Decmber 4, 2018

Hologic, Inc.
Anila Tarte
Regulatory Affairs Specialist
10210 Genetic Center Drive
San Diego, California 92121

Re: K172629
Trade/Device Name: Panther Fusion AdV/hMPV/RV Assay
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: Class II
Product Code: OOC, OEM, OOI
Dated: August 31, 2017
Received: September 1, 2017

Dear Anila Tarte:

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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

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)*
K172629

Device Name
Panther Fusion AdV/hMPV/RV Assay

Indications for Use *(Describe)*
The Panther Fusion® AdV/hMPV/RV assay is a multiplex real-time PCR (RT-PCR) in vitro diagnostic test for the rapid and qualitative detection and differentiation of Adenovirus (AdV) human Metapneumovirus (hMPV), and Rhinovirus (RV). Nucleic acids are isolated and purified from nasopharyngeal (NP) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection.

This assay is intended to aid in the differential diagnosis of Adenovirus, human Metapneumovirus, and Rhinovirus infections in humans. Negative results do not preclude Adenovirus, human Metapneumovirus, and Rhinovirus infections and should not be used as the sole basis for treatment or other management decisions. This assay is designed for use on the Panther Fusion system.

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
Panther Fusion AdV/hMPV/RV Assay

I. SUBMITTER

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Date Prepared: August 31, 2017

II. DEVICE

Proprietary Name of Device: Panther Fusion AdV/hMPV/RV Assay
Classification Name: Respiratory viral panel multiplex nucleic acid assay
Regulation Number: 21 CFR 866.3980 and 862.2570
Regulatory Class: Class II
Product Code: OEM and OCC

III. PREDICATE DEVICE

The predicate device is the FilmArray® Respiratory Panel 2 (RP2) (K170604; cleared May 30, 2017, BioFire Diagnostics, LLC, Salt Lake City, UT).

IV. DEVICE DESCRIPTION

The Panther Fusion AdV/hMPV/RV assay is a multiplex real-time PCR (RT-PCR) *in vitro* diagnostic test for the rapid and qualitative detection and differentiation of Adenovirus (AdV) human Metapneumovirus (hMPV), and Rhinovirus (RV). Nucleic acids are isolated and purified from nasopharyngeal (NP) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection.

The Panther Fusion AdV/hMPV/RV assay involves the following steps: sample lysis, nucleic acid capture and elution, and multiplex RT-PCR when analytes are simultaneously amplified, detected and differentiated. Nucleic acid capture and elution takes place in a single tube on the Panther Fusion system. The eluate is transferred to the Panther Fusion system reaction tube containing the assay reagents. Multiplex RT-PCR is then performed on the eluted nucleic acid on the Panther Fusion system.

Nucleic acid capture and elution: Prior to processing and testing on the Panther Fusion system, specimens are transferred to a Specimen Lysis Tube containing specimen transport media (STM) that lyses the viral particles, releases target nucleic acid and protects it from degradation during storage.

The Internal Control-S (IC-S) is added to each test specimen and controls via the working Panther Fusion Capture Reagent-S (wFCR-S). The IC-S in the reagent monitors specimen processing, amplification and detection.

Capture oligonucleotides hybridize to nucleic acid in the test specimen. Hybridized nucleic acid is then separated from the specimen in a magnetic field.

Wash steps remove extraneous components from the reaction tube. The elution step elutes purified nucleic acid. During the nucleic acid capture and elution step, total nucleic acid is isolated from specimens.

Elution transfer and RT-PCR: During the elution transfer step, eluted nucleic acid is transferred to a Panther Fusion reaction tube already containing oil and reconstituted mastermix.

For RV, hMPV, and internal control targets, amplification occurs via RT-PCR. A reverse transcriptase step generates DNA copies of the target sequence. For AdV, target amplification occurs via PCR. For all targets, specific forward and reverse primers and probes amplify targets while simultaneously detecting and discriminating multiple target types via multiplex PCR.

The Panther Fusion system compares the fluorescence signal to a predetermined cut-off to produce a qualitative result for the presence or absence of the analyte.

The analytes and the channel used for their detection on the Panther Fusion system are summarized in the table below.

Analyte	Gene Targeted	Instrument Channel
Adenovirus	Hexon	HEX
human Metapneumovirus	Nucleocapsid	ROX
Rhinovirus	5' UTR	FAM
Internal Control	Not applicable	RED677

Assay Components

The reagents required to perform the Panther Fusion AdV/hMPV/RV assay are packaged and sold separately. There are 7 boxes containing 9 reagents which are required for sample processing. A description of the components that are required to perform the Panther Fusion AdV/hMPV/RV assay are detailed in **Table 1.** In addition, there is one ancillary kit, Panther Fusion Specimen Lysis Tubes, which is required for processing of specimens prior to testing on the Panther Fusion system.

