DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

September 27, 2016

Ronald H. Lollar
Senior Director, Clinical and Regulatory Affairs
Quidel Corporation
2005 East State Street, Suite 100
Athens, OH 45701

Re: K161814
Trade/Device Name: Solana® Influenza A+B Assay
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OCC, OZE
Dated: June 30, 2016
Received: July 1, 2016

Dear Mr. Lollar:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Steven R. Gitterman -S

for Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K161814

Device Name
Solana® Influenza A+B Assay

Indications for Use *(Describe)*
The Solana® Influenza A+B Assay is a qualitative *in vitro* diagnostic test for the detection and differentiation of influenza A and influenza B viral RNA in nasal and nasopharyngeal swabs from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of influenza A and influenza B viral infections in humans in conjunction with clinical and epidemiological risk factors. The assay does not detect the presence of influenza C virus.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

Performance characteristics for influenza A were established during the spring of 2016 when influenza A/H3 and 2009 H1N1 influenza were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may vary.

If infection with a novel influenza A 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. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

Applicant:

Quidel Corporation
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Contact Information:

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Ron.Lollar@quidel.com

Date of preparation of 510(k) summary:

June 30, 2016

A. 510(k) Number:

k161814

B. Purpose for Submission:

To obtain substantial equivalence for the Solana® Influenza A+B Assay when performed on the Solana® instrument

C. Measurand:

Influenza A: Matrix Gene;
Influenza B: Matrix Gene

D. Type of Test:

Reverse Transcriptase - Helicase-Dependent Amplification (RT-HDA)

510(k) Summary

E. Applicant:

Quidel Corporation

F. Proprietary and Established Names:

Solana® Influenza A+B Assay

G. Regulatory Information:

Table 1. Regulatory Information

Product Code	Classification	Regulation Section	Panel
OCC	Class II	21 CFR 866.3980 Respiratory viral panel multiplex nucleic acid assay	Microbiology (83)

H. Intended Use:

1. Intended Use(s):

The Solana® Influenza A+B Assay is a qualitative *in vitro* diagnostic test for the detection and differentiation of influenza A and influenza B viral RNA in nasal and nasopharyngeal swabs from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of influenza A and influenza B viral infections in humans in conjunction with clinical and epidemiological risk factors. The assay does not detect the presence of influenza C virus.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

Performance characteristics for the Solana® Influenza A+B Assay were established during the spring of 2016 when influenza A/H3 and 2009 H1N1 influenza were the predominant influenza viruses in circulation. When other influenza viruses are emerging, performance characteristics may vary.

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. Viral 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):

   - For *in vitro* diagnostic use only
   - For prescription use only

4. Special instrument requirements:

   Solana® Instrument

I. Device Description:

The Solana Influenza A+B Assay amplifies and detects viral RNA present in viral transport media containing nasopharyngeal or nasal swab specimens obtained from symptomatic patients.

The assay consists of two major steps: 1) specimen preparation, and 2) amplification and detection of target sequences specific to influenza A and/or influenza B using isothermal Reverse Transcriptase - Helicase-Dependent Amplification (RT-HDA) in the presence of target-specific fluorescence probes.

A patient nasal or nasopharyngeal swab specimen in viral transport media is transferred to a Process Buffer Tube, subjected to heat treatment at 95°C for 5 minutes and mixed. The processed sample is transferred to a Reaction Tube. The Reaction Tube contains lyophilized RT-HDA reagents, dNTPs, primers and probes. Once rehydrated with the processed sample, the Reaction Tube is placed in Solana for amplification and detection of influenza A and influenza B-specific target sequences. In Solana, the target sequences are amplified by influenza A and influenza B specific primers and detected by influenza A and influenza B specific fluorescence probes, respectively. A competitive process control (PRC) is included in the Process Buffer Tube to monitor sample processing, inhibitory substances in clinical samples, reagent failure or device failure. The PRC target is amplified by influenza B specific primers and detected by a PRC specific fluorescence probe.

The two target probes and PRC probe are labeled with a quencher on one end and a fluorophore on the other end. In addition, the two target probes and PRC probe have one or more bases that are comprised of ribonucleic acid. Upon annealing to influenza A,

influenza B or PRC amplicons, the fluorescence probes are cleaved by RNaseH2 and the fluorescence signal increases due to physical separation of fluorophore from quencher. Solana measures and interprets the fluorescent signal, using on-board method-specific algorithms. Solana then reports the test results to the user on its display screen, and it can print out the results via an integrated printer.

