

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

A. 510(k) Number:

K143651

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Simplexa™ Group A Strep Direct and Simplexa™ Group A Strep Positive Control Pack from throat specimens.

C. Measurand:

Group A β -hemolytic *Streptococcus* (GAS; *Streptococcus pyogenes*) nucleic acids.

D. Type of Test:

The Simplexa™ Group A Strep Direct and Simplexa™ Group A Strep Positive Control Pack (Simplexa™ Group A Strep Direct) assay is a Real-Time PCR *in vitro* diagnostic test for the rapid and qualitative detection and differentiation of Group A β -hemolytic *Streptococcus* (*Streptococcus pyogenes*) nucleic acids isolated from throat swab specimens obtained from symptomatic patients.

E. Applicant:

Focus Diagnostics, Inc.

F. Proprietary and Established Names:

Simplexa™ Group A Strep Direct and Simplexa™ Group A Strep Positive Control Pack

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 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):

Simplexa™ Group A Strep Direct

The Focus Diagnostics Simplexa™ Group A Strep Direct assay is intended for use on the 3M Integrated Cycler for the in vitro qualitative detection of Group A Streptococcus (GAS) from throat swabs collected from human patients with signs and symptoms of pharyngitis, such as sore throat. This test is intended for use as an aid in the diagnosis of GAS infection. The assay is intended for use in hospital, reference, or state laboratory settings. The device is not intended for point-of-care use.

Simplexa™ Group A Strep Positive Control Pack

Focus Diagnostics' Simplexa™ Group A Strep Positive Control Pack is intended to be used as a control with Simplexa™ Group A Strep Direct. This control is not intended for use with other assays or systems.

2. Indication(s) for use:

Same as intended use.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

3M Integrated Cycler

I. Device Description:

The Simplexa™ Group A Strep Direct assay system is a real-time PCR system that enables the direct amplification and qualitative detection of Group A Strep bacterial DNA from throat swabs that have not undergone a nucleic acid extraction. The system consists of the Simplexa™ Group A Strep Direct assay, the 3M Integrated Cycler (with Integrated Cycler Studio Software), the Direct Amplification Disc (DAD) and associated accessories.

In the Simplexa™ Group A Strep Direct assay, bi-functional fluorescent probe-primers are

used together with corresponding reverse primers to amplify Group A Strep bacterial DNA and the Internal Control (DNA IC). The assay targets a conserved region of Group A Strep (pyrogenic exotoxin B gene) to identify this bacteria in the specimen. The DNA IC is used to detect PCR failure and/or inhibition.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Lyra™ Direct Strep Assay

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

k133883

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Simplexa™ Group A Strep Direct	Lyra™ Direct Strep Assay (k133883)
Intended Use	<p>Simplexa™ Group A Strep Direct</p> <p>The Focus Diagnostics Simplexa™ Group A Strep Direct assay is intended for use on the 3M Integrated Cyclor for the <i>in vitro</i> qualitative detection of Group A Streptococcus (GAS) from throat swabs collected from human patients with signs and symptoms of pharyngitis, such as sore throat. This test is intended for use as an aid in the diagnosis of GAS infection. The assay is intended for use in hospital, reference, or state laboratory settings. The device is not intended for point-of-care use.</p> <p>Simplexa™ Group A Strep Positive Control Pack</p> <p>Focus Diagnostics' Simplexa™ Group A Strep Positive Control Pack is intended to be used as a</p>	<p>The Lyra Direct Strep Assay is a Real-Time PCR <i>in vitro</i> diagnostic test for the qualitative detection and differentiation of Group A β-hemolytic Streptococcus (Streptococcus pyogenes) and pyogenic Group C and G β-hemolytic Streptococcus nucleic acids isolated from throat swab specimens obtained from patients with signs and symptoms of pharyngitis, such as a sore throat. The assay does not differentiate between pyogenic Groups C and G β-hemolytic Streptococcus.</p> <p>All negative test results should be confirmed by bacterial culture, because negative results do not preclude Group A, C or G Strep infection and should not be used as the sole basis for treatment.</p> <p>The assay is intended for use in</p>

