CLIA Waiver by Application

Approval Determination Decision Summary

A. Document Number

CW170009

B. Parent Document Number

K171976

C. Purpose of the Submission

This submission is a Dual 510(k) and CLIA Waiver by Application (Dual Submission) tracked as K171976 and CW170009. CW170009 was submitted for CLIA Waiver of the Sofia Strep A+ FIA with the Sofia 2 analyzer.

The Sofia Strep A+ FIA test for use with the Sofia analyzer in Walk Away Mode has been cleared under K141775 and CLIA waived under CW140010. A second operational mode for the Sofia analyzer (Read Now) was approved in the CLIA waived setting under CW160013. The sponsor developed another analyzer called Sofia 2 that includes modifications to the optical detection system from the original Sofia analyzer. The data supporting equivalence of the Sofia Strep A+ FIA performance when used with the Sofia and Sofia 2 analyzers (both Read Now and Walk Away Modes) were submitted under the K171976.

D. Measurand (analyte)

Group A β-hemolytic *Streptococcus* (GAS; *Streptococcus pyogenes*) antigens

E. Sample Type

Direct throat swabs

F. Type of Test

Qualitative Immunoassay

G. Applicant

Quidel Corporation

H. Proprietary and Established Names

Sofia Strep A+ FIA and Sofia 2 analyzer

I. Test System Description

1. Overview

The Sofia Strep A+ FIA is a cassette-based lateral flow immunofluorescence assay for use with the Sofia and Sofia 2 analyzers. To initiate the test, a throat swab specimen is expressed in Reagent Solution to extract the target antigens. The extracted sample is then applied to the sample pad of the lateral flow cassette, which moves by capillary action through the test strip. If Group A Streptococcal antigens are present, they are captured on the surface of fluorescent microbeads that are coated with antibodies to *Streptococcus pyogenes* antigens. Microbeads that carry bound antigen are then captured by secondary antibodies at a specific location on the test strip (Strep A Line) where they are detected by the analyzer. If no Group A Streptococcal antigens are present in the sample, the microbeads are not captured and are not detected. A procedural control is built into the assay to determine whether adequate flow of the specimen has occurred. Results are interpreted automatically. No colored test or procedural lines are evident to the user in the test window of the cassette, thus eliminating the potential for manual, subjective interpretation of results.

2. Results Interpretation

A positive result for the analyte is determined by detection of the fluorescent signal at the Test Line location on the test strip and interpretation by a specific algorithm in the Sofia 2 analyzer. There are three possible test results for the Sofia Strep A+ FIA as shown in Table 1 below. If an invalid test result is reported, the Sofia Strep A+ FIA should be repeated with a new patient sample and a new test cassette. The results are displayed on the instrument screen and can also be printed on an integrated printer if this option is selected.

Table 1. Result interpretation for Sofia Strep A+ FIA

Analyzer Display	Interpretation
Strep A: Positive Procedural Control: Valid	Positive Test for Strep A (Strep A antigen present)
Strep A: Negative Procedural Control: Valid	Negative Test for Strep A (no antigen detected)
Strep A: Invalid Procedural Control: Invalid	Result Invalid (repeat the test)

Note: The Sofia and Sofia 2 analyzers may be set to one of two operating modes: Walk Away or Read Now. Time to results for the Sofia and Sofia 2 analyzers are described below.

- In Walk Away Mode, the user inserts the test cassette into the analyzer immediately following addition of the specimen to the Sofia Strep A+ FIA sample port. The analyzer automatically monitors test development and provides positive or negative test results after 5 minutes.

- In the Read Now Mode, the user incubates the test cassette on the benchtop for 5 minutes before inserting the cassette into the analyzer. Positive and negative test results are displayed within 1 minute.

