

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

A. 510(k) Number:

K123793

B. Purpose for Submission:

Premarket notification seeking 510(k) clearance of the Sophia® Strep A FIA assay for use with the Sophia™ Analyzer.

C. Measurand:

Group A Streptococcal antigens in throat swab specimen.

D. Type of Test:

Qualitative immunofluorescence based lateral flow assay

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Sofia® Strep A FIA and Sofia™ Analyzer

Strep A immunological test system and Fluorometer

G. Regulatory Information:

1. Regulation section:

21 CFR 866.3740, 21 CFR 866.2560

2. Classification:

Class 1

3. Product code:

GTY, KHO

4. Panel:

Microbiology (83)

H. Intended Use:

1. Intended use(s):

The Sofia Strep A FIA employs immunofluorescence technology to detect Group A Streptococcal antigens from throat swabs of symptomatic patients. All negative test results should be confirmed by bacterial culture because negative results do not preclude Group A Strep infection and should not be used as the sole basis for treatment. The test is intended for professional and laboratory use as an aid in the diagnosis of Group A Streptococcal infection.

2. Indication(s) for use:

The Sofia Strep A FIA employs immunofluorescence technology to detect Group A Streptococcal antigens from throat swabs of symptomatic patients. All negative test results should be confirmed by bacterial culture because negative results do not preclude Group A Strep infection and should not be used as the sole basis for treatment. The test is intended for professional and laboratory use as an aid in the diagnosis of Group A Streptococcal infection.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

To be used only with the Sophia™ Analyzer

I. Device Description:

The Sofia Strep A FIA is an immunofluorescence-based, lateral flow assay that uses a sandwich design to detect Group A *Streptococcus pyogenes* in patient specimens. As shown in the schematic below, the design of the test strip is typical for lateral flow assays. For example, the test strip contains the following elements commonly seen in non-fluorescence-based lateral flow devices:

- A sample pad that receives the specimen;
- A label pad that contains detection particles or micro-beads coated with polyclonal antibodies that are specific for the antigens of Group A Streptococcus pyogenes;
- A nitrocellulose test strip to which are bound capture polyclonal antibodies for Group A Strep antigens at a specific location or stripe on the nitrocellulose strip;

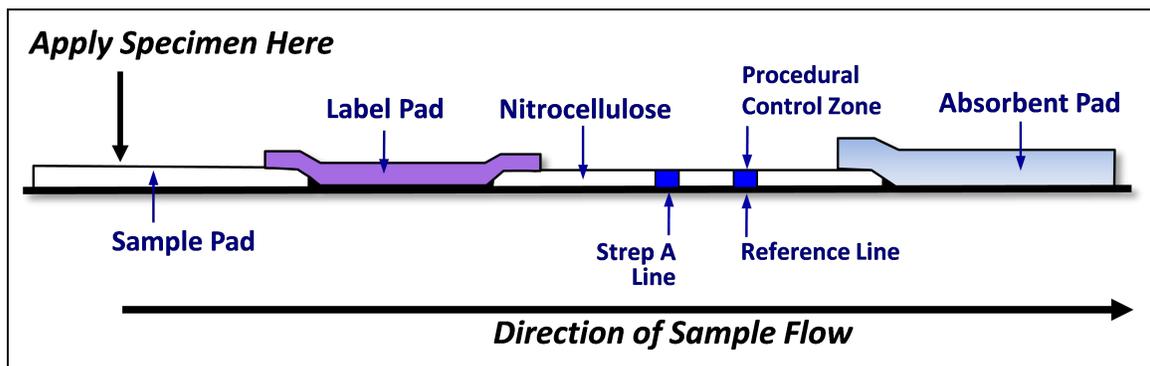
- A procedural control located after the analyte-specific test line on the nitrocellulose;
- An absorbent pad to facilitate wicking of the fluid across the nitrocellulose into the absorbent pad; and
- A desiccant that does not participate in the assay, but serves as a stabilizing agent during storage.

Elements in the Sofia Strep A FIA that are different from other lateral flow assay devices include the following:

- The fluorescent assay replaces antibody-tagged colored microparticles with antibody-tagged microparticles dyed with a highly fluorescent europium compound;
- The procedural control zone, designated at the location of the striped Reference Line, is a region located between the analyte line and the absorbent pad. The Sofia Analyzer scans this zone at the end of the assay to determine whether adequate flow of the specimen has occurred. A minimum fluorescent signal specification for this procedural control zone is an important fail-safe feature incorporated into the assay.
- No colored test or procedural control lines will be visible in the test window of the fluorescent assay cassette. The Sofia Analyzer automatically scans the test strip, collects and analyzes the fluorescence data, and then calculates and reports the result. These features eliminate the subjectivity required to interpret results in visual lateral flow assays. The operator must use the Sofia Analyzer to obtain a test result.
- The Sofia Analyzer has a number of fail-safe and failure alert procedures to help prevent the reporting of incorrect test results.