Similarities		
Item	Device	Predicate
	Simplexa™ Group A Strep Direct	Lyra™ Direct Strep Assay (k133883)
	control with Simplexa™ Group A Strep Direct. This control is not intended for use with other assays or systems.	hospital, reference, or state laboratory settings. The device is not intended for point-of-care use.
Sample Type	Throat swab	Same
Testing Time	60 minutes	Same
DNA Amplification Technology	Real-time polymerase chain reaction	Same
Detection Techniques	Automatically detects fluorescence after dissociation of fluorophore from quencher during amplification	Same

Differences		
Item	Device	Predicate
Extraction	Self-contained and automated	Manual
Target Sequence Detected	Well conserved region of the exotoxin B gene (<i>speB</i>)	Group A – 99bp product in the putative competence (<i>comX1.1</i>) gene Groups C/G – 188bp product in the tagatose-6-phosphate kinase (<i>lacC</i>) gene
Reagents/ Components	Simplexa™ Group A Strep Direct Reaction Mix Simplexa™ Group A Strep Positive Control Pack Direct Amplification Disks	Lyra™ Direct Strep Master Mix, Process Buffer, and Rehydration Solution ABI 7500 Fast Dx 96-well PCR Plate, optical plate films and plate centrifuge Dry heating block
Instrument	3M Integrated Cycler	ABI 7500 Fast DX Thermocycler
Performance Characteristics	GAS* Sensitivity: 97.4%[95% CI: 93.6% - 99.0%] GAS* Specificity: 95.2%[95% CI: 93.9% - 96.3%]	GAS* Sensitivity: 96.5%[95% CI: 91.3% - 98.6%] GAS* Specificity: 98.0%[95% CI: 97.0% - 98.6%] Pyo GCS/GGS* Sensitivity: 95.7%[95% CI: 88.1% - 98.5%] Pyo GCS/GGS* Specificity: 98.3%[95% CI: 97.4% - 98.9%]

*GAS = Group A *Streptococcus*; Pyo GCS/GGS = Pyogenic Group C/G *Streptococcus*

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

Not applicable.

L. Test Principle:

The Simplexa™ Group A Strep Direct assay system is a real-time PCR system that enables the direct amplification and qualitative detection of Group A Strep bacterial DNA from throat swabs that have not undergone a nucleic acid extraction. The system consists of the Simplexa™ Group A Strep Direct assay, the 3M Integrated Cyclor (with Integrated Cyclor Studio Software), the Direct Amplification Disc (DAD) and associated accessories. In the Simplexa™ Group A Strep Direct assay, bi-functional fluorescent probe-primers are used together with corresponding reverse primers to amplify Group A Strep bacterial DNA and the Internal Control (DNA IC). The assay targets a conserved region of Group A Strep (pyrogenic exotoxin B gene) to identify this bacteria in the specimen. The DNA IC is used to detect PCR failure and/or inhibition.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision Study

Within-laboratory, inter-lot precision was evaluated for the Simplexa™ Group A Strep Direct assay at one (1) site using two (2) strains of Group A Streptococci (GAS) representative of serotypes M1 and M3 with four (4) panel members:

- 1) Negative
- 2) Low Positive (LP), 1 x LoD and
- 3) Moderate Positive (MP), 3.0 x LoD.
- 4) Positive Control (PC)

Contrived specimens were spiked from freshly-grown bacterial stocks into a simulated negative matrix with target GAS at the final intended target concentration (confirmed by titration and plate count). Cell preparations were frozen at -70°C after preparation until testing. The LoD values were based on the values obtained in the LoD study. See section M.2.b below for details on the matrix equivalency and freeze-thaw study.

The study was conducted with three (3) different Reaction Mix lots. Each panel member was run in duplicate (2), twice (2) per day for three (3) non-consecutive days by one (1) operator at one (1) site (2 replicates x twice per day x 3 days x 3 lots = 36 replicates/panel member/strain). The results are shown in Table I.

Table I: Inter Lot Precision Study					
Strain	Panel	# Detected/ # Tested	% Detected	95% CI	CFU/ml
No Analyte	Negative	0/36	0.0%	(0.0%, 10.6%)	0
GAS M1	LP	36/36	100.0%	(90.4%, 100.0%)	6.8×10^2
	MP	36/36	100.0%	(90.4%, 100.0%)	2.4×10^3
GAS M3	LP	36/36	100.0%	(90.4%, 100.0%)	2.0×10^3
	MP	36/36	100.0%	(90.4%, 100.0%)	7.1×10^3
Positive Control	PC	36/36	100.0%	(90.4%, 100.0%)	N/A

The precision study results met the pre-defined acceptance criteria for LP, MP, and PC specimens. The results of this study are acceptable and these results are described in labeling.