The reagents and materials supplied with the 25-Test kit include:

- 25 individually Packaged Test Cassettes
- 25 Reagent Tubes with lyophilized buffer with detergents and reducing agents
- 25 Reagent Solution Bottles
- 25 Sterile Rayon Throat Swabs
- 25 small (120 µl), clear fixed volume pipettes
- 1 Positive Control Swab (coated with heat-inactivated, non-infectious GAS)
- 1 Negative Control Swab (coated with heat-inactivated, non-infectious Group C *Streptococcus*)
- Package Insert
- QC card
- Quick Reference Instructions (QRI)
- Printer Paper

A calibration cassette for the Sofia 2 analyzer is provided separately. No changes were made to test components in the Sofia Strep A+ kits or calibration cassette.

3. Description of Changes

The primary difference between the original Sofia analyzer and the Sofia 2 analyzer is the design of the optical detection system. The original Sofia uses a motorized optics unit to collect fluorescent signal data as it performs a series of scans across the longitudinal axis of the test strip whereas the Sofia 2 captures a still image of the entire test strip window using a CMOS camera. To emulate Sofia, the Sofia 2 analyzer converts pixels captured by the CMOS camera to digital data, which is then analyzed in an equivalent manner to that used by the Sofia to yield qualitative test results. Other minor adjustments to the Sofia 2 analyzer affect mainly the user interface and include the addition of a touchscreen display and an integrated barcode scanner for sample identification. Both the original Sofia and the Sofia 2 instruments utilize the same fail-safe and failure alert mechanisms, the same calibration and assay-specific cartridges, and the same ultraviolet light-emitting diodes (UV LEDs) to excite the fluorophore. The test procedure for performing the assay remains unchanged. The test cassettes used with both instruments are identical.

The Sofia 2 has a USB port for connection of an external printer provided by Quidel which allows the user to print patient test results and quality control testing results, if desired.

The built in internal barcode scanner in the Sofia 2 enables the user to enter data such as user ID numbers, patient ID numbers, and order numbers without having to manually enter the information on the Sofia 2 touchscreen.

J. Demonstrating "Simple"

The Sofia Strep A+ FIA with the Sofia 2 analyzer was designed to be simple and easy to use by incorporating the following features:

- The test uses direct unprocessed throat swab specimens.
- The test requires basic, non-technique-dependent specimen and reagent handling to obtain accurate test results.
- The provided reagents are premeasured and provided in single-use vials.
- Fixed volume pipettes are provided for sample addition.
- The test cassettes are unitized and contain all the reagents required for analysis.
- The test does not require any operator intervention during the analysis step.
- The test cassettes contain a barcode to help in determining the correct orientation for running samples.
- The Sofia 2 analyzer performs automated analysis of test results and eliminates subjectivity associated with visual reading of results by the end-user.
- The results (positive, negative or invalid) can be viewed on a touchscreen; there is no interpretation required by the end-user.
- The Sofia 2 touchscreen is designed for ease of use and features a color display that facilitates easy-to-read messages.
- Error messages are unambiguous and include easy-to-interpret solutions.
- No complex troubleshooting or interpretation of error codes are required to operate the Sofia 2 analyzer.
- General cleaning activities for the user include changing the battery and cleaning the external surfaces and Cassette drawer.
- Calibration, which is required every 30 days, is easily performed with a calibration cassette.
- There are no serviceable parts, and the instrument is to be returned to Quidel if maintenance is required.
- The test procedure is written at a 7^{th} grade comprehension level.
- An optional printer is available.

K. Demonstrating "Insignificant Risk of an Erroneous Results"- Failure Alerts and Fail-safe Mechanisms

1. Risk Assessment

   A comprehensive risk analysis of the Sofia Strep A+ FIA with the Sofia 2 analyzer has been conducted in accordance with ISO 14971. The sponsor utilized the Device Hazard Analysis and the Failure Mode Effects Analysis (FMEA) methods to assess the risks of failure that may occur during use or misuse of the device. The FMEA identified potential failure modes and contained a list of the effect(s) of various failure events, potential causes of hazards, and built-in design controls. An evaluation of the severity of hazards, frequency of occurrence, and ability to detect failures for the instrument system was also provided in the context of operator errors (human factors), sample and device handling/storage, and environmental factors.

