510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
K171552

B. Purpose for Submission:
To obtain a Substantial Equivalence Determination for a new 510(k) application for Xpert Xpress Flu Assay performed on the Cepheid GeneXpert Xpress System.

C. Measurand:
Unique sequences in the genes that encode the following proteins: influenza A matrix (M), influenza A basic polymerase (PB2), influenza A acidic protein (PA), influenza B matrix (M), and influenza B non-structural protein (NS).

D. Type of Test:

This assay is a multiplex nucleic acid assay that detects and differentiates influenza A and influenza B through nucleic acid extraction, amplification, and detection using real-time RT-PCR. All steps of the assay are automated, after sample addition, and performed in a single container.

E. Applicant:
Cepheid

F. Proprietary and Established Names:
Xpert Xpress Flu
Xpert Xpress Flu Assay

G. Regulatory Information:

1. Regulation section:
   21CFR 866.3980 - Respiratory viral panel multiplex nucleic acid assay
   21CFR 866.2390 -Transport culture medium
   21CFR 866.2570 - Instrumentation for clinical multiplex test systems

2. Classification:
   Class II

3. Product codes:
   OCC, JSM, OOI

4. Panel:
   Microbiology (83)

H. Intended Use:

1. Intended use(s):

Device Intended Use:

The Cepheid Xpert® Xpress Flu Assay, performed on the GeneXpert® Xpress System, is an automated, multiplex real-time, reverse transcriptase polymerase chain reaction (RT- PCR) assay intended for the in vitro qualitative detection and differentiation of influenza A and influenza B viral RNA. The Xpert Xpress Flu Assay uses nasopharyngeal (NP) swab and nasal swab (NS) specimens collected from patients with signs and symptoms of respiratory infection. The Xpert Xpress Flu Assay is intended as an aid in the diagnosis of influenza infections in conjunction with clinical and epidemiological risk factors.

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

Performance characteristics for influenza A were established during the 2016-2017 influenza season. When other novel 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 departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Ancillary Collection Kit for Nasal Swabs Indications for Use:

The Xpert® Nasal Sample Collection Kit is designed to collect, preserve, and transport nasal swab specimens containing viruses from patients with signs and symptoms of respiratory infection prior to analysis with the Xpert Xpress Flu Assay.

Ancillary Collection Kit for Nasopharyngeal Swabs Indications for Use:

The Xpert® Nasopharyngeal Sample Collection Kit is designed to collect, preserve, and transport nasopharyngeal swab specimens and to preserve and transport nasal aspirate/wash specimens containing viruses from patients with signs and symptoms of respiratory infection prior to analysis with the Xpert Flu Assay or the Xpert Flu/RSV XC Assay. The Xpert® Nasopharyngeal Sample Collection Kit is designed to collect, preserve, and transport nasopharyngeal swab specimens containing viruses from patients with signs and symptoms of respiratory infection prior to analysis with the Xpert Flu+RSV Xpress Assay, Xpert Xpress Flu/RSV Assay or the Xpert Xpress Flu Assay.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):
   For Prescription Use Only

4. Special instrument requirements:
   Gene Xpert Xpress System

I. Device Description:

This assay uses nasopharyngeal swab specimens from patients with signs and symptoms of respiratory infection. Viral nucleic acid is extracted from the sample and the influenza A and/or influenza B viral RNA is amplified and detected through real-time reverse transcription polymerase chain reaction (RT-PCR). Detection and differentiation of influenza A and influenza B is reported to the user.

The assay uses single use disposable cartridge that has a separate section for specimen loading. The cartridge also contains all PCR reagents and is where the PCR reaction takes place. The GeneXpert Xpress System performs all assay steps from clinical sample to reporting assay results automatically. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included in the cartridge. The SPC is present to control for adequate processing of the target viruses and to monitor the presence of inhibitors in the PCR reaction. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The GeneXpert Xpress System, comprised of the GeneXpert Dx System GX-II, which has two modules capable of performing separate sample preparation and real-time PCR and RT-PCR tests, and the GX-IV which has four modules. Each module contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells, and a proprietary thermocycler for performing real-time PCR and RT-PCR and detection.