The sensitivity of the assay is derived from the use of a unique polystyrene microbead that has been dyed with a chelate of europium. The europium compound (more than 1×10^6 fluorescent molecules per bead) that is encased within the microbeads is temperature stable, resistant to bleaching in room light, and yields a very efficient conversion of the ultraviolet (UV) energy from 365 nm to a wavelength of 618 nm. This large Stokes shift protects against many naturally occurring fluorescent compounds that may be present in the test materials and/or clinical specimens.

Schematic of the Sofia Strep A FIA Test Strip



Analyte detection with the lateral flow device begins with the pipetting of an extracted clinical sample into the test cassette’s sample port and onto the sample pad, after which the sample is drawn by capillary action into and through the label pad, through the nitrocellulose strip and into the absorbent pad. The specimen interacts with distinct chemical environments as the fluid migrates along the course of the lateral flow device. Within the label pad, the specimen comes into contact with antibodies that have been coupled to the europium chelate-impregnated microbeads. During this interaction, the beads coated with anti-Strep A polyclonal antibodies bind corresponding Strep A antigens that are present in the specimen. The bead-coupled antigen-antibody complexes then begin to flow through the test strip. As they migrate on, if Strep A antigens are present in the sample, they and the fluorescent beads to which they are bound will be subsequently captured on the surface of the nitrocellulose by the respective location-fixed, anti-Strep A-specific capture antibodies. The flow and capture of the fluorescent microbeads coated with Strep A antigens allows the accumulation of a fluorescent signal at the specific analyte line location on the test strip. Upon completion of the test, the Sofia Analyzer scans the test strip and objectively interprets the assay result. There are three possible results: (1) positive for Strep A; (2) negative for Strep A; and (3) invalid. It is important to point out that the fluorescence signals obtained with this assay are invisible to the unaided eye. The test results can only be obtained with the proper use of the Sofia Analyzer. This ensures fully objective interpretation of the test result.

Results are presented on a screen and can be printed on an integrated printer (optional).

J. Substantial Equivalence Information:

1. Predicate device name(s):

QuickVue[®] Dipstick Strep A Test, Sofia Analyzer

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

K011097, K112177

3. Comparison with predicate:

Similarities			
Item	Device	Predicate	
Features	Sofia Analyzer and Strep A FIA (K123793)	QuickVue Dipstick Strep A Test (K011097)	Sofia Analyzer and Influenza A+B FIA (K112177)
Qualitative	Yes	Yes	Yes
Storage	Room Temperature	Room Temperature	Room Temperature

Differences			
Item	Device	Predicate	
Features	Sofia Analyzer and Strep A FIA	QuickVue Dipstick Strep A Test	Sofia Analyzer and Influenza A+B FIA

Differences		
Item	Device	Predicate
Indented Use	<p>The Sofia Strep A FIA employs immunofluorescence technology to detect Group A Streptococcal antigens from throat swabs of symptomatic patients. All negative test results should be confirmed by bacterial culture because negative results do not preclude Group A Strep infection and should not be used as the sole basis for treatment. The test is intended for professional and laboratory use as an aid in the diagnosis of Group A Streptococcal infection.</p>	<p>The QuickVue Dipstick Strep A is a sensitive immunoassay for the qualitative detection of Group A Streptococcal antigen from throat swab specimens or confirmation of presumptive Group A Streptococcal colonies from culture. This test is to be used to aid in the diagnosis of disease caused by Group A Streptococcus.</p> <p>The Sofia Influenza A+B FIA employs immunofluorescence to detect influenza A and influenza B viral nucleoprotein antigens in nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens taken directly from symptomatic patients. This qualitative test is intended for use as an aid in the rapid differential diagnosis of acute influenza A and influenza B viral infections. The test is not intended to detect influenza C antigens. A negative test is presumptive and it is recommended these results be confirmed by virus culture or an FDA-cleared influenza A and B molecular assay. Negative results do not preclude influenza virus infections and should not be used as the sole basis for treatment or other management decisions. The test is intended for professional and laboratory use.</p> <p>Performance characteristics for influenza A and B were established during February through March 2011 when influenza viruses A/California/7/2009 (2009 H1N1), A/Perth/16/2009 (H3N2), and B/Brisbane/60/2008 (Victoria-Like) were the predominant influenza viruses in circulation according to the Morbidity and Mortality Weekly Report from the CDC entitled "Update: Influenza Activity--United States, 2010-2011 Season, and Composition of the 2011-2012 Influenza Vaccine". Performance characteristics may vary against other emerging influenza viruses.</p> <p>If infection with a novel influenza virus is suspected</p>

