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Real Time Solutions

K082688

NOV - 7 2008

510(k) SUMMARY

November 6, 2008

CONTACT

Dr. Karen Harrington
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Waukesha, WI 53186

NAME OF DEVICE

Trade Name:	Pro hMPV+ Assay
Regulation Number:	21 CFR 866.3980
Classification Name:	OEM

PREDICATE DEVICE

K063765 – ID-Tag Respiratory Virus Panel, Luminex Molecular Diagnostics, Inc.

INTENDED USE

The Pro hMPV+ Assay is a Real Time RT-PCR *in vitro* diagnostic test for the qualitative detection of human Metapneumovirus (hMPV) nucleic acid isolated and purified from nasopharyngeal swab (NP) specimens obtained from individuals exhibiting signs and symptoms of acute respiratory infection. This assay targets a highly conserved region of the Nucleocapsid gene of hMPV. The detection of hMPV nucleic acid from symptomatic patients aids in the diagnosis of human respiratory hMPV infection if used in conjunction with other clinical and laboratory findings. This test is not intended to differentiate the four genetic sub-lineages of hMPV.

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

PRODUCT DESCRIPTION

The Pro hMPV+ Assay enables detection human Metapneumovirus and Internal Control nucleic acid. Nasopharyngeal swab specimens are collected from patients with signs and symptoms of a respiratory infection using a polyester, rayon or nylon tipped swab and placed into viral transport medium.

An Internal Control (IC) is added to each sample prior to nucleic acid isolation to monitor for inhibitors present in the specimens. The isolation and purification of the nucleic acids is performed using either a MagNA Pure LC Instrument (Roche) and the MagNA Pure Total Nucleic Acid Isolation Kit (Roche) or a NucliSENS® easyMAG™ System (bioMérieux) and the Automated Magnetic Extraction Reagents (bioMérieux).

The purified nucleic acids are added to Pro hMPV+ Supermix along with enzymes

included in the Pro hMPV+ Assay Kit. The Pro hMPV+ Supermix contains oligonucleotide primers and target-specific oligonucleotide probes. The primers are complementary to highly conserved regions of genetic sequences for these respiratory viruses. The probes are dual-labeled with a reporter dye attached to the 5'-end and a quencher dye attached to the 3'-end (see table below).

Analyte	Gene Targeted	Probe Fluorophore	Absorbance Peak	Emission Peak	Instrument Channel
human Metapneumovirus	Nucleocapsid	FAM	495 nm	520 nm	FAM
Internal Control	NA	Quasar 670	647nm	667nm	Cy5

Reverse transcription of the RNA in the sample into complementary DNA (cDNA) and subsequent amplification of DNA is performed in a Cepheid SmartCycler® II instrument. In this process, the probe anneals specifically to the template followed by primer extension and amplification. The Pro hMPV+ Assay is based on Taqman chemistry, which utilizes the 5' – 3' exonuclease activity of the Taq polymerase to cleave the probe thus separating the reporter dye from the quencher. This generates an increase in fluorescent signal upon excitation from a light source. With each cycle, additional reporter dye molecules are cleaved from their respective probes, further increasing fluorescent signal. The amount of fluorescence at any given cycle is dependent on the amount of amplification products present at that time. Fluorescent intensity is monitored during each PCR cycle by the SmartCyclerII instrument.

SUBSTANTIAL EQUIVALENCE

Clinical Performance

Performance characteristics of the Pro hMPV+ Assay were established during a prospective study at 4 U.S. clinical laboratories during the 2008 respiratory virus season (January - March). Specimens used in the study represented excess nasopharyngeal (NP) swab specimens that were prospectively collected from symptomatic individuals suspected of respiratory infection, and were submitted for routine care or analysis by each site. Demographic details for this patient population are summarized in the following table:

Gender	Number of Subjects (Percentage of Total)
Female	617 (48.4%)
Male	654 (51.3%)
Not Determined	4 (0.3%)
Age	
≤ 5 years	596 (46.7%)
6 - 21 years	254 (19.9%)
22 – 59 years	219 (17.2%)
≥ 60 years	206 (16.2%)
Not Determined	0 (0.0%)

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Performance of the Pro hMPV+ Assay was assessed and compared to a predetermined algorithm that used composite reference methods. The composite reference methods consisted of two independent molecular (RT-PCR) tests for two separate gene targets of hMPV followed by bi-directional genetic sequencing. The two comparator methods targeted the Nucleocapsid gene (different region of the gene than targeted by the Pro hMPV+ assay) and the Fusion gene. True hMPV RNA positives were considered as any sample that had bi-directional sequencing data meeting pre-defined quality acceptance criteria for one or both gene targets that matched hMPV sequences deposited in the National Center for Biotechnology Information (NCBI) GenBank database (www.ncbi.nlm.nih.gov). True hMPV RNA negatives were considered as any sample that was tested negative by both of the comparator methods. Nucleic acid extractions on the clinical samples were carried out using either the Roche MagNA Pure LC system or the bioMérieux NucliSENS easyMAG during the clinical study.