Turnaround time for analysis of a sample is approximately 30 minutes or less. The assay results are automatically generated at the end of the process and provided in a report that can be viewed and printed.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Xpert Flu+RSV Xpress Assay

2. Predicate 510(k) number(s):
   K151226

3. Comparison with predicate:

Table 1. Differences between device and predicate

Differences		
Item	**Device**	**Predicate**
	Cepheid Xpert® Xpress Flu	**Cepheid Xpert® Flu+RSV Xpress Assay K151226**
Assay Targets	Influenza A and Influenza B viral RNA	Influenza A, Influenza B, and RSV viral RNA
Specimen Types	Nasopharyngeal (NP) swab and nasal swab (NS) specimens	Nasopharyngeal (NP) swab specimens
Assay Controls	Encapsulated (armored) RNA pseudovirus as a sample processing control. Available but not provided are inactivated virus controls for influenza A/B as external positive controls, and Coxsackie virus as an external negative control.	Encapsulated (armored) RNA pseudovirus as a sample processing control. Available but not provided are inactivated virus controls for influenza A/B and RSV as external positive controls, and Coxsackie virus as an external negative control.
Time to obtain test results	Approximately 30 minutes or less for sample preparation and RT-PCR	Approximately 60 minutes for sample preparation and real-time RT-PCR
Combinatorial Assay Selections	Not applicable	Yes, user may select combined assay with all targets or a Flu only assay or a RSV only assay.

Intended Use	The Cepheid Xpert® Xpress Flu Assay, performed on the GeneXpert® Xpress System, is an automated, multiplex real-time, reverse transcriptase polymerase chain reaction (RT- PCR) assay intended for the in vitro qualitative detection and differentiation of influenza A and influenza B viral RNA. The Xpert Xpress Flu Assay uses nasopharyngeal (NP) swab and nasal swab (NS) specimens collected from patients with signs and symptoms of respiratory infection. The Xpert Xpress Flu Assay is intended as an aid in the diagnosis of influenza infections in conjunction with clinical and epidemiological risk factors. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions. Performance characteristics for influenza A were established during the 2016-2017 influenza season. When other novel 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 departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.	The Cepheid Xpert® Flu+RSV Xpress Assay, performed on the GeneXpert® Xpress System, is an automated, multiplex real-time, reverse transcriptase polymerase chain reaction (RT-PCR) assay intended for the in vitro qualitative detection and differentiation of influenza A, influenza B, and respiratory syncytial virus (RSV) viral RNA. The Xpert Flu+RSV Xpress Assay uses nasopharyngeal swab specimens collected from patients with signs and symptoms of respiratory infection. The Xpert Flu+RSV Xpress Assay is intended as an aid in the diagnosis of influenza and respiratory syncytial virus in conjunction with clinical and epidemiological risk factors. Negative results do not preclude influenza virus or respiratory syncytial virus infection and should not be used as the sole basis for treatment or other patient management decisions. Performance characteristics for influenza A were established during the 2014-2015 influenza season. When other novel 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 departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Table 2. Similarities between device and predicate.

Similarities		
	Device	**Predicate**
Item	**Cepheid Xpert® Xpress Flu**	**Cepheid Xpert® Flu+RSV Xpress Assay 510(k)# K151226**
Regulation	866.3980	Same
Product Code	OCC, OOI	Same
Device Class	II	Same
Technology Principle of Operation	Multiplex real time RT-PCR	Same
Assay Results	Qualitative	Same
Instrument System	Cepheid GeneXpert Xpress System (instrument model GX-II and GX-IV); Cepheid I-core technology	Cepheid GeneXpert Xpress System (instrument model GX-I); Cepheid I-core technology
Primers and probes	Primers and probes to detect the presence of nucleic acid sequences of influenza A, influenza B, and RSV. Only results for influenza A and influenza B are reported.	Primers and probes to detect the presence of nucleic acid sequences of influenza A, influenza B, and RSV. Results for influenza A, influenza B and RSV analytes are reported.
Laboratory Users	Untrained operators with no clinical lab experience.	Same
Sample Preparation	Self-contained and automated after mixed specimen is added to cartridge. All other reagents are contained in the cartridge.	Same
Primers and probes for influenza A, influenza B	Primers and probes to detect the presence of nucleic acid sequences of influenza A, influenza B, and RSV A/B. The Xpert Xpress Flu Assay contains primers and probes to detect additional RNA segments in order to protect the assay sensitivity and specificity from mutations in the influenza genome due to antigenic drifts and shifts. Only results for influenza A and influenza B are reported.	Primers and probes to detect the presence of nucleic acid sequences of influenza A, influenza B, and RSV A/B. The Xpert Flu+RSV Xpress Assay contains primers and probes to detect additional RNA segments in order to protect the assay sensitivity and specificity from mutations in the influenza genome due to antigenic drifts and shifts. Results for influenza A, influenza B and RSV analytes are reported.