Reproducibility Study

The reproducibility of the Simplexa™ Group A Strep Direct assay was established in a multi-center study. The same strains and panel members were prepared and tested as listed in the precision study above (Table I). Panel members were tested in triplicate (3) in two (2) runs per day each by a different operator at three (3) sites for five (5) non-consecutive days (3 replicates x 2 operators runs x 3 sites x 5 days = 90 replicates/panel member). These studies were conducted with a single (1) lot of positive control and reagents across the three (3) sites. The results are shown in Table II.

Table II: Reproducibility Study					
Strain	Panel	# Detected/ # Tested	% Detected	95% CI	CFU/ml
No Analyte	Negative	1/90*	1.1%	(0.2%, 6.0%)	0
GAS M1	LP	84/90	93.3%	(86.2%, 96.9%)	6.8×10^2
	MP	88/90*	97.8%	(92.3%, 99.4%)	2.4×10^3
GAS M3	LP	85/90	94.4%	(87.6%, 97.6%)	2.0×10^3
	MP	87/90*	96.7%	(90.7%, 98.9%)	7.1×10^3
Positive Control	PC	90/90	100.0%	(95.9%, 100.0%)	N/A

* All observed unexpected results came from runs performed by the same operator at the same site during the first two days of the study.

These results met the predefined acceptance criteria for the various panels and are described in labeling.

b. Linearity/assay reportable range:

Not applicable.

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

The Simplexa™ Group A Strep Direct and Simplexa™ Group A Strep Positive Control Pack have been determined to be stable for at least 14 months of real-time stability over a temperature range from -14 °C to -28 °C. The products are labeled with a 12 month expiration date.

To assess the room-temperature stability of positive control aliquots of positive control were thawed and kept at room temperature for 8 hours and 24 hours and tested to determine room temperature stability. The positive control is stable up to 24 hours when stored at room temperature.

To assess the room-temperature stability of Simplexa™ Group A Strep Reaction Mix, the Reaction Mix was thawed from -20°C and kept at room temperature for 30 and 60 minutes. Positive Control (PC) was tested in quadruplicate (4) with singlet (1) of unspiked Aimes medium as a negative sample. The Reaction Mix stability was established and the labeling instructs the end user to use within 30 minutes from thawing.

Clinical studies demonstrate that swab specimens are stable for over 24 h.

d. *Detection limit:*

The limit of detection (LoD) of the Simplexa™ Group A Strep Direct assay was determined using contrived stocks of two (2) GAS serotypes which were prepared per the protocol described in the precision study section (see M.1.a above). The LoD study was conducted using two (2) lots on four (4) instruments. The LoD was defined as the point at which at least 95% of all replicates tested positive (C₉₅). Eight (8) dilutions from each serotype were screened in triplicate (3). The lowest dilution at which all three (3) replicates were detected was confirmed using twenty (20) additional replicates for each serotype at that concentration. Two invalid replicates were observed due to internal control failure. The LoD study results are shown in Table III below.

Strain	Serotype	CFU/ml
Group A Streptococcal strain 1 (<i>Streptococcus pyogenes</i>)	M1	6.82 x 10 ²
Group A Streptococcal strain 2 (<i>Streptococcus pyogenes</i>)	M3	2.35 x 10 ³

These LoD values are described in the labeling and they were used in determining spiking levels for all subsequent analytical studies.

e. *Analytical reactivity:*

Inclusivity studies were conducted for the Simplexa™ Group A Strep Direct assay

with twenty-one (21) GAS strains, in addition to those tested in the LoD studies, in replicates of three (3) per strain near at 2-3 x LoD (1.50×10^3) using the LoD determined for the M1 serotype (LoD = 682 CFU/ml) as the basis. If detection failure was experienced, the concentration of the particular strain was increased until all three (3) replicates were positively detected.

This study was performed with one (1) reagent lot on two (2) different instruments, performed by two (2) operators. Each cultured strain was prepared per the protocol described above in M.1.a above. The inclusivity study results and the final organism concentrations tested are shown in Table IV below. All GAS strains were correctly detected by the assay at the concentrations indicated.