Table 1: Reagents Required to Perform the Panther Fusion AdV/hMPV/RV Assay

Box	Components Description
1	Panther Fusion AdV/hMPV/RV Assay Cartridges
2	Panther Fusion Extraction Reagent-S • Box Contains: o Panther Fusion Capture Reagent-S o Panther Fusion Enhancer Reagent-S
3	Panther Fusion Internal Control-S
4	Panther Fusion Reconstitution Buffer I
5	Panther Fusion Elution Buffer
6	Panther Fusion Oil
7	Panther Fusion AdV/hMPV/RV Assay Controls • Box Contains: o Panther Fusion AdV/hMPV/RV Positive Control o Panther Fusion Negative Control

In addition, select components can also be ordered in the following bundles:

- Panther Fusion Universal Fluids Kit: (contains Panther Fusion Oil and Panther Fusion Elution Buffer).
- Panther Fusion Assay Fluids I-S: (contains Panther Fusion Extraction Reagents-S, Panther Fusion Internal Control-S, and Panther Fusion Reconstitution Buffer I).

Instrumentation

The Panther Fusion AdV/hMPV/RV assay has been designed for and validated on the Panther Fusion system. The Panther Fusion system is an integrated hardware and software system that together with the Panther Fusion AdV/hMPV/RV assay fully automates all the steps necessary to perform the assay.

The Panther Fusion system integrates Hologic's commercialized Panther instrument system with an add-on sidecar, the Panther Fusion module, which extends the functionality of the Panther system by increasing the assay processing capabilities to include multiplex RT-PCR. The Panther Fusion module includes instrument hardware and software and can be installed on existing Panther instruments or ordered with new Panther instruments.

The Panther Fusion system employs non-specific target capture (NSTC) for the purification of total nucleic acids from the sample, followed by nucleic acid amplification and real-time fluorescent detection. The process involves sample loading and preparation (i.e. nucleic acid extraction) on the Panther instrument using the same workflow and processing steps as for other commercialized Hologic Aptima TMA assays. The extracted nucleic acid for each sample is transferred to the Panther Fusion module where amplification and detection occur.

V. INDICATIONS FOR USE

Intended Use

The Panther Fusion® AdV/hMPV/RV assay is a multiplex real-time PCR (RT-PCR) *in vitro* diagnostic test for the rapid and qualitative detection and differentiation of Adenovirus (AdV) human Metapneumovirus (hMPV), and Rhinovirus (RV). Nucleic acids are isolated and purified

from nasopharyngeal (NP) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection.

This assay is intended to aid in the differential diagnosis of Adenovirus, human Metapneumovirus, and Rhinovirus infections in humans. Negative results do not preclude Adenovirus, human Metapneumovirus, and Rhinovirus infections and should not be used as the sole basis for treatment or other management decisions. This assay is designed for use on the Panther Fusion system.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

A comparison of the Panther Fusion AdV/hMPV/RV assay to the predicate FilmArray® Respiratory Panel 2 (RP2) (K170604) is summarized in **Table 2** (similarities) and **Table 3** (differences).

Table 2: Similarities Between Panther Fusion AdV/hMPV/RV Assay and Predicate Device

Item	FilmArray Respiratory Panel 2 Assay (Predicate Device)	Panther Fusion AdV/hMPV/RV Assay (Subject Device)
Intended Use	The FilmArray Respiratory Panel 2 (RP2) is a multiplexed nucleic acid test intended for use with FilmArray 2.0 or FilmArray Torch systems for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections. The following organism types and subtypes are identified using the FilmArray RP2: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Human Rhinovirus/Enterovirus, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype H1-2009, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Respiratory Syncytial Virus, *Bordetella parapertussis*, *Bordetella pertussis*, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae.*	The Panther Fusion AdV/hMPV/RV assay is a multiplex real-time PCR (RT-PCR) *in vitro* diagnostic test for the rapid and qualitative detection and differentiation of Adenovirus (AdV) human Metapneumovirus (hMPV), and Rhinovirus (RV). Nucleic acids are isolated and purified from nasopharyngeal (NP) swab specimens obtained from individuals exhibiting signs and symptoms of a respiratory tract infection. This assay is intended to aid in the differential diagnosis of Adenovirus, human Metapneumovirus, and Rhinovirus infections in humans. Negative results do not preclude Adenovirus, human Metapneumovirus, and Rhinovirus infections and should not be used as the sole basis for treatment or other management decisions. This assay is designed for use on the Panther Fusion system.
Organisms Detected	Adenovirus, human Metapneumovirus, Rhinovirus See below for differences.	Same
Assay Controls	Internal control in each sample. External control processed at periodic intervals.	Same
Patient Population	Male and female patients with signs/symptoms of respiratory infection	Same
Specimen Types	Nasopharyngeal (NP) swab specimens	Same
Analyte	RNA/DNA	Same
Technology Principle of Operation	Multiplex nucleic acid amplification (RT-PCR)	Same