Target Sequences	Influenza A: Matrix protein (MP), basic polymerase (PB2), and acidic protein (PA) Influenza B: Matrix protein (MP) and Non-structural proteins (NS 1 and NS 2) RSV A and RSV B: Nucleocapsid protein Only results for influenza A and influenza B are reported.	Influenza A: Matrix protein (MP), basic polymerase (PB2), and acidic protein (PA) Influenza B: Matrix protein (MP) and Non-structural proteins (NS 1 and NS 2) RSV A and RSV B: Nucleocapsid protein Results for influenza A, influenza B and RSV analytes are reported.
Internal Controls	Sample processing control (SPC) and probe check control (PCC).	Same
Early Assay termination function	Yes	Yes

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

Class II Special Controls Guidance Document: Respiratory Viral Panel Multiplex Nucleic Acid Assay

L. Test Principle:

The assay detects viral nucleic acids that have been extracted from a patient respiratory sample. A multiplex Real-time RT-PCR reaction is carried out under optimized conditions generating amplicons for influenza A, influenza B and the Sample Process Control (SPC). Identification of influenza A, influenza B and the SPC occurs by the use of target-specific primers and fluorescent-labeled probes that hybridize to conserved regions in the genomes.

Table 3. Xpert Flu+RSV Xpress Assay Probe Targets

Virus	**Target**
Influenza A	Matrix Protein gene, Polymerase B2 Protein gene, Polymerase A Protein gene
Influenza B	Matrix Protein gene, Non-Structrural Protein gene

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

A portion of the analytical studies were conducted for and described in submissions K163221 and K162456. All testing was performed using the same assay, Xpert Xpress Flu Assay, no changes to the assay were made since the 510(k) clearance of K163221 and K162456. For this submission the data from all analytical studies (except LoD and Swab Equivalency Study) were re-analyzed with the new software, version 5.0, on the Gene Xpert Xpress System instruments GX-II and GX-IV. No changes were detected in the analytical study data analyses conducted with the new software version used with the Xpert Xpress Flu Assay and Gene Xpert Xpress Sytem described in this submission.

a. Precision/Reproducibility:

Precision

Please refer to the Decision Summary for submissions K163221 and K162456.

Reproducibility

A multi-center study was conducted at 3 sites with 3 operators at each site. Each operator tested a 7-member blinded panel 2 times per day over 5 testing days. One lot of Xpert Xpress Flu/RSV Assay reagents was used for this study. All sites used the GeneXpert Xpress IV Instrument System. The panel members were comprised of influenza A (Flu A), influenza B (Flu B), and respiratory syncytial virus (RSV) viral isolates spiked into simulated matrix. Reanalysis with the Xpert Xpress Flu Assay ADF reported results of only Flu A and Flu B. The panel member composition, with viral titer, is listed in the table below.

Table 4. Reproducibility sample panel

Virus Strain	Panel Member	Expected Positivity Rate	Concentration ($TCID_{50}$/mL)	NP swab Matrix LoD	NS Matrix LoD
Negative	0	0%	N/A	N/A	N/A
Flu A (A/Victoria/361/2011)	Low positive	~95%	0.56	0.75	0.21
Flu A (A/Victoria/361/2011)	Moderate positive	100%	1.5	0.75	0.21
Flu B (B/Mass/2/2012)	Low positive	~95%	0.25	0.40	0.07
Flu B (B/Mass/2/2012)	Moderate positive	100%	0.6	0.40	0.07

Valid results were obtained for 97.5% (351/360 of samples on the first attempt. The indeterminate cases included five NO RESULT-REPEAT TEST results and four INSTRUMENT ERROR results. All nine initially indeterminate cases were retested and eight yielded valid results upon repeat testing. The overall invalid rate was 0.1% (1/360).

