July 24, 2018

Cepheid
Jim Kelly, Ph.D.
Executive Director, Regulatory Affairs
904 Caribbean Drive
Sunnyvale, California 94089

Re: K180218
Trade/Device Name: Xpert Xpress Flu/RSV, Xpert Nasopharyngeal Sample Collection Kit, Xpert Nasal Sample Collection Kit, GeneXpert Xpress II, GeneXpert Xpress IV
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OCC, OOI, JSM
Dated: January 24, 2018
Received: January 25, 2018

Dear Jim Kelly:

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 Part 801 and Part 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.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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 comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Steven R. Gitterman -S for

Uwe Scherf, 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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K180218

Device Name
Cepheid Xpert® Xpress Flu/RSV Assay

Indications for Use *(Describe)*
Device Intended Use:

The Cepheid Xpert® Xpress Flu/RSV 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 Xpress Flu/RSV Assay uses nasopharyngeal (NP) swab and nasal swab (NS) specimens collected from patients with signs and symptoms of respiratory infection. The Xpert Xpress Flu/RSV Assay is intended as an aid in the diagnosis of influenza and respiratory syncytial virus infections in conjunction with clinical and epidemiological risk factors.
Negative results do not preclude influenza virus 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 influenza A/H3N2 and A/HINI pandemic were the predominant influenza A viruses in circulation. 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 Nasopharyngeal Swab Specimen Collection Kit for Viruses:
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.

Ancillary Nasal Swab Specimen Collection Kit for Viruses:
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/RSV Assay and the Xpert Xpress Flu Assay.

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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8.0 510(k) Summary

As required by 21 CFR Section 807.92(c).

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (408) 400-6838
Contact:	Yi-Ping Lin, PhD
Date of Preparation:	May 18, 2018
Device:	
Trade name:	Xpert® Xpress Flu/RSV
Common name:	Xpert Xpress Flu/RSV Assay
Type of Test:	Automated, multiplex real-time reverse transcription-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.
Regulation number/ Classification name/ Product code:	866.3980/Respiratory viral panel multiplex nucleic acid assay/OCC 866.2570/Instrumentation for clinical multiplex test systems/OOI
Classification Advisory Panel	Class II Microbiology (83)
Prescription Use	Yes
Predicate Devices Assay:	1) *For the detection and differentiation of influenza A, influenza B, and RSV A/B viral RNA in nasopharyngeal swab specimens:* Xpert® Flu+RSV Xpress Assay [510(k) #K151226] 2) *For the Sample Collection Kits:* Cepheid Xpert® Nasopharyngeal Sample Collection Kit for Viruses[510(k) # K171552] Cepheid Xpert® Nasal Sample Collection Kit for Viruses [510(k) # K171552]

Device Description:

The Xpert Xpress Flu/RSV Assay is a rapid, automated *in vitro* diagnostic test for qualitative detection and differentiation of influenza A (Flu A), influenza B (Flu B), and respiratory syncytial virus (RSV) viral RNA directly from nasopharyngeal (NP) swab and nasal swab (NS) specimens. The assay is performed on the Cepheid GeneXpert® Xpress System.

The Xpert Xpress Flu/RSV Assay includes reagents for the detection and differentiation of influenza A, influenza B, and RSV viral RNA directly from NP swab and NS specimens from patients with signs and symptoms of respiratory tract infection. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are internal controls utilized by the GeneXpert Xpress System platform. The SPC is present to control for an adequate extraction and processing of the target sequences and to monitor for the presence of inhibitor in the PCR reaction. The PCC verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The specimens are collected in viral transport medium and transported to the GeneXpert Xpress area. The specimen is prepared according to package insert instructions and transferred to the sample chamber (large opening) of the Xpert Xpress Flu/RSV Assay cartridge. The GeneXpert cartridge is loaded onto the GeneXpert Xpress System platform, which performs hands-off automated sample processing and real-time RT-PCR for detection of Flu and RSV viral RNA. Summary and detailed test results are obtained in approximately 30 minutes or less. The results are automatically generated at the end of the process in a report that can be viewed and printed.

Device Intended Use:

The Cepheid Xpert® Xpress Flu/RSV 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 Xpress Flu/RSV Assay uses nasopharyngeal (NP) swab and nasal swab (NS) specimens collected from patients with signs and symptoms of respiratory infection. The Xpert Xpress Flu/RSV Assay is intended as an aid in the diagnosis of influenza and respiratory syncytial virus infections in conjunction with clinical and epidemiological risk factors.

Negative results do not preclude influenza virus or RSV 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 influenza A/H3N2 and A/HINI pandemic were the predominant influenza A viruses in circulation. 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 Nasopharyngeal Swab Specimen Collection Kit for Viruses

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.

Ancillary Nasal Swab Specimen Collection Kit for Viruses

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/RSV Assay and the Xpert Xpress Flu Assay.

