

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K153012

B. Purpose for Submission:

This is a new 510(k) application to expand the nasal swab, nasopharyngeal swab, and nasopharyngeal wash/aspirate specimen types to include specimens in viral transport medium (VTM) for the Quidel Sofia Influenza A+B FIA. Under recommendations from FDA, Quidel has submitted limit of detection data and clinical study performance data to support the application.

C. Measurand:

Influenza A and B virus nucleoprotein antigens

D. Type of Test:

Qualitative immunofluorescence assay

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Sofia[®] Influenza A+B FIA
Influenza A+B immunological test system

G. Regulatory Information:

1. Regulation section:

21 CFR 866.3330, Influenza virus serological reagents

2. Classification:

Class I

3. Product code:

GNX – Influenza virus serological reagents
KHO – Fluorometer for clinical use

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 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 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 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, 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.

2. Indication(s) for use:

Same as intended use

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

To be used only with the Sofia Analyzer

I. Device Description:

The Sofia Influenza A+B FIA employs immunofluorescence technology that is used with the Sofia Analyzer to detect influenza virus nucleoproteins.

The Sofia Influenza A+B FIA is a lateral-flow immunoassay that uses monoclonal antibodies that are specific for influenza antigens and have no known cross-reactivity to normal flora or other known respiratory pathogens.

Nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens are used for this test. The patient specimen is placed in the Reagent Tube, during which time the virus particles in the specimen are disrupted, exposing internal viral nucleoproteins. After disruption, the 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 influenza viral antigen is present, they will be trapped in a specific location. The Sofia Analyzer will scan the test strip and measure the fluorescent signal by processing the results using method-specific algorithms. The Sofia Analyzer will display the test results (Positive, Negative, or Invalid) on the screen.

Quality Control

See decision summary for K112177.

Results Interpretation

See decision summary for K112177.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Quidel Sofia Influenza A+B FIA

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

K112177

K131606

3. Comparison with predicate:

Table 1 – Assay Comparison with Predicate Device

	Predicate Device	Proposed Device
Item	Sofia Influenza A+B FIA	Sofia Influenza A+B FIA
510(k) Number	K112177	K153012
Regulation	866.3330	Same
Product Code	GNX, KHO	Same
Device Class	I	Same
Instrument	Sofia Analyzer	Same
Intended Use	<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 FDAcleared 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</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 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 negative test is presumptive and it is recommended these results be confirmed by virus culture or an FDAcleared 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</p>

	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 attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.	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 attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.
Assay Targets	Influenza A and Influenza B nucleoprotein antigens	Same
Specimen Types	Direct Nasal swab, Nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens	Nasal swab, Nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens both direct and in VTM
Test Time	15 Minutes	15 Minutes

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

N/A

L. Test Principle:

See decision summary for K112177.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

See decision summary for K112177.

b. *Linearity/assay reportable range:*

N/A

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

N/A

d. *Detection limit:*

Limit of Detection (LoD)

LoD was established using two influenza A strains and two influenza B strains diluted into a negative pooled clinical matrix. The clinical matrix consisted of negative nasal swabs placed in M5 or universal transport media (UTM). The LoD is defined as the lowest concentration (tissue culture infective dose, TCID₅₀/mL) per sample that can be reproducibly detected 95% of the times or lowest concentration at which 19 of 20 replicates were positive. Each strain was initially tested in a range finding study using serial dilutions of virus concentrations near the expected LoD in replicates of 10 per concentration of virus. LoD was determined using a dose response curve and interpolating the C₉₅ from the plotting software interpolation function. Verification of the estimated LoD was performed using a minimum of 20 replicates per strain. Strains tested were A/Port Chalmers/1/73 (H3N2), A/New Jersey/8/76 (H1N1), B/Allen/45, and B/Florida/07/2004.

Determined LoD concentrations as well as confirmation testing statistical data are summarized in Table 2.

Table 2 – LoD Results for the Sofia Influenza A+B FIA in nasal swab matrix/VTM

Strain	Matrix	TCID ₅₀ /ml	Influenza A Positive calls	Influenza B Positive calls
A/NJ	M5	2460	20/20	0/20
	UTM	1645	20/20	0/20
A/Port Chalmers	M5	1482	19/20	0/20
	UTM	1446	20/20	0/20
B/Allen	M5	5	0/20	20/20
	UTM	4.6	0/20	19/20
B/Florida	M5	40	0/20	20/20
	UTM	35	0/20	20/20

e. *Analytical reactivity:*

Analytical Reactivity

See decision summary for K112177.

f. *Analytical Specificity:*

See decision summary for K112177.

g. *Potentially Interfering Substances:*

See decision summary for K112177.

f. *Assay cut-off:*

The Sofia Analyzer uses a constant set of calculations to generate processed peak heights. The peak heights are used by the test method file to calculate a final test result.