A total of 1275 eligible NP swab samples were tested with the Pro hMPV+ Assay at the four clinical sites and by the composite reference methods at Prodesse. Of the Pro hMPV+ Assay run on all eligible specimens, 98.1% (1273/1298) of these specimens were successful on the first attempt. The remaining 25 specimens gave "Unresolved" results on the first attempt. Unresolved results occur when the sample is negative for both hMPV and the Internal Control, indicating potentially PCR-inhibiting samples. Of the 25 "Unresolved" specimens on the first attempt with sufficient sample for retest, 8.0% (2/25) gave a valid "negative" result on the second attempt. The remaining 23 samples were "Unresolved" on the second attempt, therefore, were not included in the analysis below. All 23 samples were tested negative by the composite reference methods.

		Composite Reference Methods			
		Positive	**Negative**	**Total**	**Comments**
Pro hMPV+ Assay	**Positive**	64	8	**72**	Percent Positive Agreement 94.1% (85.8% - 97.7%) 95% CI
	Negative	4	1199	**1203**	Percent Negative Agreement 99.3% (98.7% - 99.7%) 95% CI
	Total	**68**	**1207**	**1275**	

Reproducibility

The reproducibility of the Pro hMPV+ Assay was evaluated at 3 laboratory sites. Reproducibility was assessed using a panel of 9 simulated samples that included medium positive, low positive (near the assay limit of detection) and "high negative" hMPV samples. Panels and controls were tested at each site by 2 operators for 5 days (9 samples and 3 controls X 2 operators X 5 days X 3 sites = 360). Nucleic acid extraction on the test panel samples were carried out using either the Roche MagNA Pure LC system (Clinical Trial Site #4) or the

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bioMérieux NucliSENS easyMAG (Site #1 and Site #2). The overall percent agreement with the expected result for the Pro hMPV+ Assay was 99.2%.

	Panel Member ID	hMPV A2 High Negative [a]	hMPV A2 Low Positive	hMPV A2 Moderate Positive	hMPV B2 High Negative [a]	hMPV B2 Low Positive	hMPV B2 Moderate Positive	hMPV RNA Control	Negative Control[a]	Extraction Control hMPV A2	Total % Agreement
	Concentration	0.01 X LoD	2 X LoD	10 X LoD	0.01 X LoD	2 X LoD	10 X LoD	NA	NA	NA	
		1×10^{0} $TCID_{50}$/mL	2×10^{2} $TCID_{50}$/mL	1×10^{3} $TCID_{50}$/mL	1×10^{-1} $TCID_{50}$/mL	2×10^{1} $TCID_{50}$/mL	1×10^{2} $TCID_{50}$/mL				
Site 1	Agreement with Expected result	15/15 (100%)	15/15 (100%)	15/15 (100%)	15/15 (100%)	15/15 (100%)	15/15 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	**120/120 (100%)**
	Average Ct Value	26.6	29.2	27.1	27.5	29.3	26.6	32.5	26.2	33.1	
	% CV	1.53	2.84	1.21	1.97	2.20	1.68	0.81	0.80	2.73	
Site 2	Agreement with Expected result	15 /15 (100%)	14/15 (93.3%)	15/15 (100%)	15/15 (100%)	13/15 (86.7%)	15/15 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	**117/120 (97.5%)**
	Average Ct Value	25.8	30.7	26.9	26.9	30.7	26.3	32.8	25.6	32.9	
	% CV	0.54	3.95	2.88	1.44	4.14	1.25	1.37	0.98	4.86	
Site 4	Agreement with Expected result	15/15 (100%)	15/15 (100%)	15/15 (100%)	15/15 (100%)	15/15 (100%)	15/15 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	**120/120 (100%)**
	Average Ct Value	27.4	30.5	27.8	28.5	29.4	27.0	33.6	27.6	28.8	
	% CV	1.45	2.15	2.13	3.00	3.80	2.50	1.09	1.87	3.08	
	Total Agreement with Expected result	45/45 (100%)	44/45 (97.8%)	45/45 (100%)	45/45 (100%)	43/45 (95.6%)	45/45 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	**357/360 (99.2%)**
	95% CI	92.1% -100%	88.4% -99.6%	92.1% -100%	92.1% -100%	85.2% -98.8%	92.1% -100%	88.6% - 100%	88.6% - 100%	88.6% - 100%	**97.6% - 99.7%**
	Overall Average Ct Value	**26.6**	**30.1**	**27.63**	**27.6**	**29.7**	**26.6**	**33.0**	**26.5**	**31.6**	
	Overall %CV	**2.85**	**3.73**	**2.57**	**3.29**	**3.97**	**2.16**	**1.72**	**3.49**	**7.36**	

[a]Average Ct value calculated for the Internal Control (IC)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Karen Harrington
Manager, Clinical Affairs
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Re: k082688
Trade/Device Name: Pro hMPV+ Assay
Regulation Number: 21 CFR § 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OEM
Dated: September 12th, 2008
Received: September 15th, 2008

Dear Ms. Harrington:

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K082688

Device Name: Pro hMPV+ Assay

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

Prescription Use ___X___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

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