Table 5. Reproducibility results data

Sample	Site 1				Site 2				Site 3				% Total Agreement by Sample
	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	
Neg	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (90/90)
Flu A Low Pos	100% (10/10)	100% (10/10)	90.0% (9/10)	96.7% (29/30)	70.0% (7/10)	100% (10/10)	100% (10/10)	90.0% (27/30)	70.0% (7/10)	100% (10/10)	88.9% (8/9)[a]	86.2% (25/29)	91.0% (81/89)
Flu A Mod Pos	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (90/90)
Flu B Low Pos	90.0% (9/10)	100% (10/10)	90.0% (9/10)	93.3% (28/30)	100% (10/10)	100% (10/10)	90.0% (9/10)	96.7% (29/30)	100% (10/10)	70.0% (7/10)	100% (10/10)	90.0% (27/30)	93.3% (84/90)
Flu B Mod Pos	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (10/10)	100% (10/10)	100% (10/10)	100% (30/30)	100% (90/90)

All negative samples produced a negative result (90/90).

All moderate positive samples produced a positive result [Flu A (90/90) and Flu B (90/90)].

The low positive samples were prepared to target a concentration close the limit of detection (LoD) for both sample types. However, this resulted in the low positive samples having a titer lower than the LoD for the NP swab matrix. Overall, 91.0% (81/89) of the Flu A low positive samples and 93.3% (84/90) of the Flu B low positive samples were classified as positive for the corresponding target. Based on the virus titer used and the LoD for the different sample types, the 91% and 93% positive results for the low positive samples are acceptable.

b. Linearity/assay reportable range:
Please refer to submission K162456.

c. Traceability, Stability, controls and calibrators:
Please refer to submission K162456.

Traceability:
Please refer to submission K162456.

Calibrator
Please refer to submission K162456.

Controls
Please refer to submission K162456.

Stability:
Stability studies have been performed to support the following claims:

Sample Stability:
The following specimen stability claims are supported by study data from K162456:

- 15-30°C for up to 24 hours
- 2-8°C for up to seven days

Kit Stability:
The following kit stability claims are supported by study data from K162456:

- 2-28°C for up to 6 months

Cartridge Hold Time:
The following stability claim for prepared samples waiting on the GeneXpert Xpress GX II or IV are supported by study data from K162456:

- Up to 4.5 hours at room temperature

Carryover:
Please refer to submission K162456.

d. Detection limit:

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert Xpress Flu Assay with two lots of reagents across three testing days. The higher LoD observed per strain and per lot was selected for verification. Verification of the estimated LoD claim was performed on one reagent lot across a minimum of three testing days. LoD was established using two influenza A H3N2 strains, two influenza A 2009 H1N1 strains, and two influenza B strains. Viruses were diluted into negative pooled NP swab and NS clinical matrices for testing. The LoD is defined as the lowest concentration (tissue culture infective dose, $TCID_{50}$/mL) per sample that can be reproducibly distinguished from negative samples 95% of the times or the lowest concentration at which 19 of 20 replicates were positive. Each strain was tested in replicates of 20 per concentration of virus in each matrix, in NP swab and NS clinical matrix. The LoD point values for each strain tested are summarized in Table below.

Table 6. Confirmed LoD (TCID50/mL): Influenza A 2009 H1N1

Virus Strain	**Confirmed LoD (TCID50/mL)**	
	NP Swab Matrix	NS Matrix
Influenza A/California/7/2009	0.02	0.02
Influenza A/Florida/27/2011	0.04	0.04

Table 7. Confirmed LoD (TCID50/mL): Influenza A H3N2

Virus Strain	Confirmed LoD (TCID50/mL)	
	NP Swab Matrix	NS Matrix
Influenza A/Perth/16/2009	0.01	0.01
Influenza A/Victoria/361/2011	0.75	0.21

Table 8. Confirmed LoD (TCID50/mL): Influenza B

Virus Strain	Confirmed LoD (TCID50/mL)	
	NP Swab Matrix	NS Matrix
Influenza B/Mass/2/2012	0.40	0.07
Influenza B/Wisconsin/01/2011	0.19	0.17

e. Analytical specificity:

Interfering Substances
Please refer to submission K162456.