Table 3: Differences Between Panther Fusion AdV/hMPV/RV Assay and Predicate Device

Item	FilmArray Respiratory Panel 2 (Predicate Device)	Panther Fusion AdV/hMPV/RV Assay (Subject Device)
Organisms Detected	Adenovirus, human Metapneumovirus, Rhinovirus. Can also detect Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype H1-2009, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Respiratory Syncytial Virus, *Bordetella parapertussis*, *Bordetella pertussis*, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*. Cannot distinguish Rhinovirus and Enterovirus.	Adenovirus, human Metapneumovirus, Rhinovirus *
Platform	Automated nested multiplex PCR platform. Uses the FilmArray Pouch Loading Station to prepare FilmArray pouch (add specimen and hydrate reagents). Uses the FilmArray Instrument to process prepared FilmArray pouch for nucleic acid extraction, amplification, end-point detection and result processing.	Automated multiplex RT-PCR platform. Uses Panther Fusion system for all steps including specimen addition, reagent preparation, nucleic acid extraction, amplification, detection and result processing.
Time to Obtain Test Results	About 45 minutes	Approximately 2.5 hours

* The Panther Fusion AdV/hMPV/RV assay is specific for Rhinovirus with no cross-reactivity with Enterovirus

VII. PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

Brief Description of Analytical (Non-Clinical) Studies

The following analytical studies (non-clinical) were conducted to support the clearance of the Panther Fusion AdV/hMPV/RV Assay on the Panther Fusion System.

Analytical Sensitivity and Limit of Detection (LoD) of Nasopharyngeal Swab Specimens

Target specific LOD values were obtained using multiple strains for each targeted virus: AdV, hMPV and RV. Dilutions of AdV species A-F (strains 1, 3, 4, 9, 12, 40), four strains of hMPV and two strains of RV in pooled negative clinical Nasopharyngeal swab (NP) specimens and tested with at least 12 replicates per concentration, using three reagent lots. Testing was performed on three Panther Fusion instruments per concentration and per reagent lot for a total of at least 36 replicates per virus type. Determined LoD value for each virus type was verified by testing newly prepared samples for at least 20 replicates using one lot of reagent. Panel descriptions are shown in **Table 4.**

Table 4: LoD Determination Panel Description

Target Type	Organism	Concentration (TCID 50/mL)
Adenovirus	Strain: 1 (Species C) Source and Mfg MN: Zeptometrix, 0810050CF LN: 307673	10^1.0
		10^0.5
		10^0.0
		10^-0.5
		10^-1.0
	Strain: 3 (Species B) Source and Mfg MN: Zeptometrix, 0810062CF LN: 310503	10^1.0
		10^0.5
		10^0.0
		10^-0.5
		10^-1.0
	Strain: 4 (Species E) Source and Mfg MN: Zeptometrix, 0810070CF LN: 309013	10^-2.0
		10^-2.5
		10^-3.0
		10^-3.5
		10^-4.0
	Strain: 9 (Species D) Source and Mfg MN: TriCore, Custom LN: 112408	10^0.0
		10^-0.5
		10^-1.0
		10^-1.5
		10^-2.0
	Strain: 12 (Species A) Source and Mfg MN: TriCore, Custom LN: 120108	10^0.0
		10^-0.5
		10^-1.0
		10^-1.5
		10^-2.0

Target Type	Organism	Concentration (TCID 50/mL)
	Strain: 40 (Species F) Source and Mfg MN: Zeptometrix, 0810084CF LN: 312745	10^-1.0
		10^-1.5
		10-2.0
		10^-2.5
		10^-3.0
hMPV	Strain: A1-16 Source and Mfg MN: Zeptometrix, 0810161CF LN: 308413	10^2.0
		10^1.5
		10^1.0
		10^0.5
		10^0.0
	Strain: A2-20 Source and Mfg MN: Zeptometrix, 0810163CF LN: 308416	10^2.0
		10^1.5
		10^1.0
		10^0.5
		10^0.0
	Strain: B1-3 Source and Mfg MN: Zeptometrix, 0810156CF LN: 309673	10^1.0
		10^0.5
		10^0.0
		10^-0.5
		10^-1.0
	Strain: B2-8 Source and Mfg MN: Zeptometrix, 0810159CF LN: 308419	10^1.0
		10^0.5
		10^0.0
		10^-0.5
		10^-1.0
Rhinovirus	Strain: A-18 Source and Mfg MN: Zeptometrix, Custom LN: 313820	10^0.0
		10^-0.5
		10^-1.0
		10^-1.5
		10^-2.0
	Strain: B-26 Source and Mfg MN: Zeptometrix, Custom LN: 313819	10^1.0
		10^0.5
		10^0.0
		10^-0.5
		10^-1.0

Interference

Medications, over the counter products, and other potentially interfering substances that may be present in the samples were evaluated in the Panther Fusion AdV/hMPV/RV assay.

