510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K162438

B. Purpose for Submission:

To demonstrate equivalent performance of the Sofia® Influenza A+B FIA on the Sofia and Sofia 2 analyzers using elements of an assay migration study approach.

C. Measurand:

Influenza A and B nucleoprotein antigens

D. Type of Test:

Qualitative immunofluorescence assay

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Sofia® Influenza A+B FIA on Sofia 2

G. Regulatory Information:

1. Regulation Section:

   21 CFR 866.3328, Influenza virus antigen detection test system

2. Classification:

   Class II

3. Product Code(s):

   PSZ- Devices detecting influenza A, B, and C virus antigens

4. Panel:

   Microbiology (83)

H. Intended Use:

1. Intended Use(s):

   The Sofia Influenza A+B FIA employs immunofluorescence to detect influenza A and influenza B viral nucleoprotein antigens in direct nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens and nasopharyngeal swab and nasopharyngeal aspirate/wash specimens in transport media 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 viral 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 patient management decisions. This test is intended for professional and laboratory use.

   The Sofia Influenza A+B FIA may be used with Sofia or Sofia 2.

   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.

   If infection with a novel influenza virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, samples should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture samples.

2. Indication(s) for Use:

   Same as intended use

3. Special Conditions for Use Statement(s):

   For prescription use only

4. Special Instrument Requirements:

   To be used only with Sofia or Sofia 2 analyzers

I. Device Description:

1. Overview

The Sofia Influenza A+B FIA is a rapid lateral flow immunoassay for the qualitative detection of influenza A and influenza B nucleoprotein in direct nasal swab (NS), nasopharyngeal swab (NP), and nasopharyngeal aspirate/wash (NA/W) specimens and NP and NA/W specimens in transport media collected from patients with signs and symptoms of respiratory infection. The Sofia Influenza A+B FIA components have not been modified; detailed description of the lateral flow device is available in submissions K153012 and K112177, describing the Sofia Influenza A+B FIA use with the original Sofia analyzer.

The purpose of this submission is to obtain 510(k) clearance for the Sofia Influenza A+B FIA for use with the newly developed Sofia 2 analyzer. The Sofia and Sofia 2 analyzers are similar in function and design. Both systems utilize the same fail-safes 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 primary difference between the original Sofia and Sofia 2 analyzer is the design of the optical detection system. Sofia uses a motorized optics unit to collect fluorescent signal data as it performs a series of scans across the longitudinal axis of the Sofia Influenza A+B FIA test strip, whereas Sofia 2 captures a still image of the entire test strip window using a complimentary color-oxide semiconductor (CMOS) camera. To emulate Sofia, the Sofia 2 analyzer converts pixels captured by the CMOS camera to fluorescent signal data, which is analyzed in an equivalent manner to Sofia to yield qualitative test results.

2. Quality Control

See decision summary for K112177.

3. Results Interpretation

There are five possible test results for the Sofia Influenza A+B FIA: influenza A and/or influenza B positive, influenza A and influenza B negative, or invalid. Influenza A and B dual positive result should be re-tested and repeated; dual positive result should be confirmed by virus culture or an FDA-cleared influenza A and B molecular assay. If an invalid test result is reported, the Sofia Influenza FIA should be repeated with a new patient sample and a new test cassette.

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 analyzer 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 Influenza A+B FIA sample port. The Sofia analyzer automatically times the test development and provides positive or negative test results after 15 minutes. The Sofia 2 analyzer scans the test cassette periodically during the test development time and displays a positive test result

between 3 and 15 minutes. If the test is negative, the result will be displayed after 15 minutes.

- In the Read Now Mode, the user incubates the test cassette on the benchtop for 15 minutes before inserting the cassette into the Sofia or Sofia 2 analyzer. Positive and negative test results are displayed within 1 minute.

J. Substantial Equivalence Information:

1. Predicate Device Name(s):

   Sofia Influenza A+B FIA on Sofia

2. Predicate 510(k) Number:

   K153012

3. Comparison with Predicate:

Table 1: Comparison with the Predicate Device

Similarities and Differences		
	Predicate Device	**Proposed Device**
Item	**Sofia Influenza A+B FIA on Sofia (K153012)**	**Sofia Influenza A+B FIA on Sofia 2 (K162438)**
Regulation	866.3328	866.3328
Product code	PSZ	PSZ
Device class	II	II
Technology principle of operation	Lateral flow immunoassay	Same
Assay targets	Influenza A and B nucleoprotein	Same
Assay results	Qualitative	Same
Intended Use	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 in fresh or transport media specimens 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	The Sofia Influenza A+B FIA employs immunofluorescence to detect influenza A and influenza B viral nucleoprotein antigens in direct nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens and nasopharyngeal swab and nasopharyngeal aspirate/wash specimens in transport media from symptomatic patients. This qualitative test is intended for use as an aid in the rapid differential diagnosis of acute influenza A and