Analytical Reactivity (inclusivity)
Please refer to submission K162456

Competitive Interference
Please refer to submission K162456

Cross-Reactivity
Please refer to submission K162456.

f. Assay cut-off:
Please refer to submission K162456.

2. Comparison studies:

a. Method comparison with predicate device:
N/A

b. Matrix comparison:
Equivalency study for NP swab clinical matrix and simulated matrix was described in K162456. This study was repeated for the NS clinical matrix to show equivalency between the nasal swab specimen and simulated matrix.

Simulated matrix consisted of 2.5% (w/v) porcine mucin, 1% (v/v) human whole blood in 0.85% sodium chloride (NaCl) formulated in 1x PBS solution with 15% glycerol, which was then diluted in UTM to a final concentration of 16.7%. The NS clinical matrix was created by pooling negative NS clinical matrix, then aliquoting the pooled matrix and spiking it with the appropriate virus. This study was performed by spiking the NS clinical matrix and simulated matrix with influenza strains at four different concentrations relative to the assay LoD: low positives (2X LoD), medium positives (5X LoD), and high positives (10X and 100X LoD). The virus strains used and their concentration are shown in the table below.

Table 9. Virus strains used in matrix comparision study

Virus Strain	**LoD Estimate ($TCID_{50}$/mL)**	**Concentration ($TCID_{50}$/mL)**			
		2X LoD	**5X LoD**	**10X LoD**	**100X LoD**
Flu A/Florida/27/2011	0.04	0.08	0.2	0.4	4
Flu A/Victoria/361/2011	0.8	1.6	4	8	80
Flu B/Mass/2/2012	0.40	0.8	2	4	40

Table 10. Result data for matrix comparison study

Strain	**Level XLoD**	**Matrix**	**Number Tested**	**Percent Positive**
A_Florida_27_2011	100X	Nasal Swab - NS	5	100%
		Simulated Matrix - SIM	5	100%
	10X	Nasal Swab - NS	10	100%
		Simulated Matrix - SIM	10	100%
	5X	Nasal Swab - NS	10	100%
		Simulated Matrix - SIM	10	100%
	2X	Nasal Swab - NS	40	100%
		Simulated Matrix - SIM	40	100%
A_Victoria_361_2011	100X	Nasal Swab - NS	5	100%
		Simulated Matrix - SIM	5	100%
	10X	Nasal Swab - NS	10	100%
		Simulated Matrix - SIM	10	100%
	5X	Nasal Swab - NS	10	100%
		Simulated Matrix - SIM	10	100%
	2X	Nasal Swab - NS	40	100%
		Simulated Matrix - SIM	40	100%

B_Mass_2012	100X	Nasal Swab - NS	5	100%
		Simulated Matrix - SIM	5	100%
	10X	Nasal Swab - NS	10	100%
		Simulated Matrix - SIM	10	100%
	5X	Nasal Swab - NS	10	100%
		Simulated Matrix - SIM	10	100%
	2X	Nasal Swab - NS	40	100%
		Simulated Matrix - SIM	40	100%
Negative	0	Nasal Swab - NS	10	0%
	0	Simulated Matrix - SIM	10	0%

All samples spiked with virus were positive for the appropriate analyte. These results demonstrate NS clinical matrix and simulated matrix equivalecy for the purposes of the analytical studies conducted in K172456 and in this submission.