Substantial Equivalence**:**

The Xpert Xpress Flu/RSV Assay is substantially equivalent to the current Xpert® Flu+RSV Xpress Assay [510(k) #K151226]. The Xpert Xpress Flu/RSV Assay detects influenza A, influenza B, and RSV from nasopharyngeal (NP) swab and nasal swab (NS) specimens and the Xpert® Flu+RSV Xpress Assay detects influenza A, influenza B, and RSV from NP swab specimens. Both assays utilize the same technology by determining the presence of the target organisms through real-time RT-PCR amplification and fluorogenic target-specific hybridization detection. A multi-center clinical study was conducted and obtained data using the Xpert Xpress Flu/RSV Assay. The data were used to determine the performance characteristics of the Xpert Xpress Flu/RSV Assay relative to the reference test. The reference test was FDA cleared for testing for Flu with NP swab and NS specimens and for testing for RSV with NP swab specimens. For these studies the reference test was also validated for testing for RSV with NS specimens. The study results showed that the Xpert Xpress Flu/RSV Assay is acceptable for its intended use and is substantially equivalent to the predicate device.

Table 8-1 shows the similarities and differences between the Xpert Xpress Flu/RSV Assay and the predicate device.

Table 8-1: Comparison of Similarities and Differences of the Xpert Xpress Flu/RSV Assay with the Predicate Devices

Similarities		
	Device	**Predicate**
Item	**Cepheid Xpert® Xpress Flu/RSV**	**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

Similarities		
	Device	**Predicate**
Item	**Cepheid Xpert® Xpress Flu/RSV**	**Cepheid Xpert® Flu+RSV Xpress Assay 510(k)# K151226**
Intended Use	The Cepheid Xpert® Xpress Flu/RSV 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 Xpress Flu/RSV 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 and respiratory syncytial virus infections in conjunction with clinical and epidemiological risk factors. Negative results do not preclude influenza virus or RSV 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-	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

Similarities		
	Device	**Predicate**
Item	**Cepheid Xpert® Xpress Flu/RSV**	**Cepheid Xpert® Flu+RSV Xpress Assay 510(k)# K151226**
	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.	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.
Indication for Use	Patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors	Same
Nucleic Acid Extraction	Yes	Same
Extraction Methods	Sample preparation integrated in GeneXpert Cartridge and GeneXpert Xpress System	Same

Similarities		
	Device	**Predicate**
Item	**Cepheid Xpert® Xpress Flu/RSV**	**Cepheid Xpert® Flu+RSV Xpress Assay 510(k)# K151226**
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.	Same
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.	Same

Similarities		
	Device	**Predicate**
Item	**Cepheid Xpert® Xpress Flu/RSV**	**Cepheid Xpert® Flu+RSV Xpress Assay 510(k)# K151226**
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	Same
Internal Controls	Sample processing control (SPC) and probe check control (PCC).	Same
Early assay termination function	Yes	Yes
Assay Targets	Influenza A, Influenza B, and RSV viral RNA	Same
Assay Controls	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.	Same
Combinatorial Assay Selections	Yes, user may select combined assay with all targets or a Flu only assay or a RSV only assay.	Same

Differences		
	Device	**Predicate**
Item	**Cepheid Xpert® Xpress Flu/RSV**	**Cepheid Xpert® Flu+RSV Xpress Assay 510(k)# K151226**
Specimen Types	Nasopharyngeal (NP) swab and nasal swab (NS) specimens	Nasopharyngeal (NP) swab specimens
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

The Xpert Xpress Flu/RSV Assay and the predicate device have the same general intended use and technological characteristics, and both detect influenza A, influenza B, and RSV viral RNA from NP swab specimens. The clinical study demonstrates that the Xpert Xpress Flu/RSV Assay is acceptable for its intended use and is substantially equivalent to the predicate device.

The predicate device for the ancillary specimen collection kit, the Xpert Nasopharyngeal Sample Collection Kit for Viruses is the Cepheid Nasopharyngeal Sample Collection Kit for Viruses, [510(k) # K171552]. The similarities are shown in Table 8-2. There is no

difference between the Nasopharyngeal Sample Collection Kit for Viruses cleared in 510(k) # K171552 and this 510(k).

The predicate device for the ancillary specimen collection kit, the Xpert Nasal Sample Collection Kit for Viruses is the Xpert Nasal Sample Collection Kit for Viruses, [510(k) # K171552]. The similarities and differences are shown in Table 8-3.

