K101855

Attachment D
510(k) SUMMARY

CONTACT

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Waukesha, WI 53186

JUL 23 2010

NAME OF DEVICE

Trade Name:	ProFAST+™ Assay
Regulation Number:	21 CFR 866.3980
Classification Name:	Respiratory viral panel multiplex nucleic acid assay

PREDICATE DEVICE

- K063765, K081483, K091677 – ID Tag Respiratory Virus Panel, Luminex Molecular Diagnostics
- K080570 – Human Influenza Virus Real Time RT-PCR Detection and Characterization Panel, CDC
- K100148 – Simplexa Influenza A H1N1 (2009), Focus Diagnostics
- K073029, K081030, K092500 – ProFlu+ Assay, Gen-Probe Prodesse, Inc.

INTENDED USE

The ProFAST™+ Assay is a multiplex Real Time RT-PCR *in vitro* diagnostic test for the qualitative detection and discrimination of seasonal Influenza A/H1, seasonal Influenza A/H3 and 2009 H1N1 Influenza viral nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens from human patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors. This assay targets conserved regions of the Hemagglutinin (HA) gene for seasonal Influenza A/H1, seasonal Influenza A/H3 and 2009 H1N1 Influenza Virus, respectively. This assay is not intended to detect Influenza B or Influenza C Viruses.

A negative ProFAST+ Assay result is a presumptive negative result for Influenza A. These results should be confirmed by an FDA cleared nucleic acid-based test (NAT) detecting Influenza A.

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

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 department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

PRODUCT DESCRIPTION

The ProFAST+ Assay enables detection and discrimination of Influenza A Virus subtypes: seasonal H1, seasonal H3, and 2009 H1N1.

An overview of the procedure is as follows:

1. Collect nasopharyngeal swab specimens from symptomatic patients using a polyester, rayon, or nylon tipped swab and place into viral transport medium (refer to **Materials Required but not Provided section of this Instruction for Use**).
2. Add an Internal Control (IC) to every sample to monitor for inhibitors present in the specimens.
3. Perform isolation and purification of nucleic acids using 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).
4. Add purified nucleic acids to the ProFAST+ Supermix along with enzymes included in the ProFAST+ kit. The ProFAST+ Supermix contains target-specific oligonucleotide primers and probes. The primers are complementary to conserved regions of the Hemagglutinin (HA) gene for seasonal influenza A/H1, seasonal influenza A/H3 and 2009 H1N1 Influenza Virus (swine-origin), respectively. The probes are dual-labeled with a reporter dye and a quencher dye (see table below).
5. Perform reverse transcription of RNA into complementary DNA (cDNA) and subsequent amplification of DNA in a Cepheid SmartCycler II instrument. In this process, the probe anneals specifically to the template followed by primer extension and amplification. The ProFAST+ 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 real-time instrument.

Analyte	Gene Targeted	Probe Fluorophore	Absorbance Peak	Emission Peak
Seasonal H1 Influenza A	*Hemagglutinin*	FAM	495 nm	520 nm
Seasonal H3 Influenza A	*Hemagglutinin*	Cal Fluor Orange 560	540 nm	561 nm
2009 H1N1 Influenza Virus	*Hemagglutinin*	Cal Fluor Red 610	595 nm	615 nm
Internal Control	*E.coli* MS2 Phage *A-Protein*	Quasar 670	647 nm	667 nm

SUBSTANTIAL EQUIVALENCE

Clinical Performance

The clinical performance of the ProFAST+ Assay was established during prospective studies at 4 U.S. clinical laboratories. NP swab samples were collected and tested at three U.S. clinical laboratories during December 2009 thru May 2010. Due to the absence of seasonal (H1N1 or H3N2) and 2009 H1N1 Influenza A during the typical 2009-2010 winter season, prospectively collected archived samples were also included in the prospective studies. These samples were collected from January – March, 2008, February – March, 2009 and October – November, 2009, and tested at two U.S. clinical laboratories. All specimens used in the study meeting the inclusion and exclusion criteria represented excess, remnants of 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, and that otherwise would have been discarded.

Demographic details for the patient population included in the prospective study are summarized in the following table.