2. Comparison studies:

a. *Method comparison with predicate device:*

N/A

b. *Matrix comparison:*

N/A

c. *Fresh versus frozen equivalency*

N/A

3. Clinical studies:

a. *Clinical Sensitivity and Specificity*

A prospective clinical study for Sofia Influenza A+B FIA was conducted during February through March 2011 in the United States. A total of 17 intended use clinical sites and three (3) reference laboratories participated in the study. Three (3) different specimen types, nasal swab (NS), nasopharyngeal swab (NPS), and nasopharyngeal aspirate/wash (NPA/W), were evaluated in this study. All specimen types were tested fresh and after the sample had been suspended into viral transport media (VTM) and transported to the corresponding reference

laboratory. Testing was performed at the time of the original clinical study but data on specimens in VTM was not included in the previous submission (K112177). The data is being supplied now in order to support the specimens in VTM claim. All test results were compared to viral culture as the reference method.

A total of 2152 subject specimens were available for use in the clinical study. Of the 2152 eligible specimens, 2019 were included in the study (12 specimens had no culture data available, 55 were excluded due to site protocol deviations, 65 specimens were lost from the device SD cards, and one (1) specimen was excluded due to the instrument error). There were 28 invalid results as determined by the subject device leaving 1991 valid specimens for analysis (665 nasal swabs, 688 nasopharyngeal swabs, and 638 NA/W specimens). There were 935 specimens collected from female subjects and 1036 from male subjects. Collection and testing was performed at 17 geographically diverse locations representing intended use sites (16 sites after exclusions).

Age distribution of the patients from whom the specimens were obtained was as follows: 1410 (71%) of the specimens 5 years or younger; 439 (22%) from ages 6 to 21; 122 (6%) from ages 22 to 59; and 20 (1%) from ages 60 or older.

Sofia Influenza A+B FIA detected influenza A with a clinical sensitivity versus culture of 83%, 91% and 97% when testing nasal swab, nasopharyngeal swabs, or nasopharyngeal aspirates/washes in VTM, respectively (Table 3). The specificity ranged from 97% to 98% across all sample types.

Table 3 – Influenza A performance versus culture for all specimens in VTM

	Nasal Swab	Nasopharyngeal Swab	Nasal Wash/Aspirate
Sensitivity	83% (117/141) 95%CI (76-88%)	91% (94/103) 95%CI (84-96%)	97% (66/68) 95%CI (89-99%)
Specificity	93% (512/524) 95%CI (96-99%)	98% (573/585) 95%CI (96-99%)	97% (553/570) 95%CI (95-98%)
PPV	91% (117/129)	89% (94/106)	80% (66/83)
NPV	96% (512/536)	98% (573/582)	>99% (553/555)
Prevalence	21% (141/665)	15% (103/688)	11% (68/638)

Sofia Influenza A+B FIA detected influenza B with a clinical sensitivity versus culture of 80%, 82% and 84% when testing nasal swab, nasopharyngeal swabs, or nasopharyngeal aspirates/washes in VTM, respectively (Table 4). The specificity ranged from 97% to 99% across all sample types.

Table 4 – Influenza B performance versus culture for all specimens in VTM

	Nasal Swab	Nasopharyngeal Swab	Nasal Wash/Aspirate
Sensitivity	80% (89/111) 95%CI (72-87%)	82% (88/107) 95%CI (74-88%)	84% (43/51) 95%CI (72-92%)
Specificity	98% (540/554) 95%CI (96-99%)	99% (575/581) 95%CI (98-99%)	97% (567/587) 95%CI (95-98%)
PPV	86% (89/103)	94% (88/94)	68% (43/63)
NPV	96% (540/562)	97% (575/594)	99% (567/575)
Prevalence	17% (111/665)	16% (107/688)	8% (51/638)

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

See decision summary for K112177.

N. Proposed Labeling:

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

O. Conclusion:

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