Table 8-2: Comparison of Similarities of the Xpert Nasopharyngeal Sample Collection Kit with the Predicate Device

Similarities		
Item	**Device**	**Predicate**
	Xpert® Nasopharyngeal Sample Collection Kit for Viruses	**Xpert® Nasopharyngeal Sample Collection Kit for Viruses** **510(k)#** K171552
Intended 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.	Same
Single-use Device	Yes	Same

Similarities		
Item	**Device**	**Predicate**
	Xpert® Nasopharyngeal Sample Collection Kit for Viruses	**Xpert® Nasopharyngeal Sample Collection Kit for Viruses** **510(k)#** K171552
Transport Medium Formulation	Hank's Balanced Salt Solution Bovine Serum Albumin L-cysteine Gelatin Sucrose L-glutamic acid HEPES buffer Vancomycin Amphotericin B Colistin Phenol red	Same
pH	7.3 ± 0.2	Same
Storage Temperature	2 - 25°C (refrigerated and room temperature)	Same
Volume	3 ml	Same
Glass Beads	3 x 3 mm	Same
Container	Plastic (medical-grade polypropylene)	Same
Product Configuration	Medium Tube in Kit with individually-wrapped sterile swab.	Same

Table 8-3: Comparison of Similarities and Differences of the Xpert Nasal Sample Collection Kit for Viruses with the Predicate Device

Similarities		
Item	**Device**	**Predicate**
	Xpert® Nasal Sample Collection Kit for Viruses	**Xpert® Nasal Sample Collection Kit for Viruses 510(k)#** K171552
Intended 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/RSV and the Xpert Xpress Flu Assay.	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.
Single-use Device	Yes	Same

Similarities		
Item	**Device**	**Predicate**
	Xpert® Nasal Sample Collection Kit for Viruses	**Xpert® Nasal Sample Collection Kit for Viruses 510(k)#** K171552
Transport Medium Formulation	Hank's Balanced Salt Solution Bovine Serum Albumin L-cysteine Gelatin Sucrose L-glutamic acid HEPES buffer Vancomycin Amphotericin B Colistin Phenol red	Same
pH	7.3 $\pm$ 0.2	Same
Storage Temperature	2 - 25^{o}C (refrigerated and room temperature)	Same
Volume	3 ml	Same
Glass Beads	3 x 3 mm	Same
Container	Plastic (medical-grade polypropylene)	Same
Product Configuration	Medium Tube in Kit with individually-wrapped sterile swab.	Same
Swab	Nylon flocked	Same

Differences		
	Device	**Predicate**
Item	**Xpert Nasal Sample Collection Kit for Viruses**	**Xpert® Nasal Sample Collection Kit for Viruses 510(k)#** K171552
Intended Use	For collection, preservation and transport of nasal swab specimens containing viruses from patients with signs and symptoms of respiratory infection prior to analysis with the Xpert Xpress Flu/RSV and the Xpert Xpress Flu Assay.	For collection, preservation and transport of nasal swab specimens containing viruses from patients with signs and symptoms of respiratory infection prior to analysis with the Xpert Xpress Flu.

The proposed collection kits and predicate collection kits have the same general intended use and the same technology to collect, store and transport clinical specimens, including viruses, to the laboratory for further testing. The prospective component of the multi-center clinical study of the Xpert Xpress Flu/RSV Assay was conducted using Xpert Nasopharyngeal Sample Collection Kit for Viruses [510(k) # K171552] and Xpert Nasal Sample Collection Kit for Viruses [510(k) # K171552] demonstrating that the Xpert Nasopharyngeal Sample Collection Kit for Viruses and Xpert Nasal Sample Collection Kit for Viruses are acceptable for their intended use and substantially equivalent to the predicate devices.

Non-Clinical Studies:

Analytical Sensitivity (Limit of Detection)

Studies were performed to determine the analytical limit of detection (LoD) of the Xpert Xpress Flu/RSV 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, two influenza B strains, two respiratory syncytial virus A (RSV A) strains and two respiratory syncytial virus B (RSV 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 with 95% confidence 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 NSclinical matrix. The LoD point values for each strain tested are summarized in Tables 8-4 – 8-6.

Table 8-4 Confirmed LoD ($TCID_{50}$/mL): Influenza A 2009 H1N1

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
Influenza A/California/7/2009	0.020	0.018
Influenza A/Florida/27/2011	0.040	0.04

Table 8-5 Confirmed LoD ($TCID_{50}$/mL): Influenza A H3N2

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
Influenza A/Perth/16/2009	0.013	0.006
Influenza A/Victoria/361/2011	0.750	0.21

Table 8-6 Confirmed LoD ($TCID_{50}$/mL): Influenza B

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
Influenza B/Mass/2/2012	0.400	0.07
Influenza B/Wisconsin/01/2011	0.190	0.17

Table 8-7 Confirmed LoD ($TCID_{50}$/mL): Respiratory Syncytial Virus A

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
RSV A/2/Australia/61	0.870	0.32
RSV A/Long/MD/56	1.100	0.45

Table 8-8 Confirmed LoD ($TCID_{50}$/mL): Respiratory Syncytial Virus B

Virus Strain	Confirmed LoD Probit ($TCID_{50}$/mL)	
	NP Swab	NS
RSV B/Wash/18537/62	0.790	0.29
RSV B/9320/MA/77	2.300	0.35

Analytical Specificity (Exclusivity)

The analytical specificity of the Xpert Xpress Flu/RSV Assay was evaluated by testing a panel of 44 cultures consisting of 16 viral, 26 bacterial, and two yeast strains representing common respiratory pathogens or those potentially encountered in the nasal passage and nasopharynx. Three replicates of all bacterial and yeast strains were tested at concentrations of $\geq 1 \times 10^6$ CFU/mL with the exception of one strain that was tested at 1×10^5 CFU/mL (*Chlamydia pneumoniae*). Three replicates of all viruses

were tested at concentrations of ≥ 1 x 10^5 $TCID_{50}$/mL. The analytical specificity was 100%. Results are shown in Table 8-7.