3. Clinical studies:

a. Clinical Sensitivity and Specificity:

Clinical Studies

A total of 3610 patients were enrolled in this clinical study, 29 patient specimens were ineligible for inclusion because of improper consent documents, previously enrolled subjects and subjects deemed ineligible by the institutional review board (not an institution of employee). Of the 3576 eligible specimens there were 1784 nasal swabs (NS) and 1792 nasopharyngeal (NP) swabs. Each patient provided either an NS specimen or NP swab specimen. For nasal swab specimens one swab was used to swab both nostrils, only one nostril was swabbed for the NP swab specimen. Specimens were prospectively collected fresh and tested as soon as possible after collection and within 24 hours.

A total of 304 samples were excluded for the following reasons; 235 unresolved comparator result, 6 invalid comparator assay controls, 17 specimen frozen, 14 shipping problem 9 incorrect specimen collection, 8 not tested with GX system, 4 run on incorrect assay, and 4 not tested within protocol specified time period.

There were 3279 eligible specimens evaluated which resulted in 61 indeterminate results (33NO RESULT and 28 INSTRUMENT ERROR), 59 of those were re-tested to yield 54 valid results from repeat testing. The final indeterminate rate was 0.2%.

The total number of eligible samples with valid results was 3272; 54.8% from female subjects and 45.2% from male subjects. The table below shows the distribution of patients by age group and the number of posititves for Flu A and Flu B.

Table 11. Number and Percent of Specimens by Age Range[a]

Age Group	Number of Patients	% of Total	Flu A	Flu B
			Number of Positives by Xpert Xpress Flu	Number of Positives by Xpert Xpress Flu
≤5 years	1288	39.4%	141	58
6-21 years	518	15.8%	133	54
22-59 years	1142	34.9%	122	37
≥60 years	324	9.9%	56	5
Total	3272	100%	452	154

[a]Six subjects had multi-infections by the Xpert Xpress Flu Assay and are therefore counted more than once in this table. Of the 6 subjects with multi-infections, 1 sample Flu A and Flu B POS by comparator assay; 5 samples NEG for both targets by comparator assay.

Performance with Nasal Swabs and Nasopharyngeal Swabs

Table 12. Clinical Performance for Influenza A, Nasal Swabs

Nasal Swab Specimens (1602 specimens)		Comparator Result	
		Positive	Negative
Xpert Xpress Flu Assay	Positive	186	37
	Negative	2	1377

PPA: 98.9% (95% CI: 96.2%-99.7%)
NPA: 97.4% (95%CI: 96.4%-98.1%)

Table 13. Clinical Performance for Influenza A, Nasopharyngeal Swabs

Nasopharyngeal Swab Specimens (1670 specimens)		Comparator Result	
		Positive	Negative
Xpert Xpress Flu Assay	Positive	200	29
	Negative	5	1436

PPA: 97.6% (95% CI: 94.4%-99.0%)
NPA: 98.0% (95%CI: 97.1%-98.6%)

Table 14. Clinical Performance for Influenza B, Nasal Swabs

Nasal Swab Specimens (1602 specimens)		Comparator Result	
		Positive	Negative
Xpert Xpress Flu Assay	Positive	63	12
	Negative	1	1526

PPA: 98.4% (95% CI: 91.7%-99.7%)

NPA: 99.2% (95%CI: 98.6%-99.6%)

Table. 15. Clinical Performance for Influenza B, Nasopharyngeal Swabs

Nasopharyngeal Swab Specimens (1670 specimens)		Comparator Result	
		Positive	Negative
Xpert Xpress Flu Assay	Positive	71	8
	Negative	2	1589

PPA: 97.3% (95% CI: 90.6%-99.2%)
NPA: 99.5% (95%CI: 99.0%-99.7%)

Table 16. Clinical Performance for Influenza A, All Swabs Combined

Combined Swabs (3272 specimens)		Comparator Result	
		Positive	Negative
Xpert Xpress Flu Assay	Positive	386	66
	Negative	7	2813

PPA: 98.2% (95% CI: 96.4% -99.1%)
NPA: 97.7% (95% CI: 97.1% -98.2%)

Table 17. Clinical Performance for Influenza B, All Swabs Combined

Combined Swabs (3272 specimens)		Comparator Result	
		Positive	Negative
Xpert Xpress Flu Assay	Positive	134	20
	Negative	3	3115

PPA: 97.8% (95% CI: 93.8% -99.3%)
NPA: 99.4% (95% CI: 99.0% -99.6%)

4. Clinical cut-off**:**
   N/A

5. Expected values/Reference range:

   Expected prevalence values of influenza A and influenza B infections were calculated using the data acquired from the 3272 prospectively collected NS and NP swab specimens tested with the Xpert Xpress Flu Assay. Results are shown in Table below.