Materials Provided:

Solana® Influenza A+B Assay Kit: M300
48 Tests per kit

Table 2. Kit Components

Component	Quantity	Storage
Process Buffer	48 tubes/kit 1.55 mL	2°C to 8°C
Reaction Tubes	48 tubes/kit	2°C to 8°C

Materials required but not provided:

- External controls for Influenza A and Influenza B (e.g. Quidel Molecular Influenza A+B Control Set, which contains positive and negative controls, serves as an external processing control)
- Sterile DNAse-free filter-blocked positive displacement micropipettor tips
- Micropipettor
- Stopwatch or timer
- Scissors or a blade
- Workflow tray
- Transfer Rack
- Heat block capable of 95 ± 2°C temperature
- Thermometer
- Solana instrument
- Transport Media (BD/Copan UTM, Remel M4, Remel M4RT, Remel M5, Remel M6, or Copan eSwab)

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Lyra® Influenza A+B Assay

2. Predicate 510(k) number(s):
   K131728

510(k) Summary

3. Comparison with predicate:

Table 3. Similarities		
Item	**Solana® Influenza A+B Assay**	**Lyra® Influenza A+B Assay (k131728)**
Intended Use	The Solana® Influenza A+B Assay is a qualitative *in vitro* diagnostic test for the detection and differentiation of influenza A and influenza B viral RNA in nasal and nasopharyngeal swabs from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of influenza A and influenza B viral infections in humans in conjunction with clinical and epidemiological risk factors. The assay does not detect the presence of influenza C virus. Negative results do not preclude influenza virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Performance characteristics for influenza A were established during the spring 2016 when influenza A/H3 and 2009 H1N1 influenza were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may vary. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health	The Lyra® Influenza A+B assay is a multiplex Real Time RT-PCR assay for the *in vitro* qualitative detection and differentiation of influenza A and influenza B viral RNA in nasal and nasopharyngeal swabs from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of influenza A and influenza B viral infections in humans in conjunction with clinical and epidemiological risk factors. The assay does not detect the presence of influenza C virus. Negative results do not preclude influenza virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Performance characteristics for influenza A were established during the 2011 and 2013 influenza seasons when influenza A/H3 and 2009 H1N1

510(k) Summary

Table 3. Similarities		
Item	**Solana® Influenza A+B Assay**	**Lyra® Influenza A+B Assay (k131728)**
	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. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.	influenza were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may vary. If infection with a novel influenza A 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. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens. The assay can be performed using either the Life Technologies QuantStudio® Dx; the Applied Biosystems® 7500 Fast Dx, or the Cepheid SmartCycler® II.
Sample Types	nasal swab and nasopharyngeal swab	Same
Detection Techniques	Automated multiplex assay using different reporter dyes for each target	Same

510(k) Summary

Table 4. Differences		
Item	**Solana® Influenza A+B Assay**	**Lyra® Influenza A+B Assay (k131728)**
Viral Target	Influenza A: Matrix Gene; Influenza B: Matrix Gene	Influenza A: Matrix Gene; Influenza B: conserved influenza B sequence within the neuraminidase gene
Amplification Technology	Reverse Transcriptase - Helicase-Dependent Amplification (RT-HDA)	Real Time PCR-based system for detecting the presence or absence of viral RNA in clinical specimens
Extraction Methods	None	bioMérieux easyMAG® Automated Magnetic Extraction Reagents
Instrument	Solana	Life Technologies QuantStudio® Dx, the Applied Biosystems® 7500 Fast Dx, or the Cepheid SmartCycler® II
Performance Characteristics	The analytical sensitivity (limit of detection or LOD) of the Solana® Influenza A+B Assay was determined using quantified (TCID50/mL) cultures of three (3) influenza A strains and two (2) influenza B strains, serially diluted in negative nasopharyngeal matrix. Each dilution was run as 20 replicates in the Solana	The analytical sensitivity (limit of detection or LoD) of the Quidel Molecular Influenza A+B assay

<table>
<tr>
<td></td>
<td>Influenza A+B assay. Analytical sensitivity (LOD) is defined as the lowest concentration at which at least 95% of all replicates tested positive. The demonstrated LOD for each strain tested is shown below:
<table>
<tr><th colspan="3">LOD Values</th></tr>
<tr><td>Virus</td><td></td><td>$TCID_{50}$/mL</td></tr>
<tr><td>Influenza A</td><td>Subtype</td><td></td></tr>
<tr><td>A/Taiwan/42/06</td><td>H1N1</td><td>$7.5x10^{2}$</td></tr>
<tr><td>A/California/07/2009</td><td>H1N1p</td><td>$4.7x10^{2}$</td></tr>
<tr><td>A/Texas/50/2012</td><td>H3N2</td><td>$6.3x10^{0}$</td></tr>
<tr><td>Influenza B</td><td>Lineage</td><td></td></tr>
<tr><td>B/Brisbane/60/08</td><td>Victoria</td><td>$8.5x10^{1}$</td></tr>
<tr><td>B/Massachusetts/2/2012</td><td>Yamagata</td><td>$3.3x10^{1}$</td></tr>
</table>
</td>
<td>was determined using quantified (TCID50/mL) cultures of five (5) influenza A strains, three (3) influenza B strains, serially diluted in negative nasopharyngeal matrix. Each dilution was extracted using the NucliSENS easyMAG System and tested in replicates of 20 per concentration of virus on the Life Technologies QuantStudio® Dx; the Applied Biosystems® 7500 Fast Dx, or the Cepheid SmartCycler® II.