Similarities and Differences		
	Predicate Device	**Proposed Device**
Item	**Sofia Influenza A+B FIA on Sofia (K153012)**	**Sofia Influenza A+B FIA on Sofia 2 (K162438)**
	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. Performance characteristics for influenza A and B were established during February through March 2011 when influenza viruses A/California/7/2009 (2009 HINI), 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. If infection with a novel influenza virus is suspected 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	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 viral 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 patient management decisions. This test is intended for professional and laboratory use. The Sofia Influenza A+B FIA may be used with Sofia or Sofia 2. 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. If infection with a novel influenza virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, samples

Similarities and Differences		
	Predicate Device	**Proposed Device**
Item	**Sofia Influenza A+B FIA on Sofia (K153012)**	**Sofia Influenza A+B FIA on Sofia 2 (K162438)**
	attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.	should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture samples.
Specimen types	NS, NP, and NA/W specimens both direct and in VTM	NS, NP, and NA/W direct specimens and NP and NA/W in VTM
Internal assay controls	Negative control line, procedural control zone and reference line	Same
External controls	Test kit contains positive and negative control swab	Same
Instrument	Sofia	Sofia 2
Dimensions	24 cm x 16 cm x 10 cm	19.7 cm x 11.4 cm x 12.7cm
Weight	3 lbs	~2.5 lbs
Power supply	100-240 VAC, self-switching, or with 4 AA batteries	100-240 VAC, self-switching, or with rechargeable lithium polymer battery
Printer	Integrated	External
Assay/instrument interface	Drawer	Same
User interface	3.5 inch diagonal color LCD display and numeric keypad with function specific buttons touchscreen display	4 inch color LCD touchscreen display
Sample ID	External hand-held barcode scanner	Integrated barcode scanner
Cassette ID	Integrated barcode scanner	Integrated barcode scanner with custom 0.3MP camera
Development Modes	Two assay development modes: Walk Away and Read Now	Same
Time to obtain results	15 minutes	Potential for early read in Walk-Away Mode. Sofia 2 will image cassette at 3, 5, 8, 10, and 15 minutes until a positive result is obtained.

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

1. Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures. EP17-A2: Approved Guideline-Second Edition 2012.

L. Test Principle:

See decision summary for K153012; the FDA-cleared Sofia Influenza A+B FIA has not been modified and it is compatible with the newly developed Sofia 2 analyzer.

M. Performance Characteristics

Limit of detection, reproducibility, assay precision, early read, and method comparison studies were conducted to demonstrate equivalent performance of the Sofia Influenza A+B FIA on the Sofia and Sofia 2 analyzers. Results from each of these studies are described below. Additional analytical and clinical performance data for the Sofia Influenza A+B FIA is available under K153012.

1. Analytical Performance

   a. Limit of Detection

   The limit of detection (LoD) of the Sofia Influenza A+B FIA was established on both the Sofia and Sofia 2 analyzers. The study included two influenza A and two influenza B virus strains spiked into negative clinical nasal swab matrix, and was designed to follow the approach outlined in CLSI document EP17-A2, entitled "Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures."

   Briefly, an initial range finding study was conducted in which each of the four influenza virus strains was prepared at two different concentrations using the negative clinical matrix pool and tested in replicates of five with two lots of devices on each of the two instrument platforms (Sofia and Sofia 2). For each strain, the lowest dilution yielding all five positive results was then used as the starting concentration for two-fold serial dilutions. The lowest dilution yielding all 10 positive results was defined as the preliminary LoD.

   Additional 60 replicates of each virus strain at the preliminary LoD were tested on each of the two lots on each instrument platform. Testing spanned three days with at least 20 replicates run per day for each strain, lot and instrument combination.

   The results of the LoD study are shown in Table 1 below.