Differences			
Item	Device	Predicate	
			based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Virus culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.
Instrument	Sofia Analyzer	None	Sofia Analyzer
Analyte	Group A Streptococcal	Group A Streptococcal	Influenza A and Influenza B
Automated Analysis	Yes	No	Yes
Read Results	Read results on instrument screen or print with optional printer	Visual read for presence or absence of control and test lines	Read results on instrument screen or print with optional printer
Calibrator	Yes – Calibration Cassette and QC Card provided	Not Applicable	Yes – Calibration Cassette and QC Card provided
Read Result Time	5 Minutes	5 Minutes	15 Minutes
Specimen Types	Throat swab	Throat swab or culture colonies	Nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash
Test Principle	Immunofluorescence Device	Immunoassay	Immunofluorescence Device
Format	Lateral-flow Test Cassette	Lateral-flow dipstick	Lateral-flow Test Cassette
Antibodies Used	Polyclonal rabbit antibodies that are specific to Group A Streptococcus	Polyclonal rabbit antibodies that are specific to Group A Streptococcus	Monoclonal antibodies to influenza A nucleoprotein and monoclonal antibodies to influenza B nucleoprotein
Detection Particle	Polystyrene microparticles dyed with Europium chelate	Polystyrene microparticles dyed with red colorant	Polystyrene microparticles dyed with Europium chelate
Reagent	One reagent bottle containing sodium nitrite and acetic acid in glass ampoule	Two reagent bottles: one containing sodium nitrite and one containing acetic acid	Lyophilized buffer containing detergents
Transfer Device	Fixed volume pipette used to transfer patient sample mixed with reagent into Test Cassette	Directly add dipstick to test tube containing patient sample mixed with reagent	Fixed volume pipette used to transfer patient sample mixed with reagent into Test Cassette
External Controls	Test kit contains Positive and Negative Control Swabs	Test kit contains Positive and Negative Liquid Controls	Test kit contains Positive and Negative Control Swabs

Differences			
Item	Device	Predicate	
Quality Control Features	Built-in features include: <ul style="list-style-type: none"> Built-in procedural control zone scanned by the analyzer to determine whether adequate flow occurred Analyzer prevents used or expired cartridge from being read by the reader Cassette properly inserted 	Built-in procedural control line interpreted by the operator to determine whether adequate flow occurred and clearing of background	Built-in features include: <ul style="list-style-type: none"> Built-in procedural control zone scanned by the analyzer to determine whether adequate flow occurred Analyzer prevents used or expired cartridge from being read by the reader Cassette properly inserted Built-in negative control line scanned by the analyzer to measure degree of non-specific binding

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

Standards recognized by FDA:

- CLSI LIS01-A2 (13-29)
- CLSI LIS2-A2 (13-17)
- EP5-A2 (7-110)
- EP12-A2 (7-152)
- IEC 62304:2006 (13-32)
- ISO 14971:2007 (5-40)
- ISO 15223-1:2007 (5-73)

Other Standards:

- EN 61326-1
- EN61326-2-6
- EP17-A
- IEC 61010-1
- IEC 61010-2-081
- IEC 61010-2-101

L. Test Principle:

The Sofia Strep A FIA employs immunofluorescence technology that is used with the Sofia Analyzer to detect Group A Streptococcal antigen. The Sofia Strep A FIA involves the extraction of the antigenic components of the Group A Streptococcus (GAS) bacteria. The

patient’s swab specimen is placed in the Reagent Tube containing the Reagent Solution, during which time the bacterial antigens are extracted, making them more accessible to the specific antibodies. An aliquot of the extracted specimen is dispensed into the Cassette sample well. From the sample well, the specimen migrates through a test strip containing various unique chemical environments. If Group A Streptococcal antigens are present, they will be bound by antibodies coupled to fluorescent microparticles that migrate through the test strip. The fluorescent microparticles containing bound antigen will be captured by antibodies at a defined location on the test strip where they are detected by the Sofia Analyzer. If antigens are not present, the fluorescent microparticles will not be trapped by the capture antibodies nor detected by the Analyzer.

Depending upon the user’s choice, the Cassette, now containing the specimen, is either placed directly inside the Sofia Analyzer for automatically timed development (Walk Away Mode) or placed on the counter or bench top for a manually timed development and then placed into the Sofia Analyzer (Read Now Mode).

The Sofia Analyzer scans, measures, and interprets the immune-fluorescent signal, using on-board method-specific algorithms. The Sofia Analyzer will then report the test results to the user (Positive, Negative, or Invalid) on its display screen and it can print out the results via an on-board printer or transmit the results via an LIS connection.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The reproducibility of the Sofia Strep A FIA was evaluated at three (3) different laboratories. Two (2) different operators at each site tested a series of coded, contrived samples, prepared in negative throat swab clinical matrix, ranging from low negative to moderate positive Group A Streptococcus. Reproducibility studies were done in the Read Now mode.