Analytical sensitivity (LoD), as defined as the lowest concentration at which 95% of all replicates tested positive, ranged from 10 to 100 TCID50/mL.</td>
</tr>
</table>

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

Guidance for Industry and FDA Staff: Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests (Final, 3/13/2007)

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071287.pdf

Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Respiratory Viral Panel Multiplex Nucleic Acid Assay - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm180307.htm

Guidance on Informed Consent for In Vitro Diagnostic Device Studies Leftover Human Specimens that are Not Individually Identifiable (April 2006) – http://www.fda.gov/cdrh/oivd/guidance/1588.pdf.

Guidance for Industry and Food and Drug Administration Staff - eCopy Program for Medical Device (December 2012) http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf

L. Test Principle:

The Solana Influenza A+B Assay amplifies and detects viral RNA present in viral transport media containing nasopharyngeal or nasal swab specimens obtained from symptomatic patients.

The assay consists of two major steps: 1) specimen preparation, and 2) amplification and detection of target sequences specific to influenza A and/or influenza B using isothermal Reverse Transcriptase - Helicase-Dependent Amplification (RT-HDA) in the presence of target-specific fluorescence probes.

A patient nasal or nasopharyngeal swab specimen in viral transport media is transferred to a Process Buffer Tube, subjected to heat treatment at 95°C for 5 minutes and mixed. The processed sample is transferred to a Reaction Tube. The Reaction Tube contains lyophilized RT-HDA reagents, dNTPs, primers and probes. Once rehydrated with the processed sample, the Reaction Tube is placed in Solana for amplification and detection of influenza A and influenza B-specific target sequences. In Solana, the target sequences are amplified by influenza A and influenza B specific primers and detected by influenza A and influenza B specific fluorescence probes, respectively. A competitive process control (PRC) is included in the Process Buffer Tube to monitor sample processing, inhibitory substances in clinical samples, reagent failure or device failure. The PRC target is amplified by influenza B specific primers and detected by a PRC specific fluorescence probe.

The two target probes and PRC probe are labeled with a quencher on one end and a fluorophore on the other end. In addition, the two target probes and PRC probe have one or more bases that are comprised of ribonucleic acid. Upon annealing to influenza A, influenza B or PRC amplicons, the fluorescence probes are cleaved by RNaseH2 and the fluorescence signal increases due to physical separation of fluorophore from quencher. Solana measures and interprets the fluorescent signal, using on-board method-specific algorithms. Solana then reports the test results to the user on its display screen, and it can print out the results via an integrated printer.

M. Performance Characteristics:

1. Analytical performance:

   a. Precision/Reproducibility:

   Reproducibility
   The reproducibility of the Solana® Influenza A+B Assay was evaluated at three laboratory sites. A four sample panel consisting of three levels of a combined influenza A and influenza B contrived sample and a negative contrived sample are tested in this study. Influenza A and influenza B viruses (Influenza A/California/07/2009 and Influenza B/Brisbane/60/08, respectively) are diluted in negative nasal matrix to 2 x LOD for moderate positive, 1 x LOD for low positive and diluted to C20 to C80 for high negative / low positive. Negative nasal matrix without spiked virus is used for the negative sample. The Solana Influenza A+B assay was used according to the instructions for use.

   Panels and controls were tested at each site by two operators per instrument for five days, each sample tested in three (3) replicates, for a total of 90 results per level for each virus for each instrument (2 operators x 5 days x 3 sites x 3 replicates).

510(k) Summary

Table 5. Reproducibility Summary

	SITE						Overall Percent Agreement		95% Confidence Interval
	Site #1		Site #2		Site #3				
	#Detected positive/# tested	*% Agreement with Expected Result*	*#Detected positive/# tested*	*% Agreement with Expected Result*	*#Detected positive/# tested*	*% Agreement with Expected Result*			
Influenza A/California/07/2009 High Negative (1.4×10^2 TCID50/mL)	10/30	33.3	25/30	83.3	23/30	76.7	58/90	64.4	54.1 to 73.6
Influenza A/California/07/2009 Low Positive (4.7×10^2 TCID50/mL)	30/30	100	30/30	100	30/30	100	90/90	100	96.5 to 100
Influenza A/California/07/2009 Moderate Positive (9.4×10^2 TCID50/mL)	30/30	100	30/30	100	30/30	100	90/90	100	96.5 to 100
Negative	0/30	100	0/30	100	0/30	100	0/90	100	96.5 to 100
Influenza A Positive Control	15/15	100	15/15	100	15/15	100	45/45	100	94.2 to 100
Influenza A Negative Control	0/15	100	0/15	100	0/15	100	0/45	100	94.2 to 100
	SITE						**Overall Percent Agreement With Expected Results**		**95% Confidence Interval**
	Site #1		**Site #2**		**Site #3**				
	#Detected positive/# tested	*% Agreement with Expected Result*	*#Detected positive/# tested*	*% Agreement with Expected Result*	*#Detected positive/# tested*	*% Agreement with Expected Result*			
Influenza B/Brisbane/60/08 High Negative (2.6×10^1 TCID50/mL)	9/30	30	5/30	16.7	10/30	33.3	24/90	26.7	18.6 to 36.6
Influenza B/Brisbane/60/08 Low Positive (8.5×10^1 TCID50/mL)	30/30	100	30/30	100	30/30	100	90/90	100	96.5 to 100
Influenza B/Brisbane/60/08 Moderate Positive (1.7×10^2 TCID50/mL)	30/30	100	30/30	100	30/30	100	90/90	100	96.5 to 100
Negative	0/30	100	0/30	100	0/30	100	0/90	100	96.5 to 100