Table 18. Prevalence during the Clinical Study

Age Group	Number of Patients	Flu A		Flu B	
		Number of Positives	Positivity	Number of Positives	Positivity
≤5 years	1288	141	10.9%	58	4.5%
6-21 years	518	133	25.7%	54	10.4%
22-59 years	1142	122	10.7%	37	3.2%
≥60 years	324	56	17.3%	5	1.5%
Total	3272	452	13.8%	154	4.7%

[a]Six subjects had multi-infections by the Xpert Xpress Flu Assay and are therefore counted more than once in this table. Of the 6 subjects with multi-infections, 1 sample Flu A and Flu B POS by comparator assay; 5 samples NEG for both targets by comparator assay.

N. Instrument Name:

This assay can be run on either the GeneXpert Xpress II System or the GeneXpert IV System. Both systems run the GeneXpert Xpress Software version 5.0.

O. System Descriptions:

1. Instrument Name:

   GeneXpert Dx Systems (GX-I, GX-II, GX-IV, GX-XVI) with GeneXpert Dx software version 4.6a or higher

   GeneXpert Infinity-48 System with Xpertise software version 4.6a

   GeneXpert Infinity-80 and Infinity-48s Systems with Xpertise software version 6.2a or higher

2. System Description:

   The GeneXpert Instrument System family (GeneXpert Dx and Infinity Systems) automates and integrates sample purification, nucleic acid amplification and detection of target sequences within compatible, assay-specific, single-use cartridges. The instrument systems each contain a computer and preloaded software for running tests and viewing the results.

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 GeneXpert Instrument Systems are provided with a computer, preloaded with software for running tests and viewing results. Each instrument (Dx and Infinity) contains random access, closed-system, computer-based software and embedded firmware which run dedicated microprocessor-controlled modules to integrate sample preparation, amplification and real-time detection in a single system.

   The GeneXpert Infinity modules contain extra robotic features for cartridge handling. The Xpertise software utilized by the Infinity Systems is the user interface and provides the ordering of tests as well as automates loading and unloading of cartridges into GeneXpert modules within the system. The Xpertise user interface builds upon the existing core software functionality for handling GeneXpert modules for cartridge fluidics control, temperature control, optics control, and data analysis by the addition of automation handling for the robotic arm.

6. Specimen Identification

   Specimens are manually loaded into the Xpert Xpress Flu Assay cartridge by the user. The user can then either scan or type the sample and patient ID into the system. Prior to placing the cartridge into the GeneXpert Instrument System, the barcode on the Xpert Xpress Flu Assay cartridge is scanned. The information contained in the assay barcode is utilized by the software to run the appropriate assay definition file (ADF). If an assay is being run that does not already exist in the GeneXpert database, the user must import the ADF before starting the test.

7. Calibration

   Not required.

8. Quality Control

   Sample Processing Control

   The sample processing control (SPC) is a non-infectious armored RNA pseudovirus that is included in each cartridge to verify that adequate processing of the sample has occurred. The SPC verifies that nucleic acids have been released from the target viruses if the organism is present and detects specimen-associated PCR and RT-PCR inhibitors. The SPC should be POSITIVE in a sample that is negative for influenza A and influenza B target analytes, and can be NEGATIVE or POSITIVE in a sample containing detectable levels of one or both of the target analytes.

Probe Check Control

Before the start of the amplification process, the GeneXpert Instrument Systems measures the fluorescence signal from the probes to monitor bead rehydration, reaction tube filling, probe integrity, and dye stability. All assay reagents must be present and intact for the PCC to pass the validated acceptance criteria. If any of the PCC conditions fail, the result is reported as an ERROR and the test must be repeated using a new assay cartridge.

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

Not Applicable

Q. Proposed Labeling:

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

R. Conclusion:

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