Clinically relevant amounts of the potentially interfering substances were added to simulated clinical matrix (SCM, VTM with Hela at 2 x 10^4 cells/mL) and tested unspiked or spiked with intended targets (AdV, hMPV and RV) at their respective 3X LoD concentrations. The substances consisted of nasal sprays or drops, lozenges, exogenous and endogenous substances. No interference in performance of the Panther Fusion AdV/hMPV/RV assay was observed in the presence of a representative brand of the following potentially interfering substances at the concentrations stated in **Table 5**.

Table 5: Potentially Interfering Substances

Type	Potentially Interfering Substance	Active Ingredient(s)	Concentration
Endogenous	Mucin	Purified mucin protein	60 µg/mL
	Human blood	NA	2% v/v
Nasal sprays or drops	Neo-Synephrine®	Phenylephrine	15% v/v
	Anefrin	Oxymetazoline HCl .05%	15% v/v
	Saline	Sodium chloride with preservatives	15% v/v
	Ventolin® HFA	Albuterol (Albuterol Sulfate)	15% v/v
Nasal corticosteroids	QVAR®, Beconase AQ	Beclomethasone (Beclomethasone (Dipropionate))	5% v/v
	Dexacort	Dexamethasone	5% v/v
	AEROSPAN®	Flunisolide	5% v/v
	Nasacort	Triamcinolone	5% v/v
	Rhinocort	Budesonide	5% v/v
	Nasonex	Mometasone (Mometasone furoate)	5% v/v
	Flonase	Fluticasone (Fluticasone (propionate))	5% v/v
Nasal gel	Zicam® (Allergy Relief)	Luffa opperculata, Galphimia, Glauca, Histaminum hydrochloricum, Sulfur	5% v/v
Throat lozenges	Chloraseptic Throat Lozenges	Benzocaine	0.63 mg/mL
		Menthol	
Anti-viral drugs	Relenza®	Zanamivir	3.3 mg/mL
	TamiFlu	Oseltamivir	25 mg/mL
	Rebitol	Ribavirin	20 mg/mL
Antibiotic, nasal ointment	Bactroban cream	Mupirocin	10 mg/mL
Antibiotic, systemic	Tobramycin	Tobramycin	4.0 µg/mL

Competitive Interference

Competitive Interference of the Panther Fusion AdV/hMPV/RV assay was evaluated using a simulated clinical matrix (SCM) with pairs of target viruses at two different concentrations. One of the concentrations was near the Limit of Detection (3X LoD) while the other concentration was high (1000X LoD). The presence of two viruses at varying concentrations in a single sample had no effect on the analytical sensitivity (100% detection for both targets) at the concentration tested (see **Table 6**).

Table 6: Co-Infection Concentrations and Results

Panel Member	Target 1 (Low)	Target 2 (High)	Detection Channel (Target), % Positive (reactive n/valid n)			
			FAM (RV)	HEX (AdV)	ROX (hMPV)	RED677 (IC)
1	AdV	hMPV	0.0% (0/6)	100.0% (6/6)	100.0% (6/6)	100.0% (6/6)
2	AdV	RV	100.0% (6/6)	100.0% (6/6)	0.0% (0/6)	100.0% (6/6)
3	hMPV	AdV	0.0% (0/6)	100.0% (6/6)	100.0% (6/6)	100.0% (6/6)
4	hMPV	RV	100.0% (6/6)	0.0% (0/6)	100.0% (6/6)	100.0% (6/6)
5	RV	AdV	100.0% (6/6)	100.0% (6/6)	0.0% (0/6)	100.0% (6/6)
6	RV	hMPV	100.0% (6/6)	0.0% (0/6)	100.0% (6/6)	100.0% (6/6)

Analytical Specificity

The analytical specificity of the Panther Fusion AdV/hMPV/RV assay was evaluated by testing a panel of 64 organisms, consisting of 30 viral, 32 bacterial, and 2 yeast strains representing common respiratory pathogens or flora commonly present in respiratory tract. Bacteria and yeast were tested at concentrations of 10^5 to 10^8 CFU/mL, except where noted. Viruses were tested at concentrations of 10^3-10^7 TCID50/mL. Analytical specificity of the Panther Fusion AdV/hMPV/RV assay was 100% (0/9 detected) for AdV/hMPV/RV (see **Table 7**).