510(k) Summary

Table 5. Reproducibility Summary

	SITE						Overall Percent Agreement		95% Confidence Interval
	Site #1		Site #2		Site #3				
	#Detected positive/# tested	*% Agreement with Expected Result*	*#Detected positive/# tested*	*% Agreement with Expected Result*	*#Detected positive/# tested*	*% Agreement with Expected Result*			
Influenza B Positive Control	15/15	100	15/15	100	15/15	100	45/45	100	94.2 to 100
Influenza B Negative Control	0/15	100	0/15	100	0/15	100	0/45	100	94.2 to 100

The results suggest that there are no significant differences between different users and different sites on different days. Reproducibility studies are acceptable.

b. Linearity/assay reportable range:

Not applicable – This assay is qualitative.

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

Traceability:

Not applicable. This assay is qualitative.

Specimen Stability:

Influenza A and B strains (Influenza A/California/07/2009 and Influenza B/Brisbane/60/08, respectively) were formulated in six (6) transport medium pooled negative matrix (Copan UTM, Remel M4, Remel M5, Remel M6, Remel M4RT or Copan ESwab transport media) at a final concentration of 2x LOD level.

The transport media systems containing the contrived samples were stored at 2° to 8°C up to 9 days. The samples were processed according to the instructions for use. Each transport media was tested in 3 replicates at Day 0, 24 hours, 48 hours, 72 hours, Day 7, and Day 9.

Influenza A and influenza B are stable in transport media BD UTM (1- and 3- mL), Remel M4 (3-mL), Remel M4RT (3-mL), Remel M5 (3-mL), and Remel M6 (3-mL) at 2° to 8°C for up to 9 days.

Influenza A and influenza B are stable in Copan eSwab transport media at 2 to 8°C for up to 48 hours.

Controls:

Controls (Quidel Molecular Influenza A+B Control Set), which contains positive and negative controls, serves as an external processing and extraction control) were run on the Solana® Influenza A+B Assay each day of testing. These controls are described as follows:

a. The process control is used to monitor sample processing, to detect HDA inhibitory specimens, to confirm the integrity of assay reagents and the operation of the Solana instrument. The process control is included in the Reaction Mix tube.

b. The external positive control may be treated as a patient specimen. The control should be sampled and tested as if it were a patient specimen and processed as described above in the Assay Procedure. The external positive control is intended to monitor substantial reagent and instrument failure.

c. The external negative control may be treated as a patient specimen. The control should be sampled and tested as if it were a patient specimen and processed as described above in the Assay Procedure. The external negative control is used to detect reagent or environmental contamination (or carry-over) by influenza A or B RNA or amplicon.

d. Detection limit:

The analytical sensitivity (limit of detection or LOD) of the Solana® Influenza A+B Assay was determined using quantified ($TCID_{50}$/mL) cultures of three (3) influenza A strains and two (2) influenza B strains, serially diluted in negative nasopharyngeal matrix. Each dilution was run as 20 replicates in the Solana Influenza A+B assay. Analytical sensitivity (LOD) is defined as the lowest concentration at which at least 95% of all replicates tested positive. The demonstrated LOD for each strain tested is shown below:

Table 6. LOD Values		
Virus		$TCID_{50}$/mL
Influenza A	Subtype	
A/Taiwan/42/06	H1N1	$7.5x10^2$
A/California/07/2009	H1N1p	$4.7x10^2$
A/Texas/50/2012	H3N2	$6.3x10^0$
Influenza B	Lineage	
B/Brisbane/60/08	Victoria	$8.5x10^1$
B/Massachusetts/2/2012	Yamagata	$3.3x10^1$

e. *Analytical specificity:*

Cross Reactivity:

A study was performed to evaluate the cross-reactivity of the Solana® Influenza A+B Assay with forty-four (44) microorganisms (24 bacteria, 1 yeast, 19 viruses) potentially found in specimens that are collected from patients symptomatic for influenza. Each microorganism was diluted in negative nasal matrix to the desired concentration (10^6 or higher CFU/mL for bacteria, yeast and 10^5 or higher pfu/mL or $TCID_{50}$/mL for viruses) and tested. The organisms and their concentrations included in the cross-reactivity study are shown in the table below.