Spiked Throat Swab Panel Members

Low Negative	The low negative specimen consisted of the negative matrix containing no spiked bacteria.
High Negative	Analyte concentration below the LoD, such that results of repeated tests are negative approximately 95% of the time.
Low Positive	Analyte concentration at the LoD such that results of repeated tests are positive approximately 95% of the time
Moderate Positive	Analyte concentration three times the LoD such that the results of repeated tests should be positive 100% of the time for Strep A.

The inter-laboratory agreement for negative samples was 96.7-100% and 96.7-100% for positive samples. The intra-laboratory agreement for all samples ranged from 97.5-99.2%:

Sofia Strep A FIA Reproducibility Study Inter-laboratory Agreement

Site	Low Neg (no bacteria) (0 cfu/test)	High Negative (C ₅) (1.5x10 ³ cfu/test)	Low Positive (C ₉₅) (3.0x10 ³ cfu/test)	Mod. Positive (C _{3x}) (2.8x10 ⁴ cfu/test)
1	30/30	30/30	28/30	30/30
2	30/30	29/30	30/30	30/30
3	30/30	28/30	29/30	30/30
Total	90/90	87/90	87/90	90/90
% Overall Agreement (95% CI)	100% (90/90) (95.9 - 100%)	96.7% (87/90) (90.7 - 98.9%)	96.7% (87/90) (90.7 - 98.9%)	100% (90/90) (95.9 - 100%)

Sofia Strep A FIA Reproducibility Study Intra-laboratory Agreement

Site	Low Neg (no bacteria) (0 cfu/test)	High Negative (C ₅) (1.5x10 ³ cfu/test)	Low Positive (C ₉₅) (3.0x10 ³ cfu/test)	Mod. Positive (C _{3x}) (2.8x10 ⁴ cfu/test)	% Overall Agreement (95% CI)
1	30/30	30/30	28/30	30/30	98.3% (118/120) (94.1-99.5%)
2	30/30	29/30	30/30	30/30	99.2% (119/120) (95.4-99.9%)
3	30/30	28/30	29/30	30/30	97.5% (117/120) (92.9-99.1%)

The study further established the reliability of performance of the Positive and Negative Controls, for which 100% correct results were obtained (60/60) as shown below:

Positive and Negative Control Results

Site	Operator	Positive Control Passed	Negative Control Passed
1	1	5/5	5/5
	2	5/5	5/5
	Total	10/10	10/10
2	1	5/5	5/5
	2	5/5	5/5

	Total	10/10	10/10
3	1	5/5	5/5
	2	5/5	5/5
	Total	10/10	10/10
Total ALL:		30/30	30/30

The reproducibility panel contained low negative, high negative, low positive and moderate positive samples for Strep A. The operators obtained accurate results 98.3% (354/360) of the time.

These results demonstrate that clinical laboratory personnel from different sites and with varying levels of experience can accurately follow the Package Insert and Quick Reference Instructions, and perform the FIA correctly. No significant differences in results were observed within-run (replicates), between-runs (10 runs on at least five different assay days), or between-sites.

Reproducibility studies are acceptable.

b. Linearity/assay reportable range:

Not Applicable

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

Culture Sample Stability

A stability study was conducted to determine the impact of different storage and/or shipping conditions on the culture viability of swabs spiked with Group A Streptococcus bacteria; as well as to evaluate the impact of the same conditions on the recovery or sustenance of antigenicity. For this study, Streptococcus pyogenes strain at a concentration approximating three times its pre-determined LoD or 5.58 x 10⁴ CFU/test were selected. Swabs seeded with this amount of Streptococcus pyogenes were stored at different temperatures, from zero hours to up to more than 50 hours in some cases. At the end of each storage condition, all swabs were cultured on agar plates and subsequently interpreted for bacterial growth by examining the quadrants of each culture plate for growth. In addition, after streaking the blood agar plates, the same swabs were tested in the Sofia Strep A FIA per the draft package insert. Stability studies were done in the Read Now mode.

This study demonstrated that storage of swabs spiked with even low concentrations of bacteria (approximately 3 x LoD) can be stored, and by inference transported, at 2 to 8°C without a negative impact on recoverability in culture—even for storage periods extending up to 56 hours. The culture results, though not easily quantified, suggest that storage and transport at these temperatures is preferred over that at laboratory ambient temperature, although the differences are subtle. All samples stored at all of

the temperatures examined gave 100% accurate results in the Sofia Strep A FIA, supporting observations in other studies and attesting to the fact that the antigens measured in this assay are sufficiently stable to ensure detection. Freezing at -20°C or at -70°C, followed by culture and Sofia testing gave good results for both culture and rapid antigen detection.