Table 1: Sofia Influenza A+B FIA LoD Study Results on the Sofia and Sofia 2 Analyzers

Viral Strain	Platform	LoD ($TCID_{50}$/mL)
A/California/07/2009	Sofia	5.48
	Sofia 2	9.79
A/Hong Kong/8/68	Sofia	1.80
	Sofia 2	2.19
B/Allen/45	Sofia	113
	Sofia 2	82.3
B/Malaysia/2506/04	Sofia	8.37
	Sofia 2	8.37

The newly established LoDs (using a new preparation of the viral strains) for the Sofia Influenza A+B FIA on the Sofia and Sofia 2 analyzers differ by less than two-fold, indicating that the LoD generated on each of the two instruments is similar.

b. Reproducibility

The reproducibility of the Sofia Influenza A+B FIA on Sofia 2 analyzer was evaluated at three different laboratories. Two to three different operators at each site blindly tested a series of coded, contrived samples, prepared in negative nasal swab matrix, ranging from negative to moderate positive influenza A and influenza B. The influenza strains used were inactivated Influenza A/Hong Kong/8/68 and Influenza B/Allen/45. Testing of the same panel was also performed in parallel with Sofia in order to collect comparison data. Each operator at three study sites tested a 15-member reproducibility panel on both the Sofia and Sofia 2 analyzers once per day on 5 different days totaling 150 tests per each of the three testing sites for a total of 450 samples. The study was conducted in the Read Now mode.

The percent agreement between the expected results and the reproducibility study results for the Sofia and Sofia 2 analyzers for each analyte concentration tested is shown in Tables 2 and 3, respectively.

Table 2: Qualitative Reproducibility Study Results Using the Sofia Analyzer

Site	Operator	Influenza A+B Negative	Influenza A Low Positive (1X LoD)	Influenza A Moderate Positive (2-3X LoD)	Influenza B Low Positive (1X LoD)	Influenza B Moderate Positive (2-3X LoD)
1	1	15/15	15/15	15/15	15/15	15/15
	2	3/3	3/3	3/3	3/3	3/3
	3	12/12	12/12	12/12	12/12	12/12
2	1	15/15	15/15	15/15	15/15	15/15
	2	15/15	15/15	15/15	15/15	15/15
3	1	14*/15	15/15	15/15	15/15	14*/15
	2	15/15	15/15	15/15	15/15	15/15
Combined Total		89/90	90/90	90/90	90/90	89/90
Percent Agreement (95% CI)		98.9% (93.9-99.8%)	100% (95.9-100%)	100% (95.9-100%)	100% (95.9-100%)	98.9% (93.9-99.8%)

* The discordant result for the Negative and the 2-3X samples appeared to be a mix-up at the site as the samples were tested on the same day by the same operator

Table 3: Qualitative Reproducibility Study Results Using the Sofia 2 Analyzer

Site	Operator	Influenza A+B Negative	Influenza A Low Positive (1X LoD)	Influenza A Moderate Positive (2-3X LoD)	Influenza B Low Positive (1X LoD)	Influenza B Moderate Positive (2-3X LoD)
1	1	15/15	15/15	15/15	15/15	15/15
	2	3/3	3/3	3/3	3/3	3/3
	3	12/12	12/12	12/12	12/12	12/12
2	1	15/15	15/15	15/15	15/15	15/15
	2	15/15	15/15	15/15	15/15	15/15
3	1	14*/15	15/15	15/15	15/15	14*/15
	2	15/15	15/15	15/15	15/15	15/15
Combined Total		89/90	90/90	90/90	90/90	89/90
Percent Agreement (95% CI)		98.9% (93.9-99.8%)	100% (95.9-100%)	100% (95.9-100%)	100% (95.9-100%)	98.9% (93.9-99.8%)

* The discordant result for the Negative and the 2-3X samples appeared to be a mix-up at the site as the samples were tested on the same day by the same operator

For each analyte concentration levels listed above, the mean relative fluorescence units (RFU), standard deviation (SD), and percent coefficient of variation (% CV) were calculated. Results for samples tested using the Sofia and Sofia 2 analyzers are shown in Tables 4 and 5 below.