Table 8-7 Analytical Specificity of the Xpert Xpress Flu/RSV Assay

Organism	Concentration (per cartridge)	Result		
		Influenza A	Influenza B	RSV
No Template Control	N/A	NEG	NEG	NEG
Adenovirus Type 1	1.12E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Adenovirus Type 7	1.87E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human coronavirus OC43	2.85E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human coronavirus 229E	1.00E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Cytomegalovirus	1.00E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Echovirus	3.31E+07 $TCID_{50}$/mL	NEG	NEG	NEG
Enterovirus	3.55E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Epstein Barr Virus	7.16E+07 $TCID_{50}$/mL	NEG	NEG	NEG
HSV	8.90E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Measles	6.31E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human metapneumovirus	1.00E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Mumps virus	6.31E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Human parainfluenza Type 1	1.15E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Human parainfluenza Type 2	6.31E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Human parainfluenza Type 3	3.55E+06 $TCID_{50}$/mL	NEG	NEG	NEG
Rhinovirus Type 1A	1.26E+05 $TCID_{50}$/mL	NEG	NEG	NEG
Acinetobacter baumannii	1.00E+06 CFU/mL	NEG	NEG	NEG
Burkholderia cepacia	3.30E+06 CFU/mL	NEG	NEG	NEG
Candida albicans	3.20E+06 CFU/mL	NEG	NEG	NEG
Candida parapsilosis	3.00E+06 CFU/mL	NEG	NEG	NEG
Bordetella pertussis	3.30E+06 CFU/mL	NEG	NEG	NEG
Chlamydia pneumoniae	1.00E+05 CFU/mL	NEG	NEG	NEG
Citrobacter freundii	3.30E+06 CFU/mL	NEG	NEG	NEG
Corynebacterium sp.	3.30E+06 CFU/mL	NEG	NEG	NEG
Escherichia coli	1.00E+07 CFU/mL	NEG	NEG	NEG
Enterococcus faecalis	1.30E+06 CFU/mL	NEG	NEG	NEG
Hemophilus influenzae	1.00E+06 CFU/mL	NEG	NEG	NEG
Lactobacillus reuteri	1.00E+06 CFU/mL	NEG	NEG	NEG
Legionella spp.	1.00E+06 CFU/mL	NEG	NEG	NEG
Moraxella catarrhalis	1.00E+07 CFU/mL	NEG	NEG	NEG

Organism	Concentration (per cartridge)	Result		
		Influenza A	Influenza B	RSV
Mycobacterium tuberculosis (avirulent)	1.00E+06 CFU/mL	NEG	NEG	NEG
Mycoplasma pneumoniae	1.00E+06 CFU/mL	NEG	NEG	NEG
Neisseria meningitides	2.15E+06 CFU/mL	NEG	NEG	NEG
Neisseria mucosa	1.00E+07 CFU/mL	NEG	NEG	NEG
Propionibacterium acnes	2.40E+07 CFU/mL	NEG	NEG	NEG
Pseudomonas aeruginosa	3.70E+06 CFU/mL	NEG	NEG	NEG
*Staphylococcus aureus (*protein A producer)	2.20E+06 CFU/mL	NEG	NEG	NEG
Staphylococcus epidermidis	3.40E+06 CFU/mL	NEG	NEG	NEG
Staphyloccus haemolyticus	4.00E+06 CFU/mL	NEG	NEG	NEG
Streptococcus agalactiae	3.50E+06 CFU/mL	NEG	NEG	NEG
Streptococcus pneumoniae	1.00E+06 CFU/mL	NEG	NEG	NEG
Streptococcus pyogenes	1.00E+07 CFU/mL	NEG	NEG	NEG
Streptococcus salivarius	1.00E+07 CFU/mL	NEG	NEG	NEG
Streptococcus sanguinis	3.10E+06 CFU/mL	NEG	NEG	NEG

Analytical Reactivity (Inclusivity)

The analytical reactivity of the Xpert Xpress Flu/RSV Assay was evaluated against multiple strains of influenza A H1N1 (seasonal pre-2009), influenza A H1N1 (pandemic 2009), influenza A H3N2 (seasonal), avian influenza A (H5N1, H5N2, H6N2, H7N2, H7N3, H2N2, H7N9, and H9N2), influenza B (representing strains from both Victoria and Yamagata lineages), and respiratory syncytial virus subgroups A and B (RSV A and RSV B) at levels near the analytical LoD. A total of 53 strains comprised of 48 influenza viruses (35 influenza A and 13 influenza B) and 5 RSV strains were tested in this study with the Xpert Xpress Flu/RSV Assay. Three replicates were tested for each strain. All Flu and RSV strains tested positive in all three replicates, except for one Flu A H1N1 strain (A/New Jersey/8/76), which tested positive in 2 of 3 replicates at 0.1 $TCID_{50}$/mL. Results are shown in Table 8-8.