Table IV: Group A β-hemolytic Streptococcus Inclusivity		
Group A Streptococcus Strain #	Serotype	CFU/ml
1	M2	1.50×10^3
2	M4	1.50×10^3
3	M5	1.50×10^3
4	M6	1.50×10^3
5	M9	3.00×10^3
6	M12	1.50×10^3
7	M13	1.50×10^3
8	M14	1.50×10^3
9	M18	5.00×10^3
10	M22	1.50×10^3
11	M27	3.00×10^3
12	M28	1.50×10^3
13	M29	1.50×10^3
14	M49	1.50×10^3
15	M73	3.00×10^3
16	M75	3.00×10^3
17	M77	3.00×10^3
18	M78	1.50×10^3
19	M82	1.50×10^3
20	M87	1.50×10^3
21	M89	3.00×10^3

These study results are acceptable and they are described in the labeling.

f. Analytical specificity:

i. *Microbial cross-reactivity*

An *in silico* BLAST analysis of primers used in the Simplexa™ Group A Strep Direct assay against the NCBI database did not show evidence of cross-reactivity with organisms that might be found in throat swab specimens.

A study was performed to evaluate the performance of the Simplexa™ Group A Strep Direct assay in the presence of sixty-four (64) potentially cross-reacting bacteria and viruses commonly found in throat specimens (see Table V below). Each organism was tested in triplicate in the presence of clinically relevant levels of viruses (10⁵ PFU/ml) and bacteria (10⁶ CFU/ml) or higher. All strains were spiked into simulated negative matrix and evaluated using one (1) lot and two (2) instruments by two (2) operators.

Table V: Strains Included in Cross-Reactivity		
Strain		
<i>Arcanobacterium haemolyticum</i>	<i>Staphylococcus aureus</i> (MRSA), ATCC 43300	<i>Streptococcus sobrinus</i>
<i>Bacillus cereus</i>	<i>Staphylococcus epidermidis</i> (MRSE), ATCC 29887	<i>Streptococcus uberis</i>
<i>Bacteroides ovatus</i>	<i>Stenotrophomonas maltophilia</i>	<i>Streptococcus vestibularis</i>
<i>Bordetella pertussis</i>	<i>Streptococcus agalactiae</i>	<i>Treponema denticola</i>
<i>Burkholderia cepacia</i>	<i>Streptococcus anginosus</i>	<i>Veillonella parvula</i>
<i>Campylobacter rectus</i>	<i>Streptococcus canis</i>	Adenovirus 1
<i>Candida albicans</i>	<i>Streptococcus constellatus</i> subsp. <i>constellatus</i>	Adenovirus 7A
<i>Chlamydia pneumoniae</i>	<i>Streptococcus cristatus</i>	Coronavirus 229E
<i>Corynebacterium diphtheriae</i>	<i>Streptococcus dysgalactiae</i>	Cytomegalovirus (CMV)
<i>Enterococcus faecalis</i> vanB	<i>Streptococcus equi</i> subsp. <i>zooepidemicus</i>	Enterovirus 71
<i>Escherichia coli</i>	<i>Streptococcus equinus</i>	Epstein-Barr virus (B95-8)
<i>Fusobacterium necrophorum</i>	<i>Streptococcus gallolyticus</i>	HSV-1 McIntyre
<i>Haemophilus influenzae</i>	<i>Streptococcus gordonii</i>	HSV-2 G
<i>Klebsiella pneumoniae</i>	<i>Streptococcus intermedius</i>	Influenza A/Hong Kong/8/68 H3N2
<i>Lactobacillus acidophilus</i>	<i>Streptococcus mitis</i>	Influenza B/Panama/45/90
<i>Legionella pneumophila</i>	<i>Streptococcus mutans</i>	Metapneumovirus-9
<i>Moraxella catarrhalis</i>	<i>Streptococcus oralis</i>	Parainfluenza 1
<i>Neisseria gonorrhoeae</i>	<i>Streptococcus parasanguinis</i>	Parainfluenza 2

<i>Neisseria meningitidis</i>	<i>Streptococcus pneumoniae</i>	Parainfluenza 3
<i>Peptostreptococcus micros</i>	<i>Streptococcus salivarius</i>	Rhinovirus 1A
<i>Pseudomonas aeruginosa</i>	<i>Streptococcus sanguinis</i>	RSV-B 9320
<i>Mycoplasma pneumoniae</i>		

None of the sixty-four (64) bacteria and viruses tested that might be found in throat swab specimens cross-react with the assay.