Potential sources of errors that could adversely affect system performance were identified and mitigated by system design, as well as additional cautions in the labeling. The identified risks that could result in erroneous test results were evaluated in flex studies that stressed the functional limits of the test system (see below).

The sponsor provided detailed software validation and verification documentation, including requirements related to assay performance when using the Sofia 2 analyzer. The instrument software was reviewed under the parent 510(k) submission (K171976).

2. Fail-Safe and Failure Alert Mechanisms

The Sofia Strep A+ FIA with the Sofia 2 analyzer was designed to include numerous features and fail-safe mechanisms built into the system to prevent erroneous results.

a. Design Features

- Each test cassette is packaged in a separate foil pouch to maintain the integrity of the reagents.
- Cassette Drawer and Presence Sensor are designed to prevent the test from proceeding when the drawer is not closed or when the test cassette is not present. If the cassette drawer is opened during a test, the analysis will not continue and an invalid result will be reported.
- An Internal barcode reader is designed to read the assay cassette barcode:
  - The instrument will not proceed if the cassette is not in the correct orientation (or is absent) and the barcode cannot be read.
  - The instrument will not proceed if the assay selected does not match the test type of the cartridge.
  - The instrument will not proceed if the assay cartridge has previously been used.
  - The instrument will not proceed if the assay cartridge is expired.
- The analyzer touchscreen is designed to facilitate easy operation with clearly labeled icons and action buttons.
- Test results are interpreted automatically and a direct readout is provided on the analyzer screen.

b. Fail-Safe Features

- Temperature sensor is designed to prevent the test from proceeding when the internal temperature of the analyzer is less than 15°C or greater than 35°C.
- Calibration is required every 30 days to prevent signal drift and the instrument will not proceed until the calibration status is updated. The analyzer reminds the user to check the calibration status of the instrument after 30 days from last calibration. The calibration process takes less than two minutes and is performed with a provided calibration cassette. If the calibration fails, the system goes into an error mode and a message is displayed to contact Quidel Technical Support.
- Power-on Self-Test (POST) is initiated each time the instrument is started and it checks for the integrity of the optics, the ambient temperature, the clock

functionality, the integrity of the memory and the functionality of the electronic sensors. All measurements must be within predetermined specifications; otherwise the instrument will not proceed.

- In-test Strip Controls aid in detecting procedural errors or reagent failure. The Sofia 2 recognizes when the appropriate signal is not generated, either due to a manufacturing error or a procedural error, returning an invalid result.
  - The Procedural Control Zone is designed to control for the flow of reagents and must produce a signal within the predetermined specifications, otherwise the test will be reported as *"invalid."*
  - The Reference Line is used by the Sofia 2 to orient the cassette and locate the various regions on the test strip that will be imaged and interrogated for analysis.
- External Control Swabs—one Positive Control Swab (Group A *Streptococcus pyogenes*) and one Negative Control Swab (Group C *Streptococcus*)—are included in each reagent kit. Each control is processed using a separate test cassette. Both control swabs are ready to use and are tested using the same procedure used for patient samples. These controls monitor the entire assay and serve to detect product defects or reagent deterioration between the manufacturer's lot release date and the date of use. The controls also monitor the operator's use of the test and detect any errors in the procedure. The manufacturer-recommended frequency of running the controls is: with each new shipment, each new kit lot, and with each untrained operator, or as deemed necessary by internal quality control procedures.
- Additional checks in the system are used to ensure optimal performance of the analyzer. On-going internal performance monitoring will indicate when performance degradation is occurring. If this observation is made, the user can contact Quidel's Technical Support, in which case, the company will either repair the instrument electronics or replace the unit.
  - Condensation Check—This function is performed on the white light image. An arrow, printed on the cassette, is used as a feature to measure sharpness. When an un-sharp arrow indicating a (possible) presence of condensation on the camera lens is detected, the test will be invalid.
  - Dark Image Check—This function is used during each measurement cycle and is designed to detect leakage of ambient light which, if detected, will generate an internal error and will not allow the test to proceed.
- The Sofia 2 analyzer has enhanced connectivity compared to Sofia, which allows for transmitting and receiving information to/from an LIS or other external information systems.

c. Lockout Features and Alert Messages

The Sofia 2 analyzer has numerous built-in lockout features to minimize the potential for erroneous results, including the following:

- The analyzer calibration must be performed every 30 days. The instrument will not proceed until the calibration status is updated, preventing optics drift over time.