Table 7: Specificity Results

Organis	Concentration	AdV	hMPV	RV
Acinetobacter baumannii 307-0294	$1x10^7$ CFU/mL	-	-	-
Bordetella bronchiseptica	$1x10^7$ CFU/ml	-	-	-
Bordetella parapertussis	$1x10^7$ CFU/ml	-	-	-
Bordetella pertussis	$1x10^7$ CFU/mL	-	-	-

Burkholderia cepacia Z066	$1x10^6$ CFU/mL	-	-	-
Candida albicans	$1x10^7$ CFU/mL	-	-	-
Candida glabrata	$1x10^6$ CFU/mL	-	-	-
Chlamydia pneumoniae	$1x10^5$ CFU/mL	-	-	-
Chlamydia trachomatis	$1x10^4$ CFU/mL	-	-	-
CMV Strain AD 169	$1x10^4$ TCID50/mL	-	-	-
Coronavirus 229E	$1x10^5$ TCID50/mL	-	-	-
Coronavirus OC43	$1x10^5$ TCID50/mL	-	-	-
Corynebacterium diphtheria	$1x10^7$ CFU50/mL	-	-	-
Coxsackie B3	$1x10^6$ TCID50/mL	-	-	-
Coxsackie B4	$1x10^4$ TCID50/mL	-	-	-
Coxsackie B5/10/2006	$1x10^5$ TCID50/mL	-	-	-
Coxsackievirus A10	$1x10^4$ TCID50/mL	-	-	-
Coxsackievirus A21	$1x10^4$ TCID50/mL	-	-	-
Escherichia coli	*$1x10^7$ CFU/mL*	-	-	-
EBV	$1x10^6$ TCID50/mL	-	-	-
Echovirus 11	$1x10^6$ TCID50/mL	-	-	-
Echovirus 2	$1x10^6$ TCID50/mL	-	-	-
Echovirus 3	$1x10^4$ TCID50/mL	-	-	-
Echovirus 6	$1x10^6$ TCID50/mL	-	-	-
Enterovirus 68	$1x10^5$ TCID50/mL	-	-	-
Enterovirus 70	$1x10^4$ TCID50/mL	-	-	-
Haemophilus influenzae	$1x10^7$ TCID50/mL	-	-	-
HPIV-1	$1x10^4$ TCID50/mL	-	-	-
HPIV-2	$1x10^5$ TCID50/mL	-	-	-
HPIV-3	$1x10^5$ TCID50/mL	-	-	-
HPIV-4a	$1x10^4$ TCID50/mL	-	-	-
HSV-1 Macinytre Strain	$1x10^5$ TCID50/mL	-	-	-
HSV-2 Type 2G Strain	$1x10^5$ TCID50/mL	-	-	-
Influenza A (H1N1)	$1x10^3$ TCID50/mL	-	-	-
Influenza A (H3N2)	$1x10^3$ TCID50/mL	-	-	-
Influenza B	$1x10^3$ TCID50/mL	-	-	-
Klebsiella pneumonia	$1x10^7$ CFU/mL	-	-	-
Lactobacillus acidophilus Z048	$1x10^6$ CFU/mL	-	-	-
Lactobacillus plantarum	$1x10^6$ CFU/mL	-	-	-

Legionella pneumophila	$1x10^7$ CFU/mL	-	-	-
Measles/7/2000	$1x10^4$ TCID50/mL	-	-	-
Moraxella catarrhalis	$1x10^7$ CFU/mL	-	-	-
Mumps virus	$1x10^5$ CFU/mL	-	-	-
Mycobacterium intracellulare	$5x10^{10}$ rRNA copies/mL	-	-	-
Mycobacterium tuberculosis	$5x10^9$ rRNA copies/mL	-	-	-
Mycoplasma pneumoniae	$1x10^6$ CFU/mL	-	-	-
Neisseria gonorrhea	$1x10^7$ CFU/mL	-	-	-
Neisseria meningitides	$1x10^7$ CFU/mL	-	-	-
Neisseria mucosa	$1x10^7$ CFU/mL	-	-	-
Polio virus 1	$1x10^6$ TCID50/mL	-	-	-
Proteus mirabilis	$1x10^7$ CFU/mL	-	-	-
Proteus vulgaris	$1x10^7$ CFU/mL	-	-	-
Pseudomonas aeruginosa	$1x10^7$ CFU/mL	-	-	-
RSV A	$1x10^5$ TCID50/mL	-	-	-
RSV B	$1x10^5$ TCID50/mL	-	-	-
Serratia marcescens Z053	$1x10^7$ CFU/mL	-	-	-
Staphlycoccus aureus	$1x10^7$ CFU/mL	-	-	-
Staphlycoccus epidermidis	$1x10^7$ CFU/mL	-	-	-
Streptococcus agalactiae	$1x10^7$ CFU/mL	-	-	-
Streptococcus pneumoniae	$1x10^7$ CFU/mL	-	-	-
Streptococcus pyogenes	$1x10^7$CFU/mL	-	-	-
Streptococcus salivarius	$1x10^7$ CFU/mL	-	-	-
Tatlockia micdadei (Legionella micdadei)	$1x10^6$ CFU/mL	-	-	-
Varicella Zoster Virus	$1x10^4$ TCID50/mL	-	-	-

Carry-Over/Contamination

The carry-over/cross-contamination study was performed with negative samples alternately placed between high titer AdV/hMPV/RV samples and tested. High positive samples were prepared by spiked with RV A and AdV-1 at 10^4 TCID50/mL (over 10,000X LoD). A total of nine separate runs with negative samples and positive samples placed in a checkerboard pattern

were tested over three different instruments for a combined total of 449 positive and 450 negative samples. The carry-over rate was 0.2%.