These study results are acceptable and these results are described in labeling.

ii. *Microbial interference*

Interference studies were conducted with each of the sixty-four (64) microorganisms listed above in Table V. Each organism was tested in triplicate in the presence of clinically relevant levels of viruses (10^5 PFU/ml) and bacteria (10^6 CFU/ml) or higher. All strains were spiked into simulated negative matrix along with 2-4 x LoD Group A Streptococcus serotypes M1 and M3 and evaluated using one (1) lot and two (2) instruments by two (2) operators. None of the organisms interfered with the detection of the Group A Streptococcal strains.

iii. *Interfering substances*

Twenty-nine (29) chemical and biological substances likely to be found in throat swab specimens were evaluated for potential to interfere with the Simplexa™ Group A Strep Direct assay, including blood (10% v/v), mucin (60µg/ml) and saliva (50µl/swab). Each substance was tested in triplicate using two serotypes of *Streptococcus pyogenes* (M1 and M3), tested near 3 x LoD at medically relevant concentrations. None of the substances tested were found to interfere with the Simplexa™ Group A Strep Direct assay.

iv. *Carryover/Cross-contamination*

A study to assess carryover contamination was conducted with another previously cleared kit (k120413) and the results were determined to be acceptable. Due to the similarities of risks posed by the previous device and the Simplexa™ Group A Strep Direct device, no carryover studies were conducted for this assay.

g. *Assay cut-off:*

A Receiver Operating Characteristic (ROC) analysis was conducted to determine the cycle threshold (Ct) cutoff for the Simplexa™ Group A Strep Direct assay. Using ROC analysis and the Ct spread from the LoD as well as the clinical study, the Ct cut-off was set at 45. This value was used to determine assay results in the analytical and clinical studies.

2. Comparison studies:

a. *Method comparison with predicate device:*

Not applicable.

b. *Matrix comparison:*

A comparison study was conducted between negative clinical matrix and a contrived negative matrix in order to validate the use of the contrived negative matrix in place of a clinical negative matrix for the analytic studies in section M1 above. Contrived negative matrix was comprised of Amies medium with 9% w/v mucin and 1% v/v whole blood, constructed to mimic challenging clinical specimens. The matrix comparison study results are shown in Table VI below.

Panel ID		Simulated Negative Matrix		Swab Negative Clinical Matrix	
		Detected	% Pos	Detected	% Pos
Group A Streptococcus Serotype M1	10 x LoD	3/3	100%	3/3	100%
	2 x LoD	7/7	100%	7/7	100%
	1 x LoD	20/20	100%	20/20	100%
Group A Streptococcus Serotype M3	10 x LoD	3/3	100%	3/3	100%
	2 x LoD	7/7	100%	7/7	100%
	1 x LoD	20/20	100%	20/20	100%

These studies demonstrate that the contrived negative matrix is produces results that are equivalent to those obtained with a clinical matrix. These study results are acceptable.

3. Clinical studies:

Performance characteristics of the Simplexa™ Group A Strep Direct assay were established during a prospective study using fresh left-over throat swabs collected from and tested at four (4) clinical sites across the United States between May 6, 2014 and October 28, 2014. The assay was evaluated for the qualitative detection and differentiation of Group A β-hemolytic Streptococcus nucleic acids in comparison to culture. Discrepant analysis was conducted using bi-directional sequencing.

One thousand three hundred and ninety-seven (1397) specimens collected during clinical trials, of which one thousand three hundred and ninety-six (1396) were tested with the Simplexa™ Group A Strep Direct. Of these, one thousand three hundred and ninety-two (1392) specimens provided valid results from the Simplexa™ Group A Strep Direct and one thousand three hundred and fifty-seven (1357) were evaluable by culture. Of these, one thousand three hundred and fifty-two (1352) specimens were evaluable by both the test and reference method and could be used to evaluate the Simplexa™ Group A Strep Direct. The invalid rate observed during the clinical prospective study for this device was

0.57% (8/1396). These results are shown in Table VII below for all sites combined and for each study site separately.