- The analyzer will not proceed when the test cassette is expired; an error message is generated.
- The analyzer will not proceed when the drawer is open.
- The analyzer must scan a valid barcode on the cassette, otherwise an error message will alert the user that the barcode could not be read; the testing will not proceed.

The functionality of Fail-Safe mechanisms built into the software of the Sofia 2 analyzer was demonstrated in studies conducted using the Sofia Strep A+ FIA cassettes and the Sofia 2 analyzer. A more detailed list of Fail-Safe mechanisms for the Sofia 2 analyzer has been described previously in CW160016 and CW170001.

3. Flex Studies

The operational limits of the device were evaluated in a series of experiments simulating conditions of use outside of the intended use environment or instances of user errors. The flex studies with the Sofia 2 analyzer were limited in scope because: 1) the performance of the Sofia Strep A+ FIA with the Sofia analyzer was previously established in K141775, CW140010, and CW160013 and 2) the Sofia 2 analyzer was previously cleared under K162911 with the Sofia RSV FIA test. The studies described below are used to support migration of the Sofia Strep A+ FIA from the Sofia analyzer to the Sofia 2 analyzer. A Calibration Check of each Sofia 2 analyzer was performed prior to all testing and the results were recorded. External Positive and Negative Controls were run each day of testing on analyzers with the specified test mode.

Table 2. Flex Studies to Support CLIA Waiver Application

• Extreme Temperature and Humidity Flex Study
• Vibration Flex Study
• Environmental Light Flex Study
• Benchtop Leveling Flex Study
• Cassette Movement Flex Study
• External Controls Verification
• Sample Volume Flex Study
• Cassette Drop Flex Study
• Assay Development Time Flex Study

The effect of the following conditions on the performance of the assay was evaluated:

a. Operational Environment

(i) Temperature and Humidity

When the Sofia 2 analyzer is outside of its internal temperature range, an error message stating *"Temperature is out of range"* will appear and testing cannot be conducted until the Sofia 2 analyzer is back within its temperature range (15°C to 34.5°C). Therefore, a study was conducted to evaluate the effect of extreme

temperature and humidity on the Sofia Strep A+ FIA and Sofia 2 analyzer. Temperatures of 4°C and 40°C with up to 90% relative humidity (RH) were tested. Assay cassettes and reagents were equilibrated to the temperature and humidity conditions for 30 minutes prior to testing. The ambient temperature for the testing day was listed as 22.8°C. Table 3 shows the four different simulated environments tested and compared to conditions per the standard operating procedure (SOP).

Table 3. Extreme Temperature and Humidity Test Conditions

Condition	Instrument Condition	Assay Condition (cassette, reagent, buffer, sample)
SOP	Ambient	Ambient
1	Ambient	40°C/90% or higher humidity (RH)
2	40°C/90% or higher humidity (RH)	40°C/90% or higher humidity (RH)
3	Ambient	4°C/Ambient humidity
4	4°C/Ambient humidity*	4°C/Ambient humidity*

**Note: Relative humidity in a refrigerated chamber.*

Test cassettes were run in replicates of five using Contrived Negative Matrix as the negative samples and Strep A positive samples at 2-3X LoD. A total of 30 µl of the diluted Strep A positive sample was spiked onto a single Rayon swab for the positive swab and 30 µl of the Contrived Negative Matrix for the negative swab. The testing was conducted in Read Now Mode according to the Package Insert of the Sofia Strep A+ FIA.