Kit Stability Dating

A combination of real-time and accelerated data was used to establish the current kit dating of shelf life dating in excess of 24 months when the product is stored at 25°C.

Calibration Cassette Stability Dating

A combination of real-time and accelerated data was used to establish the current kit dating of shelf life dating in excess of 33 months when the product is stored at 25°C in a sealed protective foil pouch.

d. *Detection limit:*

The limit of detection (LoD) for the Sofia Strep A FIA was determined using three strains of Group A Streptococcus pyogenes. The LoD ranged from $9 \times 10^3 - 2 \times 10^4$ colony forming units (cfu)/test (see below).

Sofia Strep A FIA Limits of Detection for Three *Streptococcus pyogenes* Strains

Strain	Minimum Detectable Level*
Bruno [CIP 104226]	1.86×10^4 cfu/test
CDC-SS-1402	9.24×10^3 cfu/test
CDC-SS-1460	2.34×10^4 cfu/test

cfu/test = colony forming units/test

*The levels of bacteria were determined by limiting dilution, bacterial culture, and colony counting to give cfu/test.

Limit of Detection studies are acceptable.

e. *Analytical specificity:*

Analytical Reactivity: Analytical reactivity for the Sofia Strep A FIA was determined using 15 strains of Streptococcus pyogenes. Each strain listed below produced positive results in the assay.

Analytical Reactivity

<i>Streptococcus pyogenes</i> Strain	Test Quantity*
Strain #1 (ATCC 19615)	6.5×10^4 cfu/test
Strain #2 (ATCC 700942)	7.4×10^4 cfu/test

<i>Streptococcus pyogenes</i> Strain	Test Quantity*
Strain #3 (ATCC 700952)	8.3x10 ⁴ cfu/test
Strain #4 (Field Clinical Isolate)	3.1x10 ⁴ cfu/test
Strain #5 (Field Clinical Isolate)	7.6x10 ⁴ cfu/test
Strain #6 (Field Clinical Isolate)	7.1x10 ⁵ cfu/test
Strain #7 (Field Clinical Isolate)	6.3x10 ⁴ cfu/test
Strain #8 (Field Clinical Isolate)	6.3x10 ⁴ cfu/test
Strain #9 (Field Clinical Isolate)	5.3x10 ⁴ cfu/test
Strain #10 (ATCC 700482)	6.5x10 ⁴ cfu/test
Strain #11 (ATCC BAA 1315)	7.2x10 ⁴ cfu/test
Strain #12 (ATCC 700459)	5.4x10 ⁴ cfu/test
Strain #13 (ATCC 12203)	6.9x10 ⁴ cfu/test
Strain #14 ATCC 700944)	5.3x10 ⁴ cfu/test
Strain #15 (Field Clinical Isolate)	7.0x10 ⁴ cfu/test

cfu/test = colony forming units/test

*The levels of bacteria were determined by limiting dilution, bacterial culture, and colony counting to give cfu/test.

Analytical Reactivity studies are acceptable.

Cross Reactivity

The cross reactivity of the Sofia Strep A FIA was evaluated with a total of 61 non-Group A Streptococcus bacterial and fungal microorganisms, and 26 viral isolates. None of the organisms or viruses listed below showed any sign of cross reactivity in the assay. When the same organisms were pre-mixed with Group A Strep and tested in the Sofia Strep A FIA, all results are positive also indicating that the potential cross-reactants did not interfere with the detection of Strep A.

Analytical Specificity and Cross Reactivity

Organism/Virus	Test Quantity*
<i>Arcanobacterium haemolyticum</i>	3x10 ⁵ cfu/test
<i>Bacteroides fragilis</i>	3x10 ⁷ cfu/test
<i>Bordetella pertussis</i>	3x10 ⁷ cfu/test
<i>Candida albicans</i>	3x10 ⁴ cfu/test
<i>Corynebacterium diphtheria</i>	3x10 ⁵ cfu/test
<i>Corynebacterium pseudodiphtheriticum</i>	3x10 ⁶ cfu/test
<i>Enterococcus faecalis</i>	3x10 ⁶ cfu/test
<i>Enterococcus faecium</i>	3x10 ⁶ cfu/test
<i>Escherichia coli</i>	1.5x10 ⁷ cfu/test
<i>Fusobacterium necrophorum</i>	3x10 ⁶ cfu/test