a. *Clinical Sensitivity:*

Table VII: Clinical Performance Data for the Simplexa™ Group A Strep Direct vs. Composite Cultures for Group A β-hemolytic Streptococcus			
All Sites			
Simplexa™ Group A Strep Direct	Composite Culture		
	Positive	Negative	Total
Positive	152	57*	209
Negative	4**	1139	1143
Total	156	1196	1352
Sensitivity: 97.4% (152/156) 95% CI (93.6% - 99.0%) Specificity: 95.2% (1139/1196) 95% CI (93.9% - 96.3%)			
* Of the 57 discordant specimens, 46 were positive for GAS when tested with bi-directional sequencing, 9 were negative and 2 were indeterminate. ** Of the 4 discordant specimens, 2 were GAS negative when tested with bi-directional sequencing.			
Site 1			
Simplexa™ Group A Strep Direct	Composite Culture		
	Positive	Negative	Total
Positive	28	10*	38
Negative	1**	144	145
Total	29	154	183
Sensitivity: 96.6% (28/29) 95% CI (82.8% - 99.4%) Specificity: 93.5% (144/154) 95% CI (88.5% - 96.4%)			
* Of the 10 discordant specimens, 7 were positive for GAS when tested with bi-directional sequencing, 3 were negative. ** The 1 discordant specimen was GAS positive when tested with bi-directional sequencing.			

Site 2			
Simplexa™ Group A Strep Direct	Composite Culture		
	Positive	Negative	Total
Positive	47	14*	61
Negative	1**	435	436
Total	48	449	497
Sensitivity: 97.9% (47/48) 95% CI (89.1% - 99.6%)			
Specificity: 96.9% (435/449) 95% CI (94.8% - 98.1%)			
* Of the 14 discordant specimens, 11 were positive for GAS when tested with bi-directional sequencing, 2 were negative and 1 was indeterminate.			
** The 1 discordant specimen was GAS negative when tested with bi-directional sequencing.			
Site 3			
Simplexa™ Group A Strep Direct	Composite Culture		
	Positive	Negative	Total
Positive	44	23*	67
Negative	0	215	215
Total	44	238	282
Sensitivity: 100.0% (44/44) 95% CI (92.0% to 100.0%)			
Specificity: 90.3% (215/238) 95% CI (85.9% - 93.5%)			
* Of the 23 discordant specimens, 19 were positive for GAS when tested with bi-directional sequencing, 3 were negative and 1 was indeterminate.			

Site 4			
Simplexa™ Group A Strep Direct	Composite Culture		
	Positive	Negative	Total
Positive	33	10*	43
Negative	2**	345	347
Total	35	355	390
Sensitivity: 94.3% (33/35) 95% CI (81.4% - 98.4%) Specificity: 97.2% (345/355) 95% CI (94.9% - 98.5%)			
* Of the 10 discordant specimens, 9 were positive for GAS when tested with bi-directional sequencing. ** Of the 2 discordant specimens, 1 was GAS negative when tested with bi-directional sequencing.			

The positive control for this assay is an inactivated GAS strain. The negative control is a no-template control. The positive and negative external quality control isolates provided were tested at least once per day during the clinical studies for each instrument used in the study for that day. One positive control lot was used throughout the clinical trials. All valid Group A Streptococcus positive controls were detected accurately (100%, 203/203). All valid no-template controls were detected accurately (100%, 204/204). During these studies, there were four (4) invalid negative controls and five (5) invalid positive controls. In each instance, the controls were repeated successfully during the same day on the same instrument.

b. Clinical specificity:

See table 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 overall incidence of Group A β -hemolytic Streptococcus in patients tested during this study was 11.2% (152/1352) based on culture results. All clinical specimens collected during this study were collected between May 6, 2014 and October 28, 2014.

N. Instrument Name:

3M Integrated Cyclor

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 _____ or No X

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:

Specimens are identified by scanning or typing in the sample identifier.

4. Specimen Sampling and Handling:

Swab specimens are expressed in transport medium. 50µl of the expressed specimen are transferred to the Sample Well of the Direct Amplification Disk and the disk is loaded into the Integrated Cyclor for automated extraction, amplification and detection. See section I above for more information.

5. Calibration:

End-user calibration for the Integrated Cyclor is not necessary. Calibration of the optical modules (excitation and emission gain settings) is performed during the manufacturing process and the values are stored in the instrument firmware.

6. Quality Control:

See section M.1.c for information on internal and external controls.

See section M.3.a for information on external control performance during clinical trials.

P. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

Q. Conclusion:

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