Assay Precision

Panther Fusion AdV/hMPV/RV assay precision was evaluated with a seven-member panel. The panel was tested by three operators on two separate runs per day, using three reagent lots on three Panther Fusion systems over 45 calendar days. The panel members, along with a summary of the agreement with expected results for each target is presented in **Table 8**. The mean and variability analysis between instruments, between reagent lots, between operators, between days, between runs and within runs, and overall (total) for Ct are also presented in **Table 9**.

Table 8: Percent Positive and Agreement

Target	Panel Description	Member ID	Valid N	% Positive (pos n/valid n)	% Agreement (95% CI)
RV	RV 3X LoD	5	161	100.0% (161/161)	100.0% (97.7-100.0%)
	RV 1X LoD	6	162	100.0% (162/162)	100.0% (97.7-100.0%)
	RV 0.01X LoD	2	160	1.9% (3/160)	98.1% (94.6-99.4%)
	Negative	7	162	0.6% (1/162)	99.4% (96.6-99.9%)
AdV	AdV 3X LoD	3A	162	100.0% (162/162)	100.0% (97.7-100.0%)
	AdV 1X LoD	1	162	100.0% (162/162)	100.0% (97.7-100.0%)
	AdV 0.01X LoD	5	161	10.6% (17/161)	89.4% (83.7-93.3%)
	Negative	7	162	0.6% (1/162)	99.4% (96.6-99.9%)
hMPV	hMPV 3X LoD	2	160	100.0% (160/160)	100.0% (97.7 - 100%)
	hMPV 1X LoD	4	161	100.0% (161/161)	100.0% (97.7 - 100%)
	hMPV 0.01X LoD	3A	162	17.9% (29/162)	82.1% (75.5-87.2%)
	Negative	7	162	0.0% (0/162)	100.0% (97.7 - 100%)

Table 9: Signal Variability Analysis Results

Target	Panel Member	Member ID	Mean Ct	Between Instrument		Between Reagent Lot		Between Operator		Between Days		Between Runs		Within Run		Total	
				SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
RV	RV 3X LoD	5	32.5	0.1	0.5	0.1	0.3	0.0	0.1	0.0	0.0	0.3	1.0	0.6	2.0	0.7	2.4
	RV 1X LoD	6	33.8	0.1	0.5	0.1	0.5	0.0	0.0	0.1	0.4	0.0	0.0	0.8	2.6	0.9	2.8
	RV 0.01X LoD	2	40.6	1.9	4.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.6	1.6	2.0	5.0
AdV	AdV 3X LoD	3A	33.5	0.1	0.4	0.0	0.1	0.0	0.0	0.1	0.3	0.2	0.7	0.4	1.2	0.5	1.5
	AdV 1X LoD	1	35.2	0.2	0.6	0.0	0.0	0.0	0.2	0.1	0.3	0.3	0.8	0.5	1.5	0.6	1.9
	AdV 0.01X LoD	5	40.4	0.3	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.9	2.4	0.7	1.9	1.3	3.2
hMPV	hMPV 3X LoD	2	33.5	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.8	0.8	2.4	0.8	2.5
	hMPV 1X LoD	4	35.1	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.7	2.0	0.7	2.0
	hMPV 0.01X LoD	3A	40.3	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.7	0.5	1.4	1.2	3.1	1.4	3.5
IC	Negative	7	30.7	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.6	0.5	1.7	0.5	1.8

Brief Description of Clinical Studies

Clinical testing of the Panther Fusion AdV/hMPV/RV assay on the Panther Fusion system included performance and reproducibility testing. Substantial equivalence is based in part on the performance study.

Clinical Performance Study

This study was performed to demonstrate clinical performance characteristics for the Panther Fusion AdV/hMPV/RV assay. A prospective multicenter study was conducted with leftover, remnant nasopharyngeal (NP) swab specimens from male and female individuals of all ages exhibiting signs and/or symptoms of a respiratory tract infection. Four participating US pediatric/adolescent, private and/or university hospitals obtained 2961 leftover, remnant NP swab specimens. The samples were tested with the Panther Fusion AdV/hMPV/RV assay, with reference viral culture followed by direct fluorescent antibody (DFA) identification (for AdV), with an FDA-cleared assay for hMPV, and with 2 reverse transcriptase PCR assays followed by bi-directional sequencing (PCR/sequencing, for RV). FDA-cleared or validated PCR-based assays were used for discordant resolution testing for AdV and hMPV; no discordant resolution testing was performed for RV. Sensitivity and specificity (for AdV and hMPV) and negative and positive percent agreement (for RV) were estimated with corresponding 2-sided 95% Score CIs. Analyses were performed separately for each target analyte (AdV, hMPV, RV).