Organism/Virus	Test Quantity*
<i>Haemophilus influenzae</i>	3x10 ⁷ cfu/test
<i>Haemophilus parahaemolyticus</i>	3x10 ⁶ cfu/test
<i>Klebsiella pneumoniae</i>	3x10 ⁷ cfu/test
<i>Moraxella catarrhalis</i>	3x10 ⁶ cfu/test
<i>Neisseria lactamica</i>	3x10 ⁶ cfu/test
<i>Neisseria gonorrhoeae</i>	3x10 ⁶ cfu/test
<i>Neisseria meningitidis</i>	3x10 ⁶ cfu/test
<i>Neisseria sicca</i>	3x10 ⁷ cfu/test
<i>Neisseria subflava</i>	3x10 ⁷ cfu/test
<i>Proteus vulgaris</i>	3x10 ⁷ cfu/test
<i>Pseudomonas aeruginosa</i>	3x10 ⁶ cfu/test
<i>Serratia marcescens</i>	3x10 ⁷ cfu/test
<i>Staphylococcus aureus</i>	3x10 ⁶ cfu/test
<i>Staphylococcus epidermidis</i>	3x10 ⁶ cfu/test
<i>Staphylococcus haemolyticus</i>	3x10 ⁵ cfu/test
<i>Staphylococcus intermedius</i>	3x10 ⁵ cfu/test
<i>Staphylococcus saprophyticus</i>	3x10 ⁶ cfu/test
<i>Streptococcus anginosus</i>	3x10 ⁶ cfu/test
<i>Streptococcus gordonii</i>	3x10 ⁴ cfu/test
<i>Streptococcus mitis</i>	3x10 ⁴ cfu/test
<i>Streptococcus mutans</i>	3x10 ⁶ cfu/test
<i>Streptococcus oralis</i>	3x10 ⁶ cfu/test
<i>Streptococcus parasanguis</i>	3x10 ⁶ cfu/test
<i>Streptococcus pneumoniae</i>	3x10 ⁶ cfu/test
<i>Streptococcus salivarius</i>	3x10 ⁵ cfu/test
<i>Streptococcus sanguinis</i>	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group B strain #1	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group B strain #2	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group B strain #3	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group B strain #4	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group B strain #5	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group C strain #1	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group C strain #2	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group C strain #3	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group C strain #4	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group C strain #5	3x10 ⁵ cfu/test
<i>Streptococcus sp.</i> Group D strain #1	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group D strain #2	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group D strain #3	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group D strain #4	3x10 ⁶ cfu/test

Organism/Virus	Test Quantity*
<i>Streptococcus sp.</i> Group D strain #5	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group F strain #1	3x10 ⁵ cfu/test
<i>Streptococcus sp.</i> Group F strain #2	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group F strain #3	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group F strain #4	3x10 ⁵ cfu/test
<i>Streptococcus sp.</i> Group F strain #5	3x10 ⁵ cfu/test
<i>Streptococcus sp.</i> Group G strain #1	3x10 ⁷ cfu/test
<i>Streptococcus sp.</i> Group G strain #2	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group G strain #3	3x10 ⁶ cfu/test
<i>Streptococcus sp.</i> Group G strain #4	3x10 ⁶ cfu/test
<i>Yersinia enterocolitica</i>	3x10 ⁶ cfu/test
Adenovirus Type 1	3x10 ¹¹ TCID ₅₀ /test
Adenovirus Type 3	3x10 ⁵ TCID ₅₀ /test
Adenovirus Type 4	1.5x10 ² TCID ₅₀ /test
Adenovirus Type 5	3x10 ⁵ TCID ₅₀ /test
Adenovirus Type 11	3x10 ⁴ TCID ₅₀ /test
Coronavirus 229E	3x10 ⁴ TCID ₅₀ /test
Coronavirus OC43	3x10 ⁴ TCID ₅₀ /test
Coxsackievirus B5 (Faulkner)	3x10 ⁶ TCID ₅₀ /test
Cytomegalovirus	3x10 ³ TCID ₅₀ /test
Echovirus Type 3	1.5x10 ⁴ TCID ₅₀ /test
Epstein Barr virus	3x10 ⁷ TCID ₅₀ /test
Herpes Simplex virus 1	3x10 ⁴ TCID ₅₀ /test
Herpes Simplex virus 2	3x10 ⁴ TCID ₅₀ /test
Influenza A H1N1	3x10 ⁴ TCID ₅₀ /test
Influenza A H3N2	3x10 ⁴ TCID ₅₀ /test
Influenza B Hong Kong	3x10 ⁴ TCID ₅₀ /test
Influenza B Panama	1.5x10 ⁴ TCID ₅₀ /test
Influenza C Taylor	1.5x10 ⁴ TCID ₅₀ /test
Measles (Edmonston)	3x10 ⁴ TCID ₅₀ /test
Mumps (Enders)	3x10 ³ TCID ₅₀ /test
Parainfluenza virus 1	3x10 ⁴ TCID ₅₀ /test
Parainfluenza virus 2	1.2 TCID ₅₀ /test
Parainfluenza virus 3	3x10 ⁶ TCID ₅₀ /test
Parainfluenza virus 4A	3x10 ⁴ TCID ₅₀ /test
Rhinovirus Type 15	3x10 ⁴ TCID ₅₀ /test
Rhinovirus Type 1B	3x10 ³ TCID ₅₀ /test

cfu/test = colony forming units/test TCID₅₀/test = 50% tissue culture infectious dose

*The levels of bacteria were determined by limiting dilution, bacterial culture, and colony counting to give cfu/test. Virus concentrations were determined by standard

virology methods, Reed-Muench.