Table 4: RFU-based Reproducibility Results Using the Sofia Analyzer

Sample Type	Site	Mean RFU		SD		% CV	
		A	B	A	B	A	B
Influenza A+B Negative	1	543	794	95	104	17.5	13.1
	2	699	862	85	108	12.1	12.5
	3	678	1,300	95	133	14.1	10.3
	Average	640	985	92	115	14.6	12.0
Influenza A Low Positive (1X LoD)	1	4,757		847		17.8	
	2	5,616		596		10.6	
	3	5,581		1,611		28.9	
	Average	5,318		1,018		19.1	
Influenza A Moderate Positive (2-3X LoD)	1	11,173		2,233		20.0	
	2	13,979		1,752		12.5	
	3	11,847		2,992		25.3	
	Average	12,333		2,326		19.3	
Influenza B Low Positive (1X LoD)	1	8,430		1,533		18.4	
	2	10,366		1,036		10.0	
	3	8,343		1,583		19.0	
	Average	9,046		1,391		15.8	
Influenza B Moderate Positive (2-3X LoD)	1	10,469		2,305		22.0	
	2	12,806		1,325		10.3	
	3	9,761		2,039		20.9	
	Average	11,012		1,890		17.8	

Table 5: RFU-based Reproducibility Results Using the Sofia 2 Analyzer

Sample Type	Site	Mean RFU		SD		% CV	
		A	B	A	B	A	B
Influenza A+B Negative	1	552	722	114	274	20.7	38
	2	669	775	106	279	15.9	36
	3	659	1,028	107	491	16.2	47.8
	Average	626	841	109	348	17.6	40.6
Influenza A Low Positive (1X LoD)	1	4,109		615		15.0	
	2	5,620		741		13.2	
	3	5,631		1,815		32.2	
	Average	5,120		1,057		20.1	
Influenza A Moderate Positive (2-3X LoD)	1	10,051		1,691		16.8	
	2	14,224		1,539		10.8	
	3	12,007		3,387		28.2	
	Average	12,094		2,206		18.6	
Influenza B Low Positive (1X LoD)	1	7,178		1,149		16.0	
	2	10,366		1,158		11.2	
	3	8,750		1,739		19.9	
	Average	8,765		1,348		15.7	

Influenza B Moderate Positive (2-3X LoD)	1	8,955	1,392	15.5
	2	12,224	1,617	13.2
	3	10,032	2,970	29.6
	Average	10,404	1,993	19.5

Although minor differences in the measured fluorescence were observed between the Sofia and Sofia 2 analyzers, no clinically significant difference was observed in the qualitative results; all clinical samples produced equivalent qualitative results. The inter-laboratory qualitative agreement for Sofia Influenza A+B FIA with Sofia and Sofia 2 analyzers was equivalent and ranged from 98.9% to 100%. Similarly, the intra-laboratory qualitative agreement for Sofia Influenza A+B FIA with Sofia and Sofia 2 analyzers was found comparable and ranged from 98.7% to 100%.

c. Assay Precision

To supplement the reproducibility study, within-laboratory precision of the Sofia and Sofia 2 analyzers was evaluated. Influenza A/California/07/09 and influenza B/Malaysian/2506/04 strains were tested at two different analyte concentrations: a "low positive" sample with an analyte concentration approximately 1X LoD and a "moderate positive" sample with an analyte concentration 2- 3X LoD. One negative matrix sample was also included in the testing.

Five samples (negative, low positive (influenza A and B) and moderate positive (influenza A and B)) were tested on three lots of Sofia influenza A+B FIA cassettes, by two operators on 12 different days (1 sample x 3 reagent lots x 2 operators x 12 days) totaling 72 replicates per sample per instrument. The assay was run in Read Now mode on one Sofia analyzer and one Sofia 2 analyzer.

Overall percent agreement between the expected results and the precision study results for the Sofia and Sofia 2 analyzer is shown in Table 6 below.

Table 6: Qualitative Precision Study Results Summary

Sample Type	Sofia		Sofia 2	
	Overall Agreement	% Overall Agreement	Overall Agreement	% Overall Agreement
Negative A+B	72/72	100	72/72	100
Influenza A Low Positive (1X LoD)	72/72	100	72/72	100
Influenza A Moderate Positive (2-3X LoD)	72/72	100	72/72	100
Influenza B Low Positive (1X LoD)	72/72	100	72/72	100
Influenza B Moderate Positive (2-3X LoD)	72/72	100	72/72	100

For each of the sample types listed above, the mean relative fluorescence units (RFU), standard deviation (SD), and percent coefficient of variation (%CV) were calculated. Results for samples tested using the Sofia and Sofia 2 analyzers are shown in Table 7.