Table 7. Cross-reactive Organisms	
Organism	**Concentration Tested**
Adenovirus 1	$1.0x10^5$ $TCID_{50}$/mL
Adenovirus 11	$1.0x10^5$ $TCID_{50}$/mL
Bordetella bronchiseptica	$1.0x10^6$ CFU/mL
Bordetella pertussis	$1.0x10^6$ CFU/mL
Candida albicans	$1.0x10^6$ CFU/mL
Chlamydophila pneumoniae	$5.0x10^4$ $TCID_{50}$/mL*
Coronavirus 229E	$1.0x10^5$ $TCID_{50}$/mL
Corynebacterium diptheriae	$1.0x10^6$ CFU/mL

Coxsackievirus B5/10/2006	$1.0x10^5$ $TCID_{50}$/mL
Echovirus 11	$1.0x10^5$ $TCID_{50}$/mL
Echovirus 6	$1.0x10^5$ $TCID_{50}$/mL
Enterovirus 70	$1.0x10^5$ $TCID_{50}$/mL
Enterovirus 71	$2.0x10^4$ $TCID_{50}$/mL*
Epstein Barr virus	$1.0x10^5$ $TCID_{50}$/mL
Escherichia coli	$1.0x10^6$ CFU/mL
Haemophilus influenzae	$1.0x10^6$ CFU/mL
HSV 1 MacIntyre Strain	$1.0x10^5$ $TCID_{50}$/mL
HSV 2 G strain	$1.0x10^5$ $TCID_{50}$/mL
Human Rhinovirus	$1.0x10^5$ $TCID_{50}$/mL
Klebsiella pneumoniae	$1.0x10^6$ CFU/mL
Lactobacillus plantarum	$1.0x10^6$ CFU/mL
Legionella pneumophila	$1.0x10^6$ CFU/mL
Measles	$1.0x10^5$ $TCID_{50}$/mL
Metapneumovirus A1	$1.0x10^5$ $TCID_{50}$/mL
Moraxella catarrhalis	$1.0x10^6$ CFU/mL
Mumps	$1.0x10^5$ $TCID_{50}$/mL
Mycobacterium avium	$1.0x10^6$ CFU/mL
Mycobacterium tuberculosis	$1.0x10^6$ CFU/mL
Mycoplasma pneumoniae	$1.0x10^6$ CFU/mL
Neisseria gonorrhoeae	$1.0x10^6$ CFU/mL
Neisseria meningitides	$1.0x10^6$ CFU/mL
Parainfluenza Type 1	$1.0x10^5$ $TCID_{50}$/mL
Parainfluenza Type 2	$1.0x10^5$ $TCID_{50}$/mL
Parainfluenza Type 3	$1.0x10^5$ $TCID_{50}$/mL
Proteus mirabilis	$1.0x10^6$ CFU/mL
Proteus vulgaris	$1.0x10^6$ CFU/mL
Pseudomonas aeruginosa	$1.0x10^6$ CFU/mL
Respiratory syncytial virus	$1.0x10^5$ $TCID_{50}$/mL
Staphylococcus aureus	$1.0x10^6$ CFU/mL
Staphylococcus epidermidis	$1.0x10^6$ CFU/mL
Streptococcus mutans	$1.0x10^6$ CFU/mL
Streptococcus pneumoniae	$1.0x10^5$ CFU/mL*
Streptococcus pyogenes	$1.0x10^6$ CFU/mL
Streptococcus salivarius	$1.0x10^6$ CFU/mL

* Due to low concentration of the stock organism, the concentration tested was below the target. The actual concentration tested is listed in the table.

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No cross-reactivity was observed with the forty-four (44) microorganisms tested with the Solana® Influenza A+B Assay.

Interference:

The performance of Solana® Influenza A+B Assay was evaluated with potentially interfering substances that may be present in nasopharyngeal specimens. The potentially interfering substances were evaluated with influenza A (A/Mexico/ 4108/2009) and influenza B (Influenza B/Brisbane/60/08) at concentrations of 2x LOD. There was no evidence of interference caused by the substances tested at the concentrations shown below.

Table 8. Interfering Substances

Substances	Active Ingredient	Concentration Tested
Purified mucin protein	Mucin protein	2.5 mg/mL
Blood (human)	Blood	5.0%
Afrin – nasal spray	Oxymetazoline	5.0%
Saline nasal spray	Saline	15.0%
Phenylephrine hydrochloride	Phenylephrine hydrochloride	15.0%
Flonase	Fluticasone	5.0%
Zicam Gentle Allergy Relief NasalGel	*Galphimia glauca*, *Histaminum hydrochloricum*, *Luffa operculata*, Sulfur	5.0%
Mupirocin	Mupirocin	12.0 mg/mL
Oseltamivir	Oseltamivir	2.2 µg/mL
Zanamivir	Zanamivir	282.0 ng/mL
Tobramycin	Tobramycin	2.5 mg/mL
Chloraseptic	Benzocaine, Menthol	0.68 g/mL
Amantadine hydrochloride	Amantadine hydrochloride	282.0 ng/mL
Nasocort Allergy 24 hour	Triamcinolone	5.0%
Sinus Buster Nasal Spray	*Capsicum annuum* (Capsaicin)	5.0%
NasalCrom Nasal Allergy	Cromolyn Sodium	5.0%