Gender and Age Demographic Detail for ProFAST+ Prospective Study

Sex	Number of Subjects
Female	439 (52.1%)
Male	403 (47.9%)
Age	
≤ 5 years	439 (52.1%)
6 - 21 years	184 (21.9%)
22 – 59 years	168 (20.0%)
≥ 60 years	51 (6.0%)

Performance of the ProFAST+ Assay was assessed and compared to the composite comparator/reference method of the FDA cleared ProFlu+ Assay and individual well characterized Influenza A subtype specific RT-PCR assays followed by bi-directional sequencing. The sequencing assays targeted different regions of the hemagglutinin gene than the ProFAST+ Assay and were specific for each of the Influenza A subtypes (A/H1, A/H3, and A/2009 H1N1). "True" seasonal A/H1, A/H3 or A/2009 H1N1 RNA positives, were considered as any sample that was tested positive for Influenza A by the ProFlu+ Assay, and had bi-directional sequencing data meeting pre-defined quality acceptance criteria, for both the forward and the reverse sequences that matched seasonal A/H1, A/H3, and A/2009 H1N1 sequences deposited in the National Center for Biotechnology Information (NCBI) GenBank database (www.ncbi.nlm.nih.gov), respectively, with acceptable E-values. "True" seasonal A/H1, A/H3 or A/2009 H1N1 RNA negatives were considered as any sample that was tested negative for Influenza A by the ProFlu+ Assay IVD, or any sample that was tested positive for Influenza A by the ProFlu+ Assay IVD, but was tested negative by the respective Influenza A subtype specific RT-PCR assay followed by bi-directional sequencing. 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 874 prospective NP swab specimens were initially included in the prospective clinical trial. Thirty two (32) samples were excluded from the prospective clinical study data analysis because they remained "Unresolved" after repeat testing for either the ProFlu+ Assay (comparator assay), or the ProFAST+ Assay, or both assays, resulted in a total 842 eligible prospective specimens to be included in the prospective clinical study data analysis.

Of the prospective specimens run using the ProFAST+ Assay, 98.9% (864/874) of these specimens were successful on the first attempt. The remaining 10 (10/874 = 1.1%) gave "Unresolved" results on the first attempt. Unresolved results occur when the sample is negative for all three Influenza A subtype markers and the Internal Control, indicating potentially PCR-inhibiting samples. Of the 10 "Unresolved" specimens on the first attempt with sufficient nucleic acid for retest, only 50.0% (5/10) gave a valid result on the second attempt (3 from Site 1, 1 from site 2, and 1 from Site 3). The remaining 5 were "Unresolved" on the second attempt.

Seasonal Influenza A/H1 Comparison Results

		ProFlu+/Sequencing			
		Positive	**Negative**	**Total**	
ProFAST+ Assay	**Positive**	53	8[a]	**61**	Positive Percent Agreement=100.0% (93.2% - 100.0%) 95% CI
	Negative	0	781	**781**	Negative Percent Agreement=99.0% (98.0% - 99.5%) 95% CI
	Total	**53**	**789**	**842**	

[a] Two (2) samples were negative for Influenza A by the ProFlu+ Assay, but positive for seasonal A/H1 by bi-directional sequence analysis. One (1) sample was negative for Influenza A by the ProFlu+ Assay, and negative for seasonal A/H1 by bi-directional sequence analysis, but positive for Influenza A, un-subtyptable, by the FDA cleared CDC rRT-PCR Influenza Panel. Five (5) samples were positive for Influenza A by the ProFlu+ Assay, negative for A/H1, A/H3 and A/2009 H1N1 by bi-directional sequence analysis, but positive for A/H1 by the FDA cleared CDC rRT-PCR Influenza Panel.

Seasonal Influenza A/H3 Comparison Results

		ProFlu+/Sequencing			
		Positive	**Negative**	**Total**	
ProFAST+ Assay	**Positive**	25	3[a]	**28**	Positive Percent Agreement=100.0% (86.7% - 100.0%) 95% CI
	Negative	0	814	**814**	Negative Percent Agreement=99.6% (98.9% - 99.9%) 95% CI
	Total	**25**	**817**	**842**	

[a] One (1) sample was negative for Influenza A by the ProFlu+ Assay, also negative for seasonal A/H1 and A/H3, and A/2009 H1N1 by bi-directional sequence analysis. One (1) sample was positive for Influenza A by the ProFlu+ Assay, negative for A/H1, A/H3 and A/2009 H1N1 by bi-directional sequence analysis, but positive for A/H3 by the FDA cleared CDC rRT-PCR Influenza Panel. One (1) sample was positive for Influenza A by the ProFlu+ Assay, positive for A/H1 and negative for A/H3 and A/2009 H1N1 by bi-directional sequence analysis.