Predicted cross reactivity from *in silico* analyses showed 100% sequence homology for additional pH1N1 strains.

Table 8-8 Analytical Reactivity (Inclusivity) of the Xpert Xpress Flu/RSV Assay

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
No Template Control		n/a	NEG	NEG	NEG
Influenza A H1N1 (pre-2009)	A/swine/Iowa/15/30	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/WS/33	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/PR/8/34	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Mal/302/54	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Denver/1/57	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/New Jersey/8/76	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/New Caledonia/20/1999	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/New York/55/2004	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Soloman Island/3/2006	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Taiwan/42/06	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Brisbane/59/2007	0.1 $TCID_{50}$/mL	POS	NEG	NEG
Influenza A H1N1 (pdm2009)	A/swine/NY/02/2009	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Colorado/14/2012	0.1 $TCID_{50}$/mL	POS	NEG	NEG
	A/Washington/24/2012	0.1 $TCID_{50}$/mL	POS	NEG	NEG
Influenza A H3N2 (Seasonal)	A/Aichi/2/68	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/HongKong/8/68	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Port Chalmers/1/73	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Hawaii/15/2001	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Wisconsin/67/05	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Brisbane/10/2007	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Minnesota/11/2010 (H3N2)v	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Indiana/08/2011 (H3N2)v	2.0 $TCID_{50}$/mL	POS	NEG	NEG
	A/Texas/50/2012	2.0 $TCID_{50}$/mL	POS	NEG	NEG
Avian influenza	A/duck/Hunan/795/2002 (H5N1)	≤ 1ρg/μL[a]	POS	NEG	NEG

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
A	A/chicken/Hubei/327/2004 (H5N1)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/Anhui/01/2005 (H5N1)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/Japanese white eye/ Hong Kong/ 1038/2006 (H5N1)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/mallard/WI/34/75 (H5N2)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/chicken/CA431/00 (H6N2)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/duck/LTC-10-82743/1943 (H7N2)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/chicken/NJ/15086-3/94 (H7N3)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/Anhui/1/2013 (H7N9)	N/A[b]	POS	NEG	NEG
	A/Shanghai/1/2013 (H7N9)	N/A[b]	POS	NEG	NEG
	A/chicken/Korea/38349-p96323/ 1996 (H9N2)	≤ 1ρg/μL[a]	POS	NEG	NEG
	A/Mallard/NY/6750/78 (H2N2)	≤ 1ρg/μL[a]	POS	NEG	NEG
Influenza B	B/Lee/40	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Allen/45	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/GL/1739/54	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Maryland/1/59	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Panama/45/90[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Florida/07/2004[d]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Florida/02/06[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Florida/04/06[d]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Hong Kong/5/72	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Wisconsin/01/2010[d]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Malaysia/2506/04[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG
	B/Taiwan/2/62	1.0 $TCID_{50}$/mL	NEG	POS	NEG

Virus	Strain	Target Concentration	Result		
			Flu A	Flu B	RSV
	B/Brisbane/60/2008[c]	1.0 $TCID_{50}$/mL	NEG	POS	NEG

a. Purified viral RNA in simulated background matrix was used for avian influenza A viruses due to biosafety regulations.
b. Inactivated avian influenza A (H7N9) viruses without viral titer was diluted 100,000 fold in simulated background matrix and tested due to biosafety regulations.
c. Known Victoria lineage.
d. Known Yamagata lineage.

Potentially Interfering Substances

In a non-clinical study, potentially interfering substances that may be present in the nasal passage and nasopharynx were evaluated directly relative to the performance of the Xpert Xpress Flu/RSV Assay. Potentially interfering substances in the nasal passage and nasopharynx may include, but are not limited to: blood, nasal secretions or mucus, and nasal and throat medications used to relieve congestion, nasal dryness, irritation, or asthma and allergy symptoms, as well as antibiotics and antivirals. Negative samples (n = 8) were tested per each substance to determine the effect on the performance of the sample processing control (SPC). Positive samples (n = 8) were tested per substance with six influenza (four influenza A and two influenza B) and four RSV (two RSV A and two RSV B) strains spiked at 3X the analytical LoD determined for each strain. All results were compared to positive and negative simulated background matrix controls. The simulated background 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 1:5 in UTM.

The evaluated substances are listed in Table 8-9 with active ingredients and concentrations tested shown. None of the substances caused interference of the assay at the concentrations tested in this study. All positive and negative replicates were identified correctly using the Xpert Xpress Flu/RSV Assay.