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Table 8. Interfering Substances		
Substances	**Active Ingredient**	**Concentration Tested**
Spray		
Rhinocort	Budesonide (Glucocorticoid)	5.0%
Air-Vita Allergy Multi-Symptom Relief	Allium cepa, Ambrosia artemisiaefolia, Apis mellifica, Chamomilla, Eucalyptol, Eucalyptus globulus, Euphrasia officinalis, Galphimia glauca, Histaminum hydrochloricum, Natrum muriaticum, Nux vomica, Quercus robur, Silicea, Wyethia helenioides	5.0%
Ipratropium bromide	Ipratropium bromide	10.0 mg/mL
Olopatadine hydrochloride	Olopatadine hydrochloride	10.0 mg/mL
Amantadine hydrochloride	Amantadine hydrochloride	282.0 ng/mL

Analytical Reactivity (Inclusivity):

The reactivity of the Solana® Influenza A+B Assay was evaluated against multiple strains of influenza A and influenza B viruses. The clinical influenza panel consisted of fourteen (14) influenza A strains, and eight (8) Influenza B strains at concentrations near the level of detection (LOD) of the assay.

Table 9. Inclusivity Strains			
Strain	Subtype/Lineage	$TCID_{50}$/mL	Inclusive (Yes or No)
	Influenza A		
A/Mexico/4108/2009	H1N1p	$2.3x10^3$	Yes
A/Denver/1/57	H1N1	$2.3x10^3$	Yes
A/New Jersey/8/76	H1N1	$2.3x10^3$	Yes
A/PR/8/34	H1N1	$2.3x10^3$	Yes
A/FM/1/47	H1N1	$2.3x10^3$	Yes
A/Solomon Islands/3/06	H1N1	$2.3x10^3$	Yes
A/New Caledonia/20/1999	H1N1	$2.3x10^3$	Yes
A/Victoria/361/11	H3N2	$2.3x10^3$	Yes
A/Port Chalmers/1/73	H3N2	$1.4x10^4$	Yes
A/Aichi/2/68	H3N2	$2.3x10^3$	Yes
A/Victoria/3/75	H3N2	$2.3x10^3$	Yes

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Table 9. **Inclusivity Strains**			
Strain	Subtype/Lineage	$TCID_{50}$/mL	Inclusive (Yes or No)
A/Hong Kong/8/68	H3N2	$2.3x10^3$	Yes
A/Wisconsin/67/2005	H3N2	$2.3x10^3$	Yes
A/WS/33	H1N1	$2.3x10^3$	Yes
	Influenza B		
B/Malaysia/2506/04	Victoria	$2.6x10^2$	Yes
B/Florida/07/2004	Victoria	$7.7x10^2$	Yes
B/Maryland/1/59	Yamagata	$2.6x10^2$	Yes
B/Allen/45	Yamagata	$2.6x10^2$	Yes
B/Lee/40	Yamagata	$2.6x10^2$	Yes
B/Florida/04/2006	Yamagata	$7.7x10^2$	Yes
B/Panama/45/90	Yamagata	$2.6x10^2$	Yes
B/Hong Kong/5/72	Victoria	$2.6x10^2$	Yes
B/Malaysia/25/06/04	Victoria	$2.6x10^2$	Yes

Due to restrictions and availability of a number of influenza A strains, *in silico* analysis was performed for three additional strain designations:

- A total of four (4) H3N2v (1 human strain and 3 swine) sequences were analyzed *in silico*. All four sequences demonstrated 100% homology.
- A total of three hundred forty (340) H5N1 strains were analyzed *in silico*. Three hundred thirty-nine (339) strains in the database demonstrated ≥95% overall homology and ≥88% homology to any individual primer or probe sequence. One H5N1 strain demonstrated an overall homology of 88% and ≥82% homology to any individual primer or probe sequence.
- A total of one hundred sixty-four (164) H7N9 sequences were analyzed *in silico*. All 164 sequences demonstrated 100% homology.
- Fourteen (14) non-clinical avian restricted influenza A viruses (Table 10) were analyzed *in silico*.

Table 10.	**Non-clinical Avian Restricted Influenza A Viruses**
Subtype	**Strain**
H2N2	A/Mallard/NY/6750/78 (H2N2)
H7N3	A/Chicken/NJ/15086-3/94 (H7N3)
H9N2	A/Chicken/NJ/12220/97 (H9N2)
H4N8	A/Mallard/OH/338/86 (H4N8)
H6N2	A/Chicken/CA/431/00 (H6N2)

Table 10.	Non-clinical Avian Restricted Influenza A Viruses
Subtype	**Strain**
H8N4	A/Blue Winged Teal/LA/B174/86 (H8N4)
H5N1	A/Anhui/01/2005(H5N1)-PR8-IBCDC-RG5
H10N7	A/GWT/LA/169GW/88 (H10N7)
H11N9	A/Chicken/NJ/15906-9/96 (H11N9)
H12N5	A/Duck/LA/188D/87 (H12N5)
H13N6	A/Gull/MD/704/77 (H13N6)
H14N5	A/Mallard/GurjevRussia/262/82 (H14N5)
H15N9	A/Shearwater/Australia/2576/79 (H15N9)
H16N3	A/Shorebird/DE/172/2006(H16N3)