2009 H1N1 Influenza Comparison Results

		ProFlu+/Sequencing			
		Positive	**Negative**	**Total**	
ProFAST+ Assay	**Positive**	62	0	**62**	Positive Percent Agreement=95.4% (87.3% - 98.4%) 95% CI
	Negative	3	777	**780**	Negative Percent Agreement=100.0% (99.5% - 100.0%) 95% CI
	Total	**65**	**777**	**842**	

Retrospective Study

In addition to the prospective clinical study, two clinical sites also performed testing using retrospective samples that were collected from January – March, 2008, January – November 2009, and March 2010. The ProFAST+ Assay was compared to the same composite comparator/reference method that was employed for the prospective study to determine clinical Percent Positive Agreement and Percent Negative Agreement. A total of 160 retrospective nasopharyngeal (NP) swab samples were included in the retrospective study.

Demographic details for this patient population are summarized in the table below.

Gender and Age Demographic Detail for ProFAST+ Retrospective Study

Sex	Number of Subjects
Female	74 (46.3%)*
Male	84 (52.5%)*
Age	
≤ 5 years	25 (15.6%)
6 - 21 years	24 (15.0%)
22 – 59 years	91 (56.9%)
≥ 60 years	20(12.5%)

*For two of the subjects, the gender was unknown.

Seasonal Influenza A/H1 Comparison Results

		ProFlu+/Sequencing			
		Positive	**Negative**	**Total**	
ProFAST+ Assay	**Positive**	17	1[a]	**18**	Positive Percent Agreement=94.4% (74.3% - 99.0%) 95% CI
	Negative	1	141	**142**	Negative Percent Agreement=99.3% (96.1% - 99.9%) 95% CI
	Total	**18**	**142**	**160**	

[a] One (1) sample was negative for Influenza A by the ProFlu+ Assay, but positive for seasonal A/H1 by bi-directional sequence analysis.

Seasonal Influenza A/H3 Comparison Results

		ProFlu+/Sequencing			
		Positive	**Negative**	**Total**	
ProFAST+ Assay	**Positive**	72	0	**72**	Positive Percent Agreement=100.0% (94.9% - 100.0%) 95% CI
	Negative	0	88	**88**	Negative Percent Agreement=100.0% (95.8% - 100.0%) 95% CI
	Total	**72**	**88**	**160**	

2009 H1N1 Influenza A Comparison Results

		ProFlu+/Sequencing			
		Positive	**Negative**	**Total**	
ProFAST+ Assay	**Positive**	25	0	**25**	Positive Percent Agreement=100.0% (86.7% - 100.0%) 95% CI
	Negative	0	135	**135**	Negative Percent Agreement=100.0% (97.2% - 100.0%) 95% CI
	Total	**25**	**135**	**160**	

Reproducibility

The reproducibility of the ProFAST+ Assay was evaluated at 3 laboratory sites. Reproducibility was assessed using a panel of 18 simulated samples that included medium positive, low positive (near the assay limit of detection, ≥ 95% positive), and high negative (below the assay limit of detection, < 5% positive) samples for each of the three Influenza A subtypes detected by the assay. Panels and controls were tested at each site by 2 operators for 5 days. Nucleic acid extraction was carried out using either the Roche MagNA Pure LC System or the bioMérieux NucliSENS easyMAG System. The overall percent agreement with the expected result for the ProFAST+ Assay was 99.7%.