Cross-reactivity studies are acceptable.

Interfering Substances

Several over-the-counter (OTC) products, whole blood, and blood agar were evaluated and did not interfere with the Sofia Strep A FIA at the levels tested below.

Non-interfering Substances

Substance	Concentration
Crest Pro-Health Night Mint (Cetylpyridinium chloride)	25% v/v
Listerine Antiseptic (Eucalyptol, Menthol, Methyl salicylate, and Thymol)	25% v/v
Listerine Cool Mint (Eucalyptol, Menthol, Methyl salicylate, and Thymol)	25% v/v
Cepacol Dual Relief Spray (Benzocaine and Menthol)	25% v/v
Chloraseptic Max: Sore Throat Relief (Phenol and Glycerin)	25% v/v
Children's Dimetapp DM Cold & Cough Elixir (Brompheniramine maleate, Dextromethorphan HBr, and Phenylephrine HCl)	25% v/v
Children's Wal-Tap Elixir Cold & Allergy (Brompheniramine maleate and Phenylephrine HCl)	25% v/v
Children's Wal-Tap DM Elixir Cold & Cough (Brompheniramine maleate, Dextromethorphan HBr, and Phenylephrine HCl)	25% v/v
Rite Aid Tussin CF (Dextromethorphan HBr, Guaifenesin, and Phenylephrine HCl)	25% v/v
Robitussin Cough & Cold-CF Max (Dextromethorphan HBr, Guaifenesin, and Phenylephrine HCl)	25% v/v
Robitussin Nighttime Cough, Cold, & Flu (Acetaminophen, Diphenhydramine HCl, and Phenylephrine HCl)	25% v/v
Cepacol Sore Throat: Cherry Flavor (Benzocaine and Menthol)	25% w/v
Halls Cherry Mentholiptus (Menthol)	25% w/v
Halls Mentholiptus (Menthol)	25% w/v
Ricola Mountain Herb Throat Drops-Sugar Free (Menthol)	25% w/v
Sucrets Complete-Vapor Cherry (Dyclonine Hydrochloride and Menthol)	25% w/v
Sucrets Complete-Cool Citrus (Dyclonine Hydrochloride and Menthol)	25% w/v
Chloraseptic Throat Drops-Cherry (Phenol and Glycerin)	25% w/v
BreathSavers 3 Hour Mint-Spearmint (Cetylpyridinium chloride)	25% w/v
Tic Tac Freshmints (Eucalyptol, Menthol, Methylsalicylate, and Thymol)	25% w/v
Whole Blood	5% v/v
Sheep Blood Agar (5% Sheep Blood)	2.16 mg/mL
Horse Blood Agar (5% Horse Blood)	1.67 mg/mL

f. Assay cut-off:

A positive result for the analyte is determined by detection and analysis of the fluorescent signal at the test and reference lines, which are processed by an assay-specific algorithm. The algorithm employs a smoothing algorithm to the data, identifies peak maxima, minima and width, then calculates the RFU value based on peak height for the Strep A test line. When the test line value is $\geq 2,102$ RFU, the test result is positive; when $\leq 2,102$ RFU, the test result is negative. The LoB is 2,102 RFU. The procedural control zone cutoff for a valid versus invalid result is 9,500 RFU. If controls fail at any point, the result is invalid and an error code is presented.

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 Sofia Strep A FIA was compared to standard bacterial culture and identification in a multi-center clinical field study. This study was conducted by health care personnel during 2011 and 2012 at eight (8) distinct sites in various geographical regions within the United States and two (2) sites in Australia. In this multi-center, point-of-care (POC) field trial, two (2) throat swabs were collected from 736 patients with symptoms suggestive of bacterial pharyngitis.

One throat swab was transported on cold ice packs to a central Reference Laboratory, streaked on a sheep blood agar plate (SBA) and cultured for up to 48 hours. Immediately after streaking, this same swab was tested in the rapid Sofia Strep A FIA. The performance of the Sofia Strep A FIA was determined by comparison of the rapid test result to the corresponding culture result.