Table 8-9 Potentially Interfering Substances in the Xpert Xpress Flu Assay

Substance/Class	Description/Active Ingredient	Concentration Tested
Control	Simulated background matrix	100% (v/v)
Beta-adrenergic bronchodilator	Albuterol Sulfate	0.83 mg/mL (equivalent to 1 dose per day)
Blood	Blood (Human)	2% (v/v)
BD™ Universal Viral Transport System	Transport Media	100% (v/v)
Remel M4®	Transport Media	100% (v/v)
Remel M4RT®	Transport Media	100% (v/v)
Remel M5®	Transport Media	100% (v/v)
Remel M6®	Transport Media	100% (v/v)
Throat lozenges, oral anesthetic and analgesic	Benzocaine, Menthol	1.7 mg/mL
Mucin	Purified Mucin protein (Bovine or porcine submaxillary gland)	2.5% (w/v)
Antibiotic, nasal ointment	Mupirocin	10 mg/mL
Saline Nasal Spray	Sodium Chloride (0.65%)	15% (v/v)
Anefrin Nasal Spray	Oxymetazoline, 0.05%	15% (v/v)
PHNY Nasal Drops	Phenylephrine, 0.5%	15% (v/v)
Tamiflu Anti-viral drug	Zanamivir	7.5 mg/mL
Antibacterial, systemic	Tobramycin	4 µg/mL
Zicam Nasal Gel	Luffa opperculata, Galphimia glauca, Histaminum hydrochloricum Sulfur	15% (w/v)
Nasal corticosteroid	Fluticasone Propionate	5 µg/mL

Carry-Over Contamination

A study was conducted to demonstrate that single-use, self-contained GeneXpert cartridges prevent carry-over contamination of negative samples when followed by very high positive samples in the same GeneXpert module. The study consisted of a negative sample processed in the same GeneXpert module immediately followed by a very high influenza A sample (A/Victoria/361/2011, $2x10^7$ $TCID_{50}$/mL) or a very high RSV A

sample (A/Long/MD/26, $1x10^4$ $TCID_{50}$/mL) spiked into a simulated background matrix. This testing scheme was repeated 20 times on two GeneXpert modules for a total of 82 runs resulting in 40 positive and 42 negative specimens for each virus type. All 40 positive samples were correctly reported as Flu A POSITIVE; Flu B NEGATIVE; RSV NEGATIVE or Flu A NEGATIVE; Flu B NEGATIVE;RSV POSITIVE. All 42 negative samples were correctly reported as Flu A NEGATIVE; Flu B NEGATIVE; RSV NEGATIVE.

Competitive Interference Study

Competitive interference of the assay caused by the presence of two targets in the Xpert Xpress Flu/RSV Assay was evaluated by testing individual influenza strains and RSV strains near the LoD in the presence of different influenza strains at a higher concentration in a simulated background matrix. Analytical competitive interference was assessed using one (1) seasonal Flu A H3 strain (H3/Victoria/361/2011) at 0.8 $TCID_{50}$/mL, one (1) Flu B strain (B/Mass/2/2012) at 0.45 $TCID_{50}$/mL, one (1) RSV A strain (RSV-A/2/Australia/61) at 1.1 $TCID_{50}$/mL and one (1) RSV B strain (RSV-B/Wash/18537/62) at 0.9 $TCID_{50}$/mL; the strains were tested at in the presence of competing strains at either 1×10^2 $TCID_{50}$/mL or 1×10^3 $TCID_{50}$/mL. Replicates of 20 were tested for each target strain and each competitive strain combination. The normal binomial distribution with 20 replicate samples at LoD is between 17 and 20 positive results based on the binomial distribution with N=20, p=0.95 (X~Bin(20,0.95)). Therefore, sets of 20 with 16 or less positives would be rare and an indication of a competitive inhibitory effect due to high levels of a competing analyte.

- With Flu A/Victoria/361/2011 at a concentration of 0.8 $TCID_{50}$/mL no competitive inhibitory effects were observed in the presence of $1x10^3$ TCID50/mL of Flu B/Mass/2//2012; $1x10^3$ $TCID_{50}$/mL of RSV-A/2/Australia/6; or $1x10^4$ $TCID_{50}$/mL of RSV-B/Wash/18537/62.
- With Flu B/Mass/2/2012 at a concentration of 0.45 $TCID_{50}$/mL competitive inhibitory effects were observed in the presence of $1x10^3$ $TCID_{50}$/mL of Flu

A/Victoria/361/2011. No competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011; $1x10^3$ $TCID_{50}$/mL of RSV-A/2/Australia/6; or $1x10^3$ $TCID_{50}$/mL of RSV-B/Wash/18537/62.

- With RSV-A/2/Australia/6 at a concentration of 1.1 $TCID_{50}$/mL competitive inhibitory effects were observed in the presence of $1x10^3$ $TCID_{50}$/mL of Flu A/Victoria/361/2011. No competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011; or $1x10^3$ $TCID_{50}$/mL of Flu B/Mass/2/2012.
- With RSV-B/Wash/18537/62 at a concentration of 0.9 $TCID_{50}$/mL competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011 or $1x10^3$ $TCID_{50}$/mL of Flu B/Mass/2/2012. No competitive inhibitory effects were observed in the presence of 10 $TCID_{50}$/mL of Flu A/Victoria/361/2011; or $1x10^2$ $TCID_{50}$/mL of Flu B/Mass/2/2012. When the concentration of RSV-B/Wash/18537/62 was increased to 1.6 $TCID_{50}$/mL, no competitive inhibitory effects were observed in the presence of $1x10^2$ $TCID_{50}$/mL of Flu A/Victoria/361/2011; or $1x10^3$ $TCID_{50}$/mL of Flu B/Mass/2/2012.