	Panel Member ID	A/H1 negative (values from IC)	A/H1 low positive	A/H1 medium positive	A/H3 negative (values from IC)	A/H3 low positive	A/H3 medium positive	A/2009 H1N1 negative (values from IC)	A/2009 H1N1 low positive	A/2009 H1N1 medium positive	Extraction Control			Influenza A Subtyping RNA Control			Negative Control	Total % Agreement
											A/H1	A/H3	A/2009 H1N1	A/H1	A/H3	A/2009 H1N1		
	Concentration	0.001 X LoD	2 X LoD	10X LoD	0.001 X LoD	2 X LoD	10X LoD	0.001 X LoD	2 X LoD	10X LoD	N/A			N/A			N/A	
Site 1	Agreement with Expected Result	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	10/10			10/10			10/10	210/210 (100%)
	Mean Ct Value	29.3	34.7	32.1	29.5	32.5	30.3	29.4	31.3	28.6	29.3	27.5	27.9	32.4	31.3	31.6	29.5	
	% CV	1.54	1.16	0.58	1.77	0.96	0.58	1.52	0.76	1.45	0.78	1.01	3.04	0.79	0.79	0.89	0.71	
Site 2	Agreement with Expected Result	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	10/10			10/10			10/10	210/210 (100%)
	Mean Ct Value	27.0	34.1	31.0	27.1	31.7	29.5	26.9	30.6	28.0	28.1	26.5	27.3	32.1	31.0	31.2	26.4	
	% CV	1.41	3.11	0.86	1.54	0.86	0.93	1.41	2.09	0.91	0.38	0.86	1.72	0.61	0.95	0.80	0.95	
Site 3	Agreement with Expected Result	20/20	19/20	20/20	20/20	19/20	20/20	20/20	20/20	20/20	10/10			10/10			10/10	208/210 (99.0%)
	Mean Ct Value	28.5	36.1	32.0	28.6	32.4	30.2	28.3	31.5	28.7	28.9	27.2	29.4	32.0	30.9	31.0	28.8	
	% CV	4.28	7.26	1.80	4.44	1.66	2.42	3.02	2.20	1.13	1.44	1.54	1.42	1.13	1.45	1.05	4.88	
	Total Agreement with Expected Result	60/60	59/60	60/60	60/60	59/60	60/60	60/60	60/60	60/60	30/30			30/30			30/30	628/630 (99.7%)
	95% CI	94.0 - 100%	91.1- 99.7%	94.0 - 100%	94.0 - 100%	91.1- 99.7%	94.0 - 100%	94.0 - 100%	94.0 - 100%	94.0 - 100%	88.7% - 100%			88.7% - 100%			88.7 - 100%	98.8% - 99.9%
	Overall Mean Ct Value	28.2	34.9	31.7	28.4	32.2	30.0	28.2	31.1	28.5	28.8	27.1	28.3	32.2	31.0	31.3	28.2	
	Overall % CV	4.40	5.08	1.97	4.49	1.59	1.94	4.11	2.12	1.66	1.99	1.95	3.86	1.01	1.19	1.21	5.62	

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center – WO66-0609
Silver Spring, MD 20993-0002

JUL 23 2010

Karen Harrington, Ph.D.
Manager, Clinical Affairs
Gen-Probe Prodesse Inc.
W229 N1870 Westwood Dr.
Waukesha, WI, 53186

Re: K101855

Trade/Device Name:	Prodesse ProFAST+ Assay
Regulation Number:	21 CFR §866.3332
Regulation Name:	Reagents for detection of specific novel influenza A viruses
Regulatory Class:	Class II
Product Code:	OQW
Dated:	June 30, 2010
Received:	July 1, 2010

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 Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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/MedicalDevices/ResourcesforYou/Industry/default.htm.

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): K101855

Device Name: ProFAST+™ Assay

Indication For Use:

The ProFAST™+ Assay is a multiplex Real Time RT-PCR *in vitro* diagnostic test for the qualitative detection and discrimination of seasonal Influenza A/H1, seasonal Influenza A/H3 and 2009 H1N1 Influenza viral nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens from human patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors. This assay targets conserved regions of the Hemagglutinin (HA) gene for seasonal Influenza A/H1, seasonal Influenza A/H3 and 2009 H1N1 Influenza Virus, respectively. This assay is not intended to detect Influenza B or Influenza C Viruses.

A negative ProFAST+ Assay result is a presumptive negative result for Influenza A. These results should be confirmed by an FDA cleared nucleic acid-based test (NAT) detecting Influenza A.

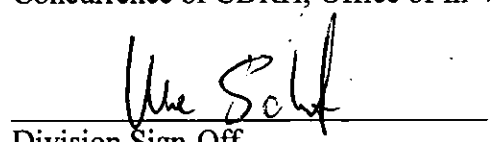
Negative results do not preclude Influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions.

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 department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

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

510(k) K101855