Of the 2961 specimens, 31 specimens/samples were withdrawn (due to incomplete reference testing results, insufficient volumes for testing, expiration prior to testing, or mishandling), 2930 samples were processed in valid Panther Fusion AdV/hMPV/RV runs, 2875 (98.1%) had final valid results, and 55 (1.9%) had final invalid results. Of the 2875 samples with valid Panther Fusion results, 1358 samples were from females and 1517 samples were from males (see **Table 10**). The positivity of each analyte by age group is presented in **Table 11**.

Table 10: Summary of Subject Demographics for Prospective Samples in the Panther Fusion AdV/hMPV/RV Assay Evaluation

	N (%)
Total	2875 (100)
Sex	
Female	1358 (47.2)
Male	1517 (52.8)
Age Group	
0 to 28 days	82 (2.9)
29 days to < 2 years	757 (26.3)
2 to 5 years	407 (14.2)
6 to 11 years	259 (9.0)
12 to 17 years	184 (6.4)
18 to 21 years	73 (2.5)
22 to 64 years	694 (24.1)
≥ 65 years	419 (14.6)

Table 11: Panther Fusion AdV/hMPV/RV **Positivity by Analyte and Age Group**

	% Positivity (n/N)		
Analyte	**AdV**	**hMPV**	**RV**
All	5.6% (160/2869)	3.6% (103/2875)	21.0% (604/2870)
0 to 28 days	1.2% (1/82)	1.2%	17.1% (14/82)
29 days to < 2	8.7% (66/757)	5.8% (44/757)	31.5% (238/756)
2 to 5 years	11.5% (47/407)	6.9% (28/407)	28.3% (115/406)
6 to 11 years	12.4% (32/258)	2.3% (6/259)	21.3% (55/258)
12 to 17 years	2.8% (5/181)	0.5% (1/184)	16.8% (31/184)
18 to 21 years	2.7% (2/73)	1.4% (1/73)	12.3% (9/73)
22 to 64 years	0.9% (6/692)	2.2% (15/694)	13.4% (93/692)
≥ 65 years	0.2% (1/419)	1.7% (7/419)	11.7% (49/419)

Of the samples with valid Panther Fusion AdV/hMPV/RV results, 11 samples with invalid reference results for AdV (n=6) or RV (n=5) were excluded from the performance analyses, leaving 2869 samples evaluable for AdV, 2875 for hMPV, and 2870 for RV.

Of the 2875 evaluable samples tested using the Panther Fusion AdV/hMPV/RV assay, 5.6%

(160/2869) were positive for AdV, 3.6% (103/2875) were positive for hMPV, and 21.0% (604/2870) were positive for RV.

Performance characteristics for detection of AdV, hMPV, and RV in prospective NP samples were calculated (see **Table 12**).

Table 12: Panther Fusion AdV/hMPV/RV Assay Performance Relative to Reference Testing

Analyte	N	TP	FP	TN	FN	Prevalence[1] (95% CI)[2]	Sensitivity/PPA[3] (95% CI)[2]	Specificity/NPA[3] (95% CI)[2]
AdV	2869	93	67[4]	2707	2[4]	3.3 (2.7-4.0)	97.9 (92.6-99.4)	97.6 (96.9-98.1)
hMPV	2875	74	29[5]	2771	1[5]	2.6 (2.1-3.3)	98.7 (92.8-99.8)	99.0 (98.5-99.3)
RV	2870	552	52[6]	2182	84[6]	22.2 (20.7-23.7)	86.8 (83.9-89.2)	97.7 (97.0-98.2)

FN= false negative, FP= false positive, NPA= negative percent agreement, PPA= positive percent agreement, TP= true positive, TN= true negative

[1]Study prevalence reported, [2]Score Confidence Interval, [3] PPA and NPA apply to RV

[4] 54/67 false positive results were confirmed positive and 2/2 false negative results were confirmed negative for AdV by an FDA-cleared assay

[5] 20/29 false positive results were confirmed positive and 0/1 false negative result was confirmed negative for hMPV by PCR

[6] No discordant resolution testing was performed for the 52 false positive and 84 false negative results for RV

Reproducibility

Panther Fusion AdV/hMPV/RV assay reproducibility was evaluated at three US sites using seven panel members. Testing was performed using one lot of assay reagents and six operators (two at each site). At each site, testing was performed for at least five days. Each run had three replicates of each panel member.

A negative panel member was created using a matrix of simulated nasal swab specimen in viral transport medium (VTM). Positive panel members were created by spiking 1-2X LoD (low-positive) or 2-3X LoD (moderate-positive) concentrations of the target analyte into a matrix of simulated nasal swab specimen, composed of cultured human cells suspended in VTM.

The agreement with expected results was 100% for all panel members containing AdV, hMPV, or RV as shown in **Table 13**.