Under the conditions of this study, internal competitive inhibitory effects were observed on the targets (Flu A, Flu B, and RSV) in the presence of two targets for the Xpert Xpress Flu/RSV Assay. The competitive inhibitory effect on the Xpert Xpress Flu/RSV targets is addressed in the Limitations section of this Package Insert.

Clinical Studies

Clinical Comparison Study

Performance characteristics of the Xpert Xpress Flu/RSV Assay were evaluated at fourteen institutions in the U.S. during the 2016-2017 influenza season.

Specimens were collected from the following:

- Individuals exhibiting signs and symptoms of respiratory infection who provided

informed consent for the collection of a NS or NP swab specimen.

The Xpert Xpress Flu/RSV Assay performance was compared to FDA-cleared molecular comparator assay.

Overall Results

A total of 3265 specimens (1598 NS and 1667 NP swab) were tested for influenza A, influenza B by the Xpert Xpress Flu/RSV Assay and the comparator method.

For NS specimens, the Xpert Xpress Flu/RSV Assay demonstrated a positive percent agreement (PPA) and a negative percent agreement (NPA) relative to the comparator method of 98.9% and 97.5% for the detection of influenza A and 98.4% and 99.3% for influenza B, respectively (Table 8-10).

For NP swab specimens, the Xpert Xpress Flu/RSV Assay demonstrated a PPA and NPA relative to the comparator method of 97.6% and 98.2% for the detection of influenza A and 97.3% and 99.6% for influenza B, respectively (Table 8-10).

For the combined dataset, the Xpert Xpress Flu/RSV Assay demonstrated a PPA and NPA relative to the comparator method of 98.2% and 97.9% for the detection of influenza A and 97.8% and 99.4% for influenza B, respectively (Table 8-10).

A total of 3103 specimens (1543 NS and 1560 NP swab) were tested for RSV by the Xpert Xpress Flu/RSV Assay and the comparator assay.

For NS specimens, the Xpert Xpress Flu/RSV Assay demonstrated a PPA and NPA relative to the comparator method of 98.2% and 99.1% for detection of RSV, respectively (Table 8-10).

For NP swab specimens, the Xpert Xpress Flu/RSV Assay demonstrated a PPA and NPA relative to the comparator method of 98.2% and 98.5% for detection of RSV, respectively (Table 8-10).

For the combined dataset, the Xpert Xpress Flu/RSV Assay demonstrated a PPA and NPA relative to the comparator method of 98.2% and 98.8% for the detection of RSV, respectively (Table 8-10).

Table 8-10 Xpert Xpress Flu/RSV Assay Performance

Target[a]	Specimen Type	N	TP	FN	TN	FP	PPA (95% CI)	NPA (95% CI)
Flu A	NS	1598	186	2[b]	1375	35[c]	98.9 (96.2-99.7)	97.5% (96.6-98.2)
	NP	1667	200	5[d]	1436	26[e]	97.6% (94.4-99.0)	98.2% (97.4-98.8)
	Overall	3265	386	7[f]	2811	61[g]	98.2% (96.4-99.1)	97.9% (97.3-98.3)
Flu B	NS	1598	63	1[h]	1523	11[i]	98.4% (91.7-99.7)	99.3% (98.7-99.6)
	NP	1667	71	2[j]	1587	7[k]	97.3% (90.6-99.2)	99.6% (99.1-99.8)
	Overall	3265	134	3[l]	3110	18[m]	97.8% (93.8-99.3)	99.4% (99.1-99.6)
RSV	NS	1543	269	5[n]	1257	12[o]	98.2% (95.8-99.2)	99.1% (98.4-99.5)
	NP	1560	275	5[p]	1261	19[q]	98.2% (95.9-99.2)	98.5% (97.7-99.0)
	Overall	3103	544	10[r]	2518	31[s]	98.2% (96.7-99.0)	98.8% (98.3-99.1)

[a] Five specimens were positive for both Flu A and Flu B.

[b]Discrepant Testing: 1 of 2 Flu A NEG; 1 of 2 Flu A POS.

[c]Discrepant Testing: 17 of 35 Flu A NEG; 11 of 35 Flu A POS; 7 of 35 inconclusive.

[d]Discrepant Testing: 3 of 5 Flu A NEG; 2 of 5 Flu A POS.

[e]Discrepant Testing: 11 of 26 Flu A NEG; 9 of 26 Flu A POS; 6 of 26 inconclusive.

[f]Discrepant Testing: 4 of 7 Flu A NEG; 3 of 7 Flu A POS.

