilus influenzae	*Streptococcus mitis*
Klebsiella pneumoniae	*Streptococcus mutans*
Lactobacillus acidophilus	*Streptococcus pneumoniae*
Moraxella catarrhalis	*Streptococcus salivarius*
Neisseria gonorrhoeae	*Streptococcus sanguinus*
Peptostreptococcaceae [1]	*Treponema denticola*
Prevotella oralis [2]	*Veillonella parvula*
Pseudomonas aeruginosa	
Yeast	
Candida albicans	

[1] Formerly *Peptostreptococcus micros*
[2] Formerly *Bacteroides oralis*

Bioinformatic Analysis
To evaluate the potential for cross-reaction of Alere i Strep A 2 with non-target organisms, BLAST analyses were performed against the NCBI Nucleotide database using the assay target region as the query sequence. The search showed no evidence of homology between the Alere i Strep A 2 target sequence and clinically relevant species that is likely to result in cross-reaction and generation of false-positive results.

Contamination Study
The potential for contamination between samples tested on the same Alere i Instrument was assessed by testing an alternating series of Alere i Strep A (K141757) Positive and Negative Control Swabs. The Positive Control Swabs resulted in a final

concentration of *S. pyogenes* of 1.5-2.5 CFU/mL of Elution Buffer while the Negative Controls delivered Group C *Streptococcus* at a concentration of 5 x 10^6 CFU/mL. Thirty 30 Positive and 30 Negative Control Swabs were tested on each of two Alere i Instruments (i.e., 60 Positive and 60 Negative Swabs in total). All the controls produced the expected results and no false positive results were observed, indicating that the risk of contamination between runs is acceptably low.

f. *Assay cut-off:*

Alere i Strep A 2 is comprised of two separate amplification reactions that occur in separate tubes; one for the *S. pyogenes* target and one for the Internal Control. The products of each amplification reaction are detected in separate optical channels by monitoring the accumulation of fluorescent signal in real-time. The gradient and amplitude of the fluorescence curve generated in each optic are analyzed and used in a decision algorithm to determine the final assay result. Once a definitive result for a sample is obtained, the assay is terminated. The gradient thresholds (cut-offs) for the assay were established through analysis of known positive and negative samples and were validated in the Clinical Study described in **Section M(3)(a)**.

g. *Assay Interference*

The potential for interference with Alere i Strep A 2 was evaluated with 21 endogenous and exogenous substances that may be present in throat swab specimens. Each substance was tested in triplicate in the presence and absence of *S. pyogenes* ATCC 19615 at a concentration of 3X LoD (1537 genomic copies/mL of Elution Buffer). False negative results were obtained with both human saliva and mucin at concentrations of 10% v/v and 2% w/v, respectively. In addition, a false positive result was observed in the presence of Listerine Antiseptic Mouthwash at 20% v/v. In each case, the expected results were obtained when the substances were tested at lower concentration. These results are reflected in the device labeling. No interference was observed with any of the substances when tested at the concentrations listed in **Table 6**.

Table 6. Substances tested for potential interference with Alere i Strep A 2

Substance	Concentration Tested [1]
Acetaminophen	60.4 mg/mL
Acetylsalicylic Acid	0.65 mg/mL
ACT Total Care	20% (v/v)
Albuterol	0.40 mg/mL
Cepacol Mouthwash	20% (v/v)
Cepacol Sore Throat Lozenges	20% (w/v)
Children’s Dimetapp Cough & Cold	20% (v/v)
Chloraseptic Max Sore Throat Relief + Coating Action	20% (v/v)
Contact Cold & Flu Tablets	20% (w/v)

Substance	Concentration Tested [1]
Crest Complete Multi-Benefit Whitening + Deep Clean Toothpaste	20% (w/v)
Diphenhydramine HCl	1 mg/mL
Halls Plus	20% (w/v)
Human Saliva	5% (v/v) [2]
Ibuprofen	20 mg/mL
Listerine Antiseptic Mouthwash	10% (v/v) [3]
Mucin	1% (w/v) [4]
Robitussin Maximum Strength Nighttime Cough DM	20% (v/v)
Sucrets Sore Throat & Cough	20% (w/v)
Tylenol Cold Multi-Symptom Liquid	20% (v/v)
Whole Blood	5% (v/v)
Zicam Oral Mist	20% (v/v)

[1] Highest concentration in throat swab matrix at which no interference was observed (i.e., no false positive, false negative or invalid results obtained)
[2] 1/3 replicates at 10% v/v saliva produced a false negative result
[3] 1/3 replicates at 20% v/v Listerine Antiseptic Mouthwash produced a false positive result
[4] 1/3 replicates at 2% w/v mucin produced a false-negative result

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Not applicable.

   b. *Matrix comparison:*

      The compatibility of alternative specimen collection and transport devices with Alere i Strep A 2 was demonstrated in the context of the Specimen Stability Studies described in **Section M(1)(c)**.

3. Clinical studies:

   a. *Clinical Sensitivity:*

      The clinical performance of Alere i Strep A 2 was established in a multi-center, prospective Clinical Study that was conducted at nine (9) geographically diverse U.S. sites in 2017 among patients who presented with a sore throat or symptoms of pharyngitis. A total of 1028 subjects were initially enrolled in the study of whom 43 were excluded from the analysis of performance for the following reasons: error in sample handling (21), failure to meet eligibility criteria (11), failure to comply with informed consent procedures (11). Of the remaining subjects, 976/985 (99.1%) generated valid Alere i Strep A 2 results on initial testing (initial invalid rate 9/985; 0.9%). Of the nine (9) samples that initially produced invalid results, eight (8) were

retested and five (5/8) produced valid results for a final invalid rate of 4/985 (0.2%).

