K123838

Attachment D
510(k) SUMMARY

Modification of Prodesse Pro hMPV+ Assay

JAN 16 2013

INTRODUCTION: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis of substantial equivalence.

SUBMITTED BY:

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Contact: Karen Harrington, PhD
Date Submitted: 12/10/2012

NAME AND CLASSIFICATION OF DEVICE

Trade Name:	ProhMPV+ Assay
Regulation Number:	21 CFR 866.3980
Product Code:	OEM
Classification Name:	Nucleic acid amplification assay for human metapneumovirus RNA

PREDICATE DEVICE

- K082688, Gen-Probe Prodesse Pro hMPV+ Assay
- K112490, Quidel Molecular hMPV Assay
- K063765, K081483, K091667 Luminex ID-Tag RVP Assay

INTENDED USE

The Pro hMPV™+ Assay is a Real-Time PCR (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 hMPVnucleic 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

The Pro hMPV+ Assay is substantially equivalent to the Pro hMPV+ Assay (K082688), Quidel Molecular hMPV Assay (K112490) and the Luminex RVP Assay (K063765, K081483, and K091667). All were determined to be class II devices.

The following table compares the Pro hMPV+ Assay to the previously cleared Pro hMPV+ Assay (K082688), Quidel Molecular hMPV Assay (K112490) and the Luminex RVP Assay (K063765, K081483, and K091667).

Features	New Device	Predicate Devices	
	New Pro hMPV+ Assay	**Current Pro hMPV+ Assay**	**Luminex RVP**
510(k)	TBD	K082688	K063765, K081483, K091667
Regulation	866.3980	866.3980	866.3980
Product Code	OEM	OEM	OCC, OEM, OEP
Device Class	Class II	Class II	Class II
Intended Use	For the *in vitro*	For the *in vitro*	Direct and differential

Features	New Device	Predicate Devices	
	New Pro hMPV+ Assay	**Current Pro hMPV+ Assay**	**Luminex RVP**
	qualitative detection of human metapneumovirus nucleic acids.	qualitative detection of human metapneumovirus nucleic acids.	qualitative detection of human metapneumovirus, influenza types A and B, RSV types A and B, Parainfluenza types 1, 2 and 3, Adenovirus, and Rhinovirus viral nucleic acids.
Technology/ Detection	Real Time RT-PCR Detection	Real Time RT-PCR Detection	RT-PCR Detection: Amplified products are coupled to microspheres and detected using spectrofluorometric analysis.
Specimen Types	NP swabs	NP swabs	NP swabs
Nucleic Acid Isolation	Roche MagNA Pure LC System and bioMérieux NucliSENS easyMAG	Roche MagNA Pure LC System and bioMérieux NucliSENS easyMAG	NucliSENS®miniMAG extraction Kit (bioMérieux) QIAamp®MiniElute® Virus Spin Kit (Qiagen)
Instrument /Assay Platform	Cepheid SmartCycler II System	Cepheid SmartCycler II System	Luminex 100 or 200
Assay Controls	hMPV positive RNA transcript control and an Internal RNA control provided	hMPV positive RNA transcript control and an Internal RNA control provided	Bacteriophage lambda positive control and *E. coli* MS2 phage Internal Control – ancillary reagents not provided

Element	New Device: Pro hMPV+ Assay	Predicate: Current Pro hMPV+ Assay (K082688)
Assay Cutoff Cycle for hMPV detection	35	40
hMPV Positive RNA Control	Provided "at use" concentration for RT-PCR (no dilution prior to RT-PCR required).	Dilute 1:10 prior to use for RT-PCR

Clinical Comparison Study

The Pro hMPV+ Assay's supermix was reformulated and performance characteristics were established by comparing the reformulated assay to the original Pro hMPV+ Assay. One hundred eighty-three retrospective nasopharyngeal swab samples collected during 2011 – 2012 at two sites (Milwaukee, WI and Chicago, IL) were used for this study. hMPV positive and negative NP swab samples were selected for inclusion based on previous site-specific molecular test results. One sample was not used in the final analysis as it was Unresolved upon initial and repeat testing with both the original and reformulated

ProhMPV+ Assays.

"True" hMPV positives were considered as any sample that tested positive for hMPV by the original Pro hMPV+ Assay. "True" hMPV negatives were considered as any sample that tested negative for hMPV by the original Pro hMPV+ Assay. Discrepant analysis for samples where the reformulated Pro hMPV+ Assay and the original Pro hMPV+ results were in disagreement was performed using RT-PCR with hMPV specific primers targeting the hMPV phosphoprotein gene followed by bi-directional genetic sequencing.

hMPV Comparison Results

		Current Pro hMPV+ Assay			
		Positive	**Negative**	**Total**	**Comments**
New Pro hMPV+ Assay	**Positive**	43	2*	**45**	Percent Positive Agreement 100% (91.80%-100%) 95% CI
	Negative	0	137	**137**	Percent Negative Agreement 98.6% (94.91%-99.61%) 95% CI
	Total	**43**	**139**	**182**	

* Two samples tested positive for hMPV by bi-directional sequencing.

Select Analytic Studies

Limit of Detection

The analytical sensitivity (limit of detection or LoD) of the Pro hMPV+ Assay was determined using quantified ($TCID_{50}$/mL) cultures of two hMPV (subtype A2 and subtype B2) strains serially diluted in nasopharyngeal clinical matrix. Each viral strain was processed using the bioMérieux NucliSENS EasyMAG system for extraction and the SmartCycler II Instrument for RT-PCR. The LoD was identical to the original Pro hMPV+ Assay for hMPV strain A2 and 0.5 log lower for hMPV strain B2.

Viral Strain	**LoD Concentration (Original Pro hMPV+)**	**LoD Concentration (Reformulated Pro hMPV+)**
hMPV subtype A2	$10^2 TCID_{50}$/mL	$10^2 TCID_{50}$/mL
hMPV subtype B2	10^1 $TCID_{50}$/mL	$10^{0.5}$ $TCID_{50}$/mL

Positive Control Effectiveness

The Pro hMPV+ Control (PC) is a non-infectious *in vitro* transcribed RNA of the hMPV viral sequence targeted by the New Pro hMPV+ Assay. Its purpose is to test for procedural errors (absence of reagent, instrument failure, etc.) that may result in failure of the assay to detect hMPV. The New Pro hMPV+ Assay uses the PC at a higher concentration than Current Pro hMPV. "Defective" RT-PCR master mixes (e.g. no reverse transcriptase, no Taq polymerase, decreased hMPV primer concentration) were prepared and tested to assess the PC's ability to detect global errors. Each defective mix was tested using 20 replicates of the New Pro hMPV+ Control. A Negative Control (NC) consisting of Internal Control (IC) in viral transport media was included in each run. For each defective mix, none of the hMPV PC replicates were detected and thus, the New PC was considered effective.

CONCLUSION:

The results of the clinical study indicate that the New Pro hMPV+ Assay is sensitive and specific as compared to the Current Pro hMPV+ Assay (K082688). Furthermore, analytical studies support substantial equivalence to the predicate device, the current Pro hMPV+ Assay (K082688).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

JAN 16 2013

Gen-Probe Prodesse, Inc.
C/O Karen Harrington, PhD
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Waukesha, WI, 53186

Re: K123838
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: December, 12, 2012
Received: December 17, 2012

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

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. 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.

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 (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Uwe Scherf for

Sally A. Hojvat, M.Sc., Ph.D.
Director
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Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): K

Device Name: Pro hMPV+ Assay

Indication For Use:

The Prodesse® Pro hMPV™+ Assay is a Real-Time PCR (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.

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)

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

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