The results from these analyses are presented below:

Sofia Strep A FIA Results: Read Now + Walk Away

	Culture			
	Pos*	Neg	Total:	
Sofia Pos	116	24	140	Sens. = 90.6% (116/128) (95% CI: 84.3 - 94.6%)
Sofia Neg	12	584	596	Spec. = 96.1% (584/608) (95% CI: 94.2 - 97.3%)
Total:	128	608	736	PPV = 82.9% (116/140) NPV = 98.0% (584/596) Prev. = 17.4% (128/736)

Sofia Strep A FIA Results: Read Now Mode

	Culture			
	Pos	Neg	Total:	
Sofia Pos	100	23	123	Sens. = 89.3% (100/112) (95% CI: 82.2 - 93.8%)
Sofia Neg	12	549	561	Spec. = 96.0% (549/572) (95% CI: 94.0 - 97.3%)
Total:	112	572	684	PPV = 81.3% (100/123) NPV = 97.9% (549/561) Prev. = 16.4% (112/684)

Sofia Strep A FIA Results: Walk Away Mode

	Culture			
	Pos	Neg	Total:	
Sofia Pos	16	1	17	Sens. = 100% (16/16) (95% CI: 80.6 - 100%)
Sofia Neg	0	35	35	Spec. = 97.2% (35/36) (95% CI: 85.8 - 99.5%)
Total:	16	36	52	PPV = 94.1% (16/17) NPV = 100% (35/35) Prev. = 30.8% (16/52)

b. *Clinical specificity:*

See 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:

Group A Streptococcus bacteria are responsible for about 19% of all upper respiratory tract infections (Lauer B.A., Reller L.D., and Mirrett S., Journal of Clinical Microbiology, 17:338-340, 1983). Infection is most prevalent in winter and early spring, with most cases arising in patients living in highly populated areas. Consistent with these figures, in the multi-center clinical study conducted by Quidel during 2011 and 2012, 17.4% (128/736) of the patients presenting with pharyngitis were found to be culture positive for Strep A. Nearly half of these subjects, 46%, were female. The subjects' ages ranged from 3 to 72 years and eighty-eight percent (647/736) were children (3 to 17 years of age).

N. Instrument Name:

Sophia™ Analyzer

O. System Descriptions:

1. Modes of Operation:

The Sofia® Strep A FIA can be operated on the Sofia Analyzer in Walk Away Mode (for single use) and in a Read Now Mode (for batch testing in ≥ 1 minute increments), accommodating different workload operating environments. These are operator-selected modes that allow either the device or the operator to be responsible for the time the sample resides on the strip.

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:

Not Applicable

4. Specimen Sampling and Handling:

Specimen Handling:

The antigen extraction reagent is prepared, added to a tube (up to a predetermined volume line) before the specimen swab is added, agitated and incubated in the reagent. The swab is squeezed dry upon removal and 100 µl of sample is applied to the test strip using an included fixed-volume pipette. The specimen is allowed to sit in the cartridge at room temperature for 5 minutes either in the analyzer or on the bench dependent on the mode of operation selected. User ID and patient ID is then entered either manually or using the external barcode scanner. In Read Now Mode, the cartridge is then inserted and the user presses start. Test results are provided within one minute.

5. Calibration:

The sponsor recommends that the Calibration Check Procedure should be performed every thirty (30) days. The Sofia Analyzer is set to remind the user to complete the Calibration Check Procedure.

The Calibration Check is a required function that checks the Sofia Analyzer optics and calculation systems using a specific Calibration Cassette. This Calibration Cassette is shipped with the Sofia Installation Pack. The Calibration Cassette should be stored in the provided storage pouch between uses to protect it from exposure to light. The Sofia Analyzer User Manual details the Calibration Check Procedure.

6. Quality Control:

QC is performed every 30 days. There are three types of Quality Control for the Sofia Analyzer and Strep A FIA: Sofia Analyzer Calibration Check Procedure (See O 5 above), built-in procedural control features, and External Controls.

External Controls: Each 25-test kit will contain one Positive and one Negative Control swab—each provided separately in a foil pouch with desiccant. The Positive Control swab is spiked with Group A Streptococcus pyogenes cells. The Negative Control swab is spiked with Group C Streptococcus antigens.

The sponsor recommends that External Positive and Negative Controls be run:

- Once for each untrained operator to the Analyzer, and to the specific type of test.
- Once for each new shipment of kits provided that each different lot received in the shipment is tested.
- In accordance with local, state and federal regulations or accreditation requirements.

In-Test Assay Controls: The test strip also has several other chemically built-in control features to ensure that each test run is performed properly. These include the Negative Control (NC) line and the Procedural Control zone.

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

Not Applicable

Q. Proposed Labeling:

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

R. Conclusion:

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