Of the 981 subjects with evaluable Alere i Strep A 2 test results, 582 (59.3%) were female and 399 (40.7%) were male.

Two throat swabs were collected from each subject. One swab was used for the reference bacterial culture according to standard procedures (inoculation of sheep blood agar followed by identification of β-hemolytic colonies by latex agglutination); while the other swab was tested with Alere i Strep A 2. Swabs for analysis by the reference culture method were shipped to a central laboratory in dry transport tubes. All reference cultures were inoculated within 48 hours of specimen collection and culture plates were incubated for 48 hours before being discarded as negative. The overall performance of Alere i Strep A 2 in relation to the reference culture method is summarized in **Table 7** and stratified by site in **Table 8**. The performance of Alere i Strep A 2 observed in the Clinical Study was considered acceptable.

Table 7. Overall clinical performance of Alere i Strep A 2 versus bacterial culture

		Reference Culture		
		Positive	**Negative**	**Total**
Alere i Strep A 2	**Positive**	195	52 [1]	**247**
	Negative	3 [2]	731	**734**
	Total	**198**	**783**	**981** [3]
Sensitivity		98.5% (195/198); 95% CI: 95.6-99.5%		
Specificity		93.4% (731/783); 95% CI: 91.4-94.9%		
Positive Predictive Value		78.9% (195/247)		
Negative Predictive Value		99.6% (731/734)		
Prevalence		20.2% (198/981)		

95% CI: 95% score confidence interval

[1] 38/52 (73.1%) samples with Alere i Strep A 2 false-positive results relative to culture were positive by an alternative laboratory developed real-time PCR method

[2] 2/3 (66.7%) samples with Alere i Strep A 2 false-negative results relative to culture were positive by an alternative laboratory developed real-time PCR method

[3] 943/981 (96.1%) of specimens were tested with Alere i Strep A 2 within 2 hours of collection

Table 8. Alere i Strep A 2 performance stratified by site

Site	Samples (%)	Culture Positive (% Prevalence)	Percent (%; 95% Score Confidence Interval)	
			Sensitivity	Specificity
001A	50 (5.1)	19 (38.0)	18/19 (94.7; 75.4-99.1)	26/31 (83.9; 67.4-92.9)
009A	150 (15.3)	21 (14.0)	21/21 (100; 84.5-100)	120/129 (93.0; 87.3-96.3)
024A	57 (5.8)	15 (26.3)	15/15 (100; 79.6-100)	36/42 (85.7; 72.2-93.3)
033A	119 (12.1)	23 (19.3)	23/23 (100; 85.7-100)	92/96 (95.8; 89.8-98.4)
060A	195 (19.9)	11 (5.6)	10/11 (90.9; 62.3-98.4)	179/184 (97.3; 93.8-98.8)
061A	98 (10.0)	15 (15.3)	14/15 (93.3; 70.2-98.8)	74/83 (89.2; 80.7-94.2)
066A	163 (16.6)	39 (23.9)	39/39 (100; 91.0-100)	120/124 (96.8; 92.0-98.7)
071A	89 (9.1)	31 (34.8)	31/31 (100; 89.0-100)	50/58 (86.2; 75.1-92.8)
074A	60 (6.1)	24 (40.0)	24/24 (100; 86.2-100)	34/36 (94.4; 81.9-98.5)
Total	**981 (100)**	**198 (20.2)**	**195/198 (98.5; 95.6-99.5)**	**731/783 (93.4; 91.4-94.9)**

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 Alere i Strep 2 was evaluated in a prospective Clinical Study conducted at nine (9) sites in the US (**Section M(3)(a)**). The overall prevalence of *S. pyogenes* (Group A *Streptococcus*) in throat swab specimens was 25.2% (247/981) as determined by Alere i Strep A 2 and 20.2% (198/981) as determined by culture. In **Table 9**, the prevalence of *S. pyogenes* as determined by Alere i Strep A 2 is stratified by the age and gender of the subjects.

Table 9. Prevalence of *S. pyogenes* positive subjects by age and gender

Age/Gender	Number	Alere i Strep A 2 Positive	% Prevalence [1]
<2 years	25	5	20.0
2-11 years	421	155	36.8
12-21 years	240	38	15.8
22-59 years	254	47	18.5
≥60 years	41	2	4.9
Male	399	99	24.8
Female	582	148	25.4
Total	**981**	**247**	**25.2**

[1] As determined using Alere i Strep A 2

N. Instrument Name:

Alere i Instrument

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 ____________ No _____X_____

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

   Yes ____________ No _____X_____

2. Software:

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

   Yes _____X_____ No ____________

3. Specimen Identification:

   Specimens are identified by scanning or typing in the applicable patient identification code.

4. Specimen Sampling and Handling:

   Swab specimens are expressed in the Elution Buffer contained within the Sample Receiver. The operator transfers 2 x 100µL aliquots of the expressed specimen to the Test Base using the Transfer Cartridge to rehydrate the reagents for target and Internal Control amplification/detection. Refer to **Section I** above for additional information.

5. Calibration:

   End-user calibration for the Alere i Instrument is not required. Calibration of the optical and thermal systems is performed during the manufacturing process. The instrument is maintenance-free and has no serviceable parts. However, if the instrument is transported or moved, a performance check using Alere i Positive and Negative Controls is recommended by the manufacture prior to testing patient specimens to ensure proper functionality.

6. Quality Control:

   Refer to **Section M(1)(c)**.

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

The Alere i Instrument was initially cleared under K141520 (Alere i Influenza A&B on the Alere i Instrument).

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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