The ambient laboratory (SOP) condition and condition 1 (instrument at ambient temperature and assay reagents at 40°C/90% humidity) yielded expected positive or negative results. Conditions 2 and 4 produced no results due to the Sofia 2's internal temperature parameters—Sofia 2 analyzers were locked out when the instrument was not within the internal temperature range. Condition 3 produced false negative and invalid results. The risk of erroneous results under the circumstances of exposing the test cards to extremes of operating conditions is minimized by the packaging of the units in individual air-tight foil pouches and specifying temperature conditions for the test run. Additionally, caution statements are included in the test procedure instructing the user to leave the test card sealed in the pouch until just prior to testing and having test materials and samples at room temperature before beginning a test.

(ii) Vibration Flex Study

The purpose of this study was to evaluate the effect of vibrations produced by nearby laboratory equipment on the performance of the Sofia Strep A+ FIA with Sofia 2. Five (5) Sofia 2 analyzers were used in the study. Samples were prepared as described in the Temperature and Humidity Study *3a(i)* above. The prepared samples were then run on Sofia 2 in a location in close proximity to a centrifuge

running at 10,000 rpm. Testing was conducted in Walk Away Mode. No failure modes were found in the study, and all testing conditions yielded expected results. Vibrations coming from a centrifuge within the ranges tested had no impact on the performance of the Sofia Strep A+ FIA with Sofia 2.

(iii) Environmental Light Flex Study

The purpose of this study was to document the effect of environmental light on performance of the Sofia Strep A+ FIA prior to scanning in a Sofia 2 analyzer.

- The environmental conditions in the study included a procedure where the cassette and analyzer were exposed to natural sunlight entering through a window during test preparation, incubation, and scanning. An additional test was conducted with just with the cassette exposed to natural sunlight during preparation and incubation. Test cassettes were then inserted into Sofia 2 analyzers in Read Now Mode. Exposure to environmental sunlight was enough to heat the Sofia 2 analyzers past the maximum allowable temperature of 34.5°C. As a consequence, no testing could be conducted with the Sofia 2 analyzers because of the temperature lockout function (internal temperature specifications are 15°C to 34.5°C).

- In the study where only the test cassettes were exposed to direct environmental sunlight and the Sofia 2 analyzers left under ambient laboratory conditions, all tests gave the expected results.

This study verified that exposure to direct sunlight is effectively controlled by the analyzer and does not affect the performance of the Sofia Strep A+ FIA with Sofia 2 analyzer. Although no erroneous results were generated, a warning against operating the Sofia 2 analyzer in direct sunlight is included in the Sofia 2 user manual.

(iv) Benchtop Leveling Flex Study

The purpose of this study was to evaluate the effect of non-leveled benchtop or work surface on the test performance of the Sofia Strep A+ FIA with the Sofia 2 analyzer. Cassettes were prepared, loaded with sample, and run in the analyzer at two (2) longitudinal angles (15 °fore and aft), as well as two (2) latitudinal angles (15° left and right), before comparing results to those obtained with the standard condition (SOP). Five (5) Sofia 2 analyzers were used in the study, and the testing was conducted in the Walk Away Mode. A minimum of five (5) separate replicates of each sample type (negative samples and Strep A positive samples at 2-3X LoD) were tested according to the Package Insert of the Sofia Strep A+ FIA. All angles tested produced the same results. A 15° angle, whether it be left, right, forward or backward, did not change the output for the Sofia Strep A+ FIA using Sofia 2 analyzers. This study verified the performance when changing the angle of the benchtop or work surface containing both Sofia 2 analyzer and Sofia Strep A+ FIA test cassette.

b. Operator Errors/Human Factors

(i) Cassette Movement Flex Study

The purpose of this study was to evaluate the effect of tilting the Sofia Strep A+ FIA test cassette to a vertical position for varying lengths of time (1, 2, and 3 minutes) during the incubation period. Five (5) Sofia 2 analyzers were used in the study, and testing was conducted in Read Now Mode. Five (5) separate replicates of each sample type (negative samples and Strep A positive samples at 2-3X LoD) were tested for each movement condition. The testing procedure was conducted according to the Package Insert of the Sofia Strep A+ FIA. All samples yielded the expected results for each condition tested.