[g]Discrepant Testing: 26 of 61 Flu A NEG; 22 of 61 Flu A POS; 13 of 61 inconclusive

[h]Discrepant Testing: 1 of 1 inconclusive.

[i]Discrepant Testing: 5 of 11 Flu B POS; 6 of 11 inconclusive.

[j]Discrepant Testing: 1 of 2 Flu B POS; 1 of 2 inconclusive.

[k]Discrepant Testing: 1 of 7 Flu B NEG; 5 of 7 Flu B POS; 1 of 7 inconclusive.

[l]Discrepant Testing: 1 of 3 Flu B POS; 2 of 3 inconclusive

[m]Discrepant Testing: 1 of 18 Flu B NEG; 10 of 18 Flu B POS; 7 of 18 inconclusive

[n]Discrepant Testing: 3 of 5 RSV NEG; 1 of 5 inconclusive; 1 of 5 not done.

[o]Discrepant Testing: 5 of 12 RSV NEG; 3 of 12 RSV POS, 4 of 12 inconclusive.

[p]Discrepant Testing: 2 of 5 RSV NEG; 2 of 5 inconclusive; 1 of 5 not done.

[q]Discrepant Testing: 6 of 19 RSV NEG; 2 of 19 RSV POS, 6 of 19 inconclusive; 5 of 19 not done.

[r]Discrepant Testing: 5 of 10 RSV NEG; 3 of 10 inconclusive; 2 of 10 not done.

[s]Discrepant Testing: 11 of 31 RSV NEG; 5 of 31 RSV POS; 10 of 31 inconclusive; 5 of 31 not done.

Of the Xpert Xpress Flu/RSV Assay runs performed with eligible specimens, 98.0% (3212/3279) of these specimens were successful on the first attempt. The remaining 67 gave indeterminate results on the first attempt (38 NO RESULT-REPEAT TEST results and 29 INSTRUMENT ERROR). Fifty-eight of the 67 indeterminate cases were retested, of which 53 yielded valid results upon repeat testing; nine specimens were not retested. The overall rate of assay success was 99.6% (3265/3279). The overall indeterminate rate was 0.4%.

Reproducibility Study

Reproducibility was established in a multi-center, blinded study using a 7-member specimen panel. Testing was performed at three sites using the GeneXpert Xpress System.

Testing was conducted for five (not necessarily consecutive) days, with one lot of Xpert Xpress Flu/RSV cartridges. Each site had three operators, who tested each panel twice each day. Results are summarized in Table 8-11.

Table 8-11 Summary of Reproducibility Results

Sample	Titer of Virus ($TCID_{50}$/mL)	Site 1				Site 2				Site 3				% Total Agreement by Sample[a]
		Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	Op 1	Op 2	Op 3	Site	
Neg	0	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	0.75	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)[b]	86.2% (25/29)	91.0% (81/89)
Flu A Mod Pos	1.5	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	0.2	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	0.4	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)
RSV Low Pos	1.1	80.0% (8/10)	90.0% (9/10)	100% (10/10)	90.0% (27/30)	100% (10/10)	80.0% (8/10)	100% (10/10)	93.3% (28/30)	90.0% (9/10)	80.0% (8/10)	100% (10/10)	90.0% (27/30)	91.0% (82/90)
RSV Mod Pos	2.2	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)

a. Agreement calculated based on expected result: Negative for Negative (targeted positivity: 0%); Positive for Low Pos (targeted positivity: 95%) and Mod Pos (targeted positivity: 100%) samples.

b. One sample 2x indeterminate (Flu A Low Pos)

The reproducibility of the Xpert Xpress Flu/RSV Assay was also evaluated in terms of the fluorescence signal expressed in Ct values for each target detected. The mean, standard deviation (SD), and coefficient of variation (CV) between-sites, between-days, between-lots and between-operators for each panel member are presented in Table 8-12.

Table 8-12 Summary of Reproducibility Data

Sample	Assay Channel (Analyte)	N[a]	Mean Ct	Between-Site		Between-Day		Between-Operator		Within-Assay		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Neg	SPC	90	32.2	0.2	0.6	0.2	0.6	0.2	0.7	0.4	1.4	0.6	1.8
Flu A Low Pos	A	80	36.4	0.1	0.4	0	0	0	0	1.8	4.9	1.8	4.9
Flu A Mod Pos	A	90	33.7	0.1	0.2	0	0	0	0	0.6	1.7	0.6	1.8
Flu B Low Pos	B	84	35.8	0	0	0	0	0.6	1.8	1.5	4.1	1.6	4.5
Flu B Mod Pos	B	90	33.7	0	0.1	0.1	0.4	0	0	0.5	1.6	0.6	1.7
RSV Low Pos	RSV	82	36.8	0.7	2.0	0.1	0.4	0	0	1.1	2.9	1.3	3.6
RSV Mod Pos	RSV	90	33.1	0	0.1	0.2	0.6	0	0	0.5	1.4	0.5	1.5

a. Results with non-zero Ct values of 90.

Conclusions

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the Xpert Xpress Flu/RSV Assay is substantially equivalent to the predicate device.