A total of twenty-seven (27) sequences were available for analysis. The Solana™ FluA primers and probe are 90-100% conserved to the specified avian strains and to representative avian strains.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

510(k) Summary

Performance characteristics of the Solana Influenza A+B Assay were established during a prospective study with specimens collected between February and April 2016. One thousand four hundred seventy-three (1473) prospectively collected specimens have been included in this study at five (5) sites across the United States. A single nasal or nasopharyngeal swab specimen (302 and 1171, respectively) was collected per patient in viral transport media (BD/Copan UTM, Remel M5, Remel M6). All specimens were transported to a central location at 2°C to 8°C for testing by the comparator methods (culture for influenza A and B using the R-Mix Too mixed cells and direct specimen DFA (DSFA), and extraction with the NucliSENS® easyMAG® and testing with a FDA-cleared Influenza A+B molecular assay). The specimens were processed and tested with Solana Influenza A+B Assay (frozen (731) and fresh (742)) on the Solana instrument at the sites.

COMPARISON VERSUS CULTURE WITH DFA AND DSFA

One thousand four hundred seventy-three (1473) fresh specimens were included in this study. Each specimen was cultured for influenza A and B using the R-Mix Too mixed cells and stained with an FDA-cleared device and processed for direct specimen DFA (DSFA). All comparator testing was performed on fresh specimens within 72-hours of their collection. A specimen was recorded as positive for influenza A or B if either comparator test was positive.
Seven hundred and forty-two (742) of these specimens were tested fresh using the Solana Influenza A+B Assay for the presence influenza A or B. Seven hundred and thirty-one (731) specimens were frozen and stored at -70°C prior to testing with the Solana Influenza A+B Assay. Fifteen (15) specimens were contaminated or toxic in the cell culture (1.0%). Fifty (50) specimens were invalid in the Solana Assay (3.4%). These sixty-five (65) specimens have been excluded from further analysis. Tables 11 and 12 detail the performance of the Solana Assay for influenza A and influenza B respectively for the remaining one thousand four hundred eight (1408) specimens, across all testing sites combined, as compared to viral culture with DSFA results.

Table 11. Performance Characteristics of the Solana Influenza A+B Assay for Influenza A Compared to Culture and DSFA (Across all Sites Combined)

Source Category	N	TP	FP	TN	FN	Sensitivity% (95% CI)	Specificity% (95% CI)
Fresh	709	180	24	503	2	98.9 (96.1 to 99.7)	95.4 (93.3 to 96.9)
Frozen	699	176	27	493	3	98.3 (95.2 to 99.4)	94.8 (92.6 to 96.4)
All	1408	356	51*	996	5**	98.6 (96.8 to 99.4)	95.1 (93.7 to 96.3)

*Of the fifty-one (51) discordant specimens (Solana Positive/Culture and DSFA Negative) reported in Table 11, twenty-eight (28) of these specimens were positive by an alternate molecular assay.

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**Of the five (5) discordant specimens (Solana Negative/Culture and DSFA Positive) reported in Table 11, two (2) of these specimens were positive by an alternate FDA cleared molecular assay.

Table 12. Performance Characteristics of the Solana Influenza A+B Assay for Influenza B Compared to Culture and DSFA (Across all Sites Combined)

Source Category	N	TP	FP	TN	FN	Sensitivity% (95% CI)	Specificity% (95% CI)
Fresh	709	62	1	646	0	100 (94.2 to 100)	99.8 (99.1 to 100)
Frozen	699	23	8	668	0	100 (85.7 to 100)	98.8 (97.7 to 99.4)
All	1408	85	9*	1314	0	100 (95.7 to 100)	99.3 (98.7 to 99.6)

*Of the nine (9) discordant specimens (Solana Positive/Culture and DSFA Negative) reported in Table 12, two (2) of these specimens were positive by an alternate FDA cleared molecular assay.

COMPARISON WITH A FDA-CLEARED INFLUENZA A+B MOLECULAR ASSAY

One thousand four hundred seventy-three (1473) specimens were processed using the NucliSENS® easyMAG® and tested with a FDA-cleared Influenza A+B molecular assay according to the assay's package insert. The comparator testing was performed on fresh specimens within 72-hours of their collection.

Seven hundred and thirty-one (731) of the original specimens were frozen and stored at -70°C prior to testing with the Solana® Influenza A+B Assay. Seven hundred and forty-two (742) of the original specimens were tested fresh using the Solana® Influenza A+B Assay for the presence of influenza A or B. Thirty one (31) specimens were invalid in the comparator assay (2.1%). Fifty (50) specimens were invalid in the Solana® Assay (3.4%)(one specimen was invalid in both assays). These eighty (80) specimens have been excluded from further analysis.