Table 7: RFU-based Precision Study Results Summary

Platform	Sample Type	Mean RFU	SD	% CV
Sofia	Negative Influenza A	651.9	165.7	25.4
	Negative Influenza B	846.0	223.3	26.4
	Influenza A Low Positive (1X LoD)	4497.7	595.9	13.2
	Influenza B Low Positive (1X LoD)	4652.1	626.1	13.5
	Influenza A Moderate Positive (2-3X LoD)	9942.3	1460.1	14.7
	Influenza B Moderate Positive (2-3X LoD)	12201.5	1565.3	12.8
Sofia 2	Negative Influenza A	582.6	149.3	25.6
	Negative Influenza B	425.5	440.4	103.5
	Influenza A Low Positive (1X LoD)	4283.4	590.9	13.8
	Influenza B Low Positive (1X LoD)	4480.7	593.2	13.2
	Influenza A Moderate Positive (2-3X LoD)	9649.1	1225.0	12.7
	Influenza B Moderate Positive (2-3X LoD)	11684.7	1548.0	13.2

Though a difference was observed between Sofia and Sofia 2 analyzers for negative influenza B samples, the qualitative result of the analyzers did not change and all negative samples were 100% negative by both Sofia and Sofia 2 analyzers. Overall, the study results showed that Sofia and Sofia 2 analyzers generated clinically equivalent qualitative results when used by multiple operators, on multiple device lots, and operated over multiple days.

d. Early Read

Additional study was performed to support the multi-read feature of the Sofia 2 analyzer in Walk Away mode i.e., the test cassettes were scanned and interpreted by the Sofia 2 analyzer at 3, 5, 8, 10, and 15 minutes. Positive samples were prepared using one strain each of influenza A (A/California/07/09) and influenza B (B/Malaysian/2506/04) spiked in M4-RT transport media. Negative samples were contrived with extraction reagent reconstituted with solutions of 0.2% to 0.8% mucin in 50% M4-RT and M6 viral transport media in saline. The study results demonstrated that positive samples (depending on the viral load) can be interpreted as positive as early as 3 minutes with Sofia 2 in Walk Away mode.

2. Comparison Studies

a. Method Comparison

A method comparison study using clinical samples was conducted to demonstrate comparable performance of the Sofia Influenza A+B FIA using the Sofia and Sofia 2 analyzers. The study was conducted at three sites testing identical specimen panels that consisted of 100 influenza A positive, 50 influenza B positive, and 100 influenza negative clinical samples. Each panel member was assigned to one of the analyte concentration levels based on the signal-to-cutoff ratio (S/CO) that was obtained from a single replicate on the Sofia analyzer. The Table 8 below shows the S/CO for each level.

Table 7: S/CO Target Values

Panel Member	Influenza A S/CO	Influenza B S/CO
Negative	<0.5	
High Negative	0.75-0.95	0.75-0.95
Low Positive (1X LoD)	1.45-1.76	2.32-2.42
Moderate Positive(2-3X LoD)	3.0-5.1	4.64-6.96
High Positive (4-5X LoD)	6.5-8.5	9.28-11.6
Very High Positive (>5X LoD)	>9	>12

The final composition of the Method Comparison Panel was as follows in Table 9 below.

Table 9: Method Comparison Panel

Panel Member	Quantity per panel
Negative for both influenza A and influenza B	66
High Negative for influenza A	20
High Negative for influenza B	14
Low Positive for influenza A (1X LoD)	35
Low Positive for influenza B (1X LoD)	15
Moderate Positive for influenza A (2-3X LoD)	30
Moderate Positive for influenza B (2-3X LoD)	17
High Positive for influenza A (4-5X LoD)	15
High Positive for influenza B (4-5X LoD)	11
Very High Positive for influenza A (>5X LoD)	20
Very High Positive for influenza A (>5X LoD)	7

A total of 250 tests were performed at each of the three testing sites resulting in a total of 749 results (one specimen test result was not recoverable) across the three testing sites utilizing 15 Sofia and 14 Sofia 2 analyzers. To assess the potential for early read with Sofia 2, the testing for all specimens was conducted in Walk Away Mode. In this mode,

Sofia 2 captured the images of each test cassette at 5, 8, and 15 minutes. The overall study results obtained after the full 15 minutes are shown in Tables 10 and 11 below. Agreement between the results obtained on the Sofia and Sofia 2 analyzers for each of the individual analyte levels tested is shown in Tables 12 and 13.