(ii) External Controls Verification

The purpose of this study was to confirm the test performance of the External Positive and Negative Controls in the Sofia Strep A+ FIA kit on the Sofia 2 analyzer. Three (3) lots of the External Positive and Negative Controls were tested with two (2) different lots of Sofia Strep A+ FIA Cassettes on both Sofia and Sofia 2 analyzer platforms. The testing was conducted in Read Now Mode and Walk Away Mode for each Sofia platform. All the replicates (n=10) for each condition yielded expected results. This study confirmed that the External Positive and Negative Controls provided in the Sofia Strep A+ FIA kit can be used on Sofia 2 analyzer similar to the Sofia analyzer.

(iii) Sample Volume Flex Study

The purpose of this study was to evaluate the effect of varied sample volume on the performance of the Sofia Strep A+ FIA prior to scanning in the Sofia 2 analyzer. Five (5) Sofia 2 analyzers were used in the study, and testing was conducted in Read Now Mode. Five (5) separate replicates of each sample type (negative samples and Strep A positive samples at 2-3X LoD) were tested. All valid replicates yielded expected results with sample volumes of 60-160 µl. Two (2) invalid results were observed with a sample volume of 60 µl due to insufficient volume flowing through the test cassette. At sample volumes of 180, 200 and 240 µl, false negative results were observed due to flooding of the test cassette. The possibility of this error is minimized by the fixed volume pipette that is included with the kit. In addition, the test procedure includes a clear caution directing the operator to use the provided transfer pipette and not to pour the sample directly onto the sample pad.

(iv) Cassette Drop Flex Study

The study examined the effect of dropping test cassettes from various heights prior to use—unpouched cassettes dropped from 36 inches and pouched cassettes dropped from 8 feet. Five (5) Sofia 2 analyzers were used in the study, and testing was conducted in Read Now Mode. Five (5) separate replicates of each sample type (negative samples and Strep A positive samples at 2-3X LoD) were tested for each condition according to the Package Insert of the Sofia Strep A+ FIA. No visible damage was seen on any cassette under drop conditions. All cassettes tested yielded expected results with the negative swab (producing negative results) and the Strep A positive swab (producing positive results). In the package insert, it is advised that if the cassette looks visibly damaged, it should be replaced with a new test cassette.

(v) Assay Development Time Flex Study

The purpose of this study was to evaluate varied development time and result stability of the Sofia Strep A+ FIA with the Sofia 2 analyzer. The study was conducted in Read Now Mode with thirty (30) replicates each of spiked negative and Strep A positive (2-3X LoD) swabs. The following development times were evaluated: 3 minutes, 5 minutes, 8 minutes, 10 minutes, and 15 minutes using Sofia 2 analyzers. The Sofia Strep A+ FIA test cassettes were re-barcoded for scanning of the same Sofia Strep A+ FIA test cassette at multiple time-points on the same Sofia 2 analyzer. Five (5) Sofia 2 analyzers were used for each development time in this study. All valid replicates produced expected results for all testing conditions. Both positive and negative samples produced valid results for the 5-15 minute development time. Sofia Strep A+ FIA results were stable for up to ten (10) minutes after the designated development time of 5 minutes. Invalid results were reported for both positive and negative sample types at the three (3) minute development time.

Based on: 1) an assessment of the design features, 2) robustness of the assay system and device labeling submitted in K171976, and 3) data supported by previous 510(k) clearances and CLIA waiver approvals associated with the Sofia Strep A+ FIA test and/or Sofia 2 analyzer, all the hazards and sources of potentials errors have been mitigated to reasonably acceptable levels.

L. Demonstrating "Insignificant Risk of an Erroneous Result" - Accuracy

The Sofia Strep A+ FIA with the Sofia 2 analyzer was evaluated in a method comparison study to demonstrate comparable performance between the Sofia 2 and the Sofia analyzers (K171976). An additional field study was conducted at CLIA waived sites to demonstrate that untrained operators could obtain accurate results when testing weakly reactive samples using the Sofia Strep A+ FIA test with Sofia 2 analyzer.