Tables 13 and 14 detail the positive percent agreement (PPA) and the negative percent agreement (NPA) of the Solana Influenza A+B Assay results for influenza A and influenza B respectively, as compared with an FDA cleared molecular comparator, for the remaining one thousand three hundred ninety-three (1393) specimens.

Table 13. Percent Agreement of the Solana® Influenza A+B Assay for Influenza A Compared to an FDA cleared Influenza A+B Molecular Assay (Across all Sites Combined)

Source Category	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Fresh	710	195	9	499	7	96.5 (93.0 to 98.3)	98.2 (98.7 to 99.1)
Frozen	683	180	24	475	4	97.8 (94.5 to 99.2)	95.2 (92.9 to 96.7)

510(k) Summary

Table 13. Percent Agreement of the Solana® Influenza A+B Assay for Influenza A Compared to an FDA cleared Influenza A+B Molecular Assay (Across all Sites Combined)							
Source Category	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
All	1393	375	33	974	11	97.2 (95.0 to 98.4)	96.7 (95.4 to 97.7)

There were a total of forty-four (44) discordant specimens among the hundred ninety-three (1393) specimens evaluated. Of the thirty-three (33) discordant specimens (Solana Positive/ Comparator Negative) reported in Table 13, nine (9) of these specimens were positive by culture/DSFA. Of the eleven (11) discordant specimens (Solana Negative/Comparator Positive) reported in Table 13, two (2) of these specimens were positive by culture/DSFA.

Table 14. Percent Agreement of the Solana® Influenza A+B Assay for Influenza B Compared to an FDA-cleared Influenza A+B Molecular Assay (Across all Sites Combined)							
Source Category	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Fresh	710	57	6	647	0	100 (93.7 to 100)	99.1 (98.0 to 99.6)
Frozen	683	23	8	652	0	100 (85.7 to 100)	98.8 (97.6 to 99.4)
All	1393	80	14	1299	0	100 (95.4 to 100)	98.9 (98.2 to 99.4)

There were a total of fourteen (14) discordant specimens among the one thousand three hundred ninety-three (1393) specimens evaluated. Of the fourteen (14) discordant specimens (Solana Positive/ Comparator Negative) reported in Table 14, seven (7) of these specimens were positive by culture/DSFA.

b. Clinical specificity:

See Section 3a.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values:

The expected values of the Solana Influenza A+B Assay were established during a prospective study conducted between February and April 2016. One thousand four hundred seventy-three (1473) specimens (fresh (742) and frozen (731)) have been included in this study at five (5) sites across the United States. A single specimen was

collected per patient. The specimens were processed and tested with Solana® Influenza A+B Assay on the Solana® instrument at the sites.

The expected value of influenza A and influenza B with the Solana Influenza A+B Assay has been calculated for the combined sites based on the age of the patient.

Fifty-three (53) of the one thousand four hundred seventy-three (1473) specimens were removed from analysis: (three (3) specimens did not have the age provided; fifty (50) specimens were invalid). Table 15 provides the percentage of influenza A and influenza B positive cases per specified age group, as determined by the Solana Influenza A+B Assay, for the remaining one thousand four hundred twenty (1420) specimens.

Table 15. Expected Values (N=1420)

Age Group	Influenza A			Influenza B		
	Number of Patients	Number of Positives	Prevalence	Number of Patients	Number of Positives	Prevalence
≤ 5 years	377	91	24.1%	377	26	6.9%
6 to 21 years	297	89	30.0%	297	48	16.2%
22 to 59 years	504	191	37.9%	504	17	3.4%
≥ 60 years	242	37	15.3%	242	3	1.2%

The prospective clinical study had a dual infection rate for Influenza A and Influenza B of 0.2% (3/1420) using the Solana Influenza A+B Assay. All three (3) of these dual detections were only positive for influenza A by culture and DSFA and also by an alternate molecular comparator.

N. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Instrument: Solana® Instrument

O. System Descriptions:

1. Modes of Operation:

The Solana instrument heats each reaction tube to 58°C. If present, the target RNA sequence is reverse transcribed into cDNA by the Reverse Transcriptase and influenza A or B specific primers that are present in the reaction mix. After the completion of the Reverse Transcriptase step, the Solana instrument heats each reaction tube to 65°C where the isothermal DNA polymerase amplifies the cDNA strands using the influenza A or B specific primers. Influenza A or B specific fluorescence probes are also included in the Reaction Tube. The target probes are labeled with a quencher on one end and a fluorophore specific for the recognition sequence on the other end. In addition, the

target probes carry a ribonucleic acid. Upon annealing to amplicons, the fluorescence probes are cleaved by RNaseH2 and the fluorescence signal increases due to physical separation of fluorophore from quencher. The Solana instrument measures and interprets the fluorescent signal, using on-board method-specific algorithms. Solana instrument will then report the test results to the user on its display screen, and it can print out the results via a printer.

2. Software:

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

Yes ____X____ No _____

P. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10, 21 CFR 801.109, and the special controls.