Table 10: Method Comparison Study Influenza A Results for the Sofia and Sofia 2 Analyzers

	Sofia Positive	**Sofia Negative**		
Sofia 2 Positive	304	15	Positive % Agreement (95% CI)	304/311=98% (95.4-98.9%)
Sofia 2 Negative	7	423	Negative % Agreement (95% CI)	423/438=97% (94.4-97.9%)

Table 11: Agreement Stratified by Influenza A Level

Analyte Level	**Qualitative Method Comparison Results**		
		Sofia Positive	Sofia Negative
Negative	Sofia 2 Positive	0	0
	Sofia 2 Negative	0	198
High Negative	Sofia 2 Positive	11	12
	Sofia 2 Negative	6	31
Low Positive (1X LoD)	Sofia 2 Positive	98	3
	Sofia 2 Negative	1	3
Moderate Positive (2-3X LoD)	Sofia 2 Positive	90	0
	Sofia 2 Negative	0	0
High Positive (4-5X LoD)	Sofia 2 Positive	45	0
	Sofia 2 Negative	0	0
Strong Positive (>5X LoD)	Sofia 2 Positive	60	0
	Sofia 2 Negative	0	0

Table 12: Method Comparison Study Influenza B Results for the Sofia and Sofia 2 Analyzers

	Sofia Positive	**Sofia Negative**		
Sofia 2 Positive	154	5	Positive % Agreement (95% CI)	154/157=98% (94.5-99.4%)
Sofia 2 Negative	3	587	Negative % Agreement (95% CI)	587/592=99% (98.1-99.6%)

Table 13: Agreement Stratified by Influenza B Level

Analyte Level	Qualitative Method Comparison Results		
		Sofia Positive	Sofia Negative
Negative	Sofia 2 Positive	0	0
	Sofia 2 Negative	0	198
High Negative	Sofia 2 Positive	5	5
	Sofia 2 Negative	3	29
Low Positive (1X LoD)	Sofia 2 Positive	45	0
	Sofia 2 Negative	0	0
Moderate Positive (2-3X LoD)	Sofia 2 Positive	50	0
	Sofia 2 Negative	0	0
High Positive (4-5X LoD)	Sofia 2 Positive	33	0
	Sofia 2 Negative	0	0
Strong Positive (>5X LoD)	Sofia 2 Positive	21	0
	Sofia 2 Negative	0	0

The method comparison study results demonstrate that the performance of the Sofia Influenza A+B FIA on the Sofia 2 is comparable to the predicate device. There were 22 discordant results for influenza A and 8 discordant results for influenza B across all the three sites. Eighteen samples of the 22 discordant influenza A results were categorized as "high negative" and four samples were characterized as "Low positive (1X LoD)". All eight influenza B discordant results were characterized as "high negative". These discordant results were observed across all three sites and were generated by multiple operators, no trend indicating any instrument bias was observed.

For influenza A specimens, 100% of the specimens yielded positive results by 8 minutes and at least 91% by 5 minutes at ≥2-3X LoD; more than 80% were positive by 8 minutes at 1X LoD. For influenza B specimens, 100% of the specimens yielded positive results by 5 minutes at ≥2-3X LoD; 89% were positive by 5 minutes and 100% were positives by 8 minutes at 1X LoD.

N. Instrumentation/System Description

1. Instrument Name:

   Sofia and Sofia 2

2. System Description:

   The Sofia instruments are equipped with UV LED lighting and optical detection systems that are designed to collect and analyze fluorescent data emitted from the Sofia influenza

A+B FIA test cassettes. The instrument software contains embedded assay-specific algorithms that are used to convert the fluorescent signal data into a qualitative test result.

3. Software:

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

   Yes ___X___ or No _____

4. Level of Concern

   Moderate

5. Software Description

   The Sofia 2 Analyzer images the test strip and utilizes an embedded software algorithm to process the resulting data set into a qualitative test result. A positive test result for the analyte is determined by detection and analysis of the fluorescent signal at the test and reference lines, which are processed by the assay-specific algorithm. The algorithm employs a smoothing filter to the data and, identifies a peak maxima, minima and width, then calculates the RFU value based on peak height for the analyte test line. Results are presented on a screen and can be printed on an integrated printer.

6. Specimen Identification

   Each cassette is labeled with a barcode that is detected by the Sofia 2 internal barcode reader. The 2-dimensinal barcode contains lot, expiration, and test method information. If the cassette is not in the correct orientation, the barcode cannot be read and the analyzer will display an error.

7. Calibration

   To ensure that signal drift is controlled, the Sofia 2 analyzer has a calibration algorithm that reminds the operator to check the calibration status of the instrument every 30 days. The calibration cassette uses a highly stable fluorescent reagent along with a unique barcode. The insertion of this cassette triggers the Sofia 2 analyzer to self-check its calibration.

O. Other supportive Instrument Characteristics Data Not Covered in the "Performance Characteristics" Section Above

N/A

P. Proposed Labeling

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

Q. Conclusion

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