Table 13: Agreement of Panther Fusion AdV/hMPV/RV Assay Results With Expected Results

Panel			Expected Results			Agreement with Expected Results					
						AdV		hMPV		RV	
Description	Comp.	Conc. (TCID 50/mL)	AdV	hMPV	RV	N[1]	(%) 95% CI	N[1]	(%) 95% CI	N[1]	(%) 95% CI
AdV Low Pos	1-2X LoD	1.00E+00	+	-	-	88/88	100 (95.8-100)	88/88	100 (95.8-100)	88/88	100 (95.8-100)
AdV Mod Pos	2-3X LoD	3.00E+00	+	-	-	89/89	100 (95.9-100)	89/89	100 (95.9-100)	89/89	100 (95.9-100)
hMPV Low Pos	1-2X LoD	1.00E+01	-	+	-	88/88	100 (95.8-100)	88/88	100 (95.8-100)	88/88	100 (95.8-100)
hMPV Mod Pos	2-3X LoD	3.00E+01	-	+	-	89/89	100 (95.9-100)	89/89	100 (95.9-100)	89/89	100 (95.9-100)
RV Low Pos	1-2X LoD	3.16E-01	-	-	+	89/89	100 (95.9-100)	89/89	100 (95.9-100)	89/89	100 (95.9-100)
RV Mod Pos	2-3X LoD	9.48E-01	-	-	+	87/87	100 (95.8-100)	87/87	100 (95.8-100)	87/87	100 (95.8-100)
Neg	N/A	N/A	-	-	-	87/87	100 (95.8-100)	87/87	100 (95.8-100)	87/87	100 (95.8-100)

Comp.=composition, Conc.=concentration, CI=Score confidence interval, Mod=moderate, N/A=not applicable, Neg=negative, Pos=positive, $TCID_{50}$/mL=50% tissue culture infective dose (measure of virus titer)

[1] A total of 13 samples had final invalid results and were not included in the calculation of overall agreement

The total AdV, hMPV, and RV signal variability measured as %CV ranged from 1.70% to 4.90% in low and moderate positive panel members. For the sources of variation except the 'within-run' factor, %CV values were ≤1.72% as shown in **Table 14**.

Table 14: Signal Variability of the Panther Fusion AdV/hMPV/RV Assay by Panel Member

			Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
Panel Description	N	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
AdV Low Pos	88	35.1	0.35	0.99	0.13	0.38	0.0	0.0	0.0	0.0	0.58	1.65	0.69	1.96
AdV Mod Pos	89	33.5	<0.1	0.18	0.17	0.49	0.21	0.63	<0.1	<0.1	0.50	1.49	0.57	1.70
hMPV Low Pos	88	35.1	0.23	0.64	0.0	0.0	0.0	0.0	0.0	0.0	1.14	3.25	1.16	3.32
hMPV Mod Pos	89	33.1	0.0	0.0	0.24	0.71	0.57	1.72	<0.1	<0.1	1.50	4.53	1.62	4.90
RV Low Pos	89	33.7	0.14	0.43	0.24	0.72	0.22	0.66	<0.1	<0.1	0.83	2.45	0.90	2.67
RV Mod Pos	87	32.3	0.16	0.48	<0.1	0.16	0.38	1.18	<0.1	0.13	0.71	2.20	0.83	2.55

Ct=threshold cycle, CV=coefficient of variation, Mod=moderate, Pos=positive, SD=standard deviation

Note: If variability from some factors was numerically negative, SD and CV are shown as 0.0.

The signal variability, measured as %CV, was ≤1.94% between sites, between operators, between days, or overall for the Panther Fusion AdV/hMPV/RV assay positive controls (see **Table 15**).

Table 15: Signal Variability of the Panther Fusion AdV/hMPV/RV Assay Controls

				Between Sites		Between Operators		Between Days		Between Runs		Within Runs		Total	
Control	Analyte	N	Mean Ct	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Pos	AdV	30	33.0	0.0	0.0	0.0	0.0	<0.1	0.24	0.0	0.0	0.27	0.82	0.28	0.85
	hMPV	30	34.0	<0.1	0.21	<0.1	0.18	0.0	0.0	0.0	0.0	0.30	0.89	0.32	0.93
	RV	30	31.8	0.0	0.0	0.0	0.0	0.32	1.02	0.0	0.0	0.53	1.65	0.62	1.94

Ct=threshold cycle, CV=coefficient of variation, Mod=moderate, Pos=positive, SD=standard deviation

Note: If variability from some factors was numerically negative, SD and CV are shown as 0.0.

VIII. CONCLUSIONS

The analytical and clinical study results demonstrate that the Panther Fusion AdV/hMPV/RV assay on the Panther Fusion system performs comparably to the predicate device that is currently marketed for the same intended use. Hardware and software verification and validation demonstrate that the Panther Fusion AdV/hMPV/RV assay on the Panther Fusion system performs as intended.