1. Comparison of Sofia and Sofia 2 Analyzers

Similar performance of the Sofia Strep A+ FIA when used with either the Sofia or Sofia 2 analyzer was demonstrated in a study conducted in support of K171976. Briefly, the method comparison study was conducted at three clinical sites using a panel of known positive and negative clinical and contrived samples prepared in clinical negative matrix. One-hundred (100) Strep A positive and 100 Strep A negative samples were incorporated into each panel (tested positive or negative with the current FDA-cleared Sofia Strep A+ FIA on Sofia). According to the test protocol, positive panel members were prepared so that approximately 60% to 80% of the samples had Strep A levels close to the Sofia Strep A+ FIA cut-off, with approximately one-half around the LoD and the remainder as moderate positive samples. The remaining positive samples were evenly distributed across the range of the assay based on the signal-to-cutoff ratio (S/CO). Negative panel members were prepared so that approximately 30% to 40% were High Negatives. All samples were coded and used to prepare randomized panels, with an identical panel of specimens prepared for each of three sites. Each site received a set of two hundred (200) numbered tubes each containing 2 swabs, as well as Positive and Negative Control swabs. The study demonstrated that the Sofia Strep A+ FIA had comparable performance when used with Sofia and Sofia 2 analyzers (See Table 4 below).

Table 4. Method Comparison Study of GAS Results Between the Sofia and Sofia 2 Analyzers

	Sofia Positive	**Sofia Negative**	**Total**
Sofia 2 Positive	369	7	376
Sofia 2 Negative	5	219	224
Total	374	226	600
	PPA: 98.7% (369/374), 95%CI: (96.9%-99.4%) NPA: 96.9% (219/226), 95%CI: (93.7%-98.5%)		

Additional details of the comparison study may be found in the Decision Summary for K171976, which can be accessed from the 510(k) database.

Because the Sofia and Sofia 2 analyzers are similar in design and function, with limited changes to the user interface and minimal changes to the test procedure in the QRI, an additional comparison of the Sofia Strep A+ FIA test with the Sofia 2 vs. Sofia in the hands of untrained operators was not needed.

2. Performance with Analyte Concentrations Near the Assay Cut-off

A study designed to evaluate the ability of the intended untrained users to perform testing and obtain accurate results with samples at bacterial concentrations near the assay cut-off was conducted. A contrived negative matrix was prepared and portions of this were spiked with Strep A bacteria in order to prepare the following panel members for the study: Strep A negative sample (C_0) and weak Strep A positive samples (C_{95}). A total of nine operators across three sites performed testing with the Sofia Strep A+ FIA with the Sofia 2 analyzer. The protocol required all testing to be equally split between Walk Away Mode and Read Now Mode. Each site received a set of forty-eight (48) numbered tubes, which included a mix of twenty-four (24) negative and twenty-four (24) weak positive samples. A total of forty-eight (48) results per CLIA site were obtained, where a total of 144 samples were tested across the three (3) sites.

The operators were selected from among the staff of the healthcare providers enrolled in the study. The participating operators included nurses, phlebotomists, and clerical office staff. Information on the operators' current job title, education, laboratory experience and the number of years of relevant work experience was also provided. The education of the operators ranged from high school graduates to those with bachelor degrees. The operators at each site (3 per site) tested sixteen (16) coded samples for 10 days over an approximate two week period. All operators were untrained in laboratory procedures and qualified as intended operators encountered at CLIA waived sites. On the day of testing, each operator tested blinded swab samples at random from their designated sample swab panel using only the Quick Reference Instructions (QRI). The number of sample swabs tested each day was at the discretion of the test operator allowing the testing to be integrated into their normal work day. This practice simulated how testing may actually happen in the intended use environment. The results from this study are shown below in Table 5.

Table 5. Performance of the Sofia Strep A+ FIA with the Sofia 2 analyzer and Samples Near the Assay Cut-off: Percent Agreement with Expected Results

Percent Agreement with Expected Results					
Sample Type	**Site 1**	**Site 2**	**Site 3**	**Overall**	**95% CI**
Low Positive (C_{95})	100% (24/24)	100% (24/24)	100% (24/24)	100% (72/72)	93.9%- 100%
True Negative	100% (24/24)	100% (24/24)	100% (24/24)	100% (72/72)	93.9%- 100%

There were no significant differences in the observed reactivity of the device with weakly reactive samples between sites, between operators, or between the two operational modes. All negative samples yielded negative results. The study results demonstrated that untrained users were able to perform the test correctly, and the test provided the expected results for samples with bacterial concentrations near the assay cut-off. There was one (1) invalid test result that had to be repeated during this study.

Quick Reference Instructions (QRI)

The QRI for the use of the Sofia Strep A+ FIA with the Sofia 2 analyzer is written in simple language (at 7th grade reading level) and contains pictorial descriptions of the individual steps. The QRI has separate sections for Sofia and Sofia 2 analyzers for easy reference by the end-user. In addition to the test procedure for patient samples, the QRI includes a section on performing QC testing with external controls. The user is instructed to refer to the package insert for Warnings and Precautions, Specimen Collection and Handling, and Quality Control.

Operator Questionnaire Results

Upon completion of the contrived sample testing study, operators at each site were asked to complete a questionnaire to help assess whether participants understood how to use the Sofia Strep A + FIA with the Sofia 2 analyzer correctly. The questionnaire consisted of a series of questions pertaining to the ease of use of the test with answers rated on a scale from 1 to 5. Participants found the test to be easy to use and the instructions easy to understand; however, additional language was added to the package insert to ensure operators can run the external controls successfully.

M. Labeling for Waived Devices

The labeling consists of:

a. Package insert
b. QRI
c. Sofia 2 User Manual

The following elements are appropriately present:

- The QRI is written at no higher than a 7th grade reading level and, where appropriate, contain graphic representation of system components and procedure steps.
- The package insert and the QRI identify the test as CLIA waived, and the package insert contains a statement that a Certificate of Waiver is required to perform the test in a waived setting; information on how users can obtain a certificate is also provided.
- The package insert contains a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test [42 CFR 493.15(e)(1)].
- Instructions for QC are integrated with procedural instructions for performing the test in the package insert and the QRI.
- Appropriate cautions have been added to the package insert and QRI to ensure safe use of the product.
- The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

N. Conclusion

Quidel conducted an appropriate study evaluating the performance of the assay with contrived samples near the assay cut-off with untrained operators in CLIA waived healthcare settings. The sponsor also conducted appropriate flex studies to demonstrate that the test system is robust, including design and labeling mitigations, to minimize erroneous results.

FDA has evaluated the benefits and risks of using the Sofia Strep A+ FIA with the Sofia 2 analyzer in CLIA waived settings and concluded that the medical benefit/risk profile favors the decision to grant CLIA waiver for this test. As a general consideration, the benefits of rapid antigen-based Group A Strep detection tests include the following:

- Simplicity, allowing healthcare professionals not skilled in laboratory testing to perform the test with ease;
- Short time to results, leading to early diagnosis and treatment; and
- Widespread use of the tests allowing for prompt detection and better infection control.

The specific benefits of the Sofia Strep A+ FIA with the Sofia 2 analyzer in CLIA waived settings include the following:

- The test system includes a digital reader for result interpretation eliminating the subjectivity associated with the visual interpretation of results inherent in older rapid Strep A detection tests;
- The intended use of the test clearly states that negative test results should be confirmed by culture or an FDA-cleared molecular method, mitigating the risk of false negative results.
- The product labeling incorporates bold cautions in the written test procedure to safeguard against procedural errors.
- The test includes a built-in procedural control to further safeguard against procedural errors or reagent malfunction.

In summary, the Sofia Strep A+ FIA with the Sofia 2 analyzer presents low risk of erroneous results and is suitable for use in CLIA waived environments.

The submitted information in this CLIA waiver application supports a CLIA Waiver approval decision.