NOV 1 0 2010

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of the SMDA 1990 and 21 CFR Part 807.92.

The assigned 510(k) number is: K083746

1. Date of Summary: August 17, 2010

2. Submitted by: Princeton BioMeditech Corporation
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3. Device Name: Trade Names: BioSign® Flu A+B
   Status™ Flu A & B
   Common or Usual Name: Influenza test
   Classification Name: Influenza virus serological reagents (21CFR 866.3330)

4. Identification of legally marketed devices to which claims of equivalence are made:
   K053146: QuickVue Influenza A+B Test by Quidel Corp.

5. Device Description:

   BioSign® Flu A+B is an immuno-chromatographic test for the rapid, qualitative detection of influenza A and B. The test device has two test lines, thereby allowing the separate identification of type A and/or type B viral antigens from the same specimen.
   In the test procedure, a specimen is collected and placed into the Extraction Well of the test device containing extraction solution for one minute, during which time antigen is extracted from disrupted virus particles. The test device is then raised, tapped and laid back down onto a level surface to allow the solution in the Extraction Well to migrate through the pads containing lyophilized detector antibodies conjugated to gold dye and then through the test membrane. If influenza antigens are present in the specimen, they will react with anti-influenza antibody coupled to gold dye particles, migrate through the membrane as antigen-antibody-dye complexes, bind to the immobilized anti-influenza antibody on the membrane, and generate a colored line in the Test line position (A and/or B). The rest of the sample and unbound/bound dye complexes continue to migrate to the Control line position, where antibody to the anti-influenza antibody is immobilized, and anti-influenza antibody-unbound/bound dye complexes form the Control line (internal procedural control).

6. Intended Use:

   The BioSign® Flu A+B test is an *in vitro* rapid qualitative test that detects influenza type A and type B antigens directly from nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens obtained from patient with signs and symptoms of respiratory infection. It is intended to aid in the rapid differential diagnosis of influenza A and B viral infections. A negative test result is presumptive and it is recommended these results be confirmed by viral

culture. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other management decisions. The test is intended for professional and laboratory use.

7. Technological Characteristics

Both BioSign® Flu A+B and the predicate, QuickVue® Influenza A+B tests are *in vitro* rapid qualitative tests that detect influenza type A and type B antigens directly from nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens. The scientific principle of both tests is a solid phase chromatographic immunoassay. Both tests are lateral flow rapid assays that employ specific antibodies immobilized onto solid phases to capture and visualize influenza nucleoprotein antigens.

8. Performance Summary

Clinical Study

A prospective clinical study was conducted from January 2007 to March 2008 and during March and April 2009 to determine the performance of BioSign® Flu A+B for aspirate, nasopharyngeal swab, and nasal swab specimens. The samples were collected at 5 sites in the USA from patients who visited physicians' offices and clinics with signs and symptoms of respiratory infection during the study period. All collected samples were tested with BioSign® Flu A+B, and were cultured to confirm the results of BioSign® Flu A+B. The total number of patients tested was 862, of which 30% were 5 and younger, 38% were 6-21 years old, and the rest were older than 21. Forty eight (48) percent were male and 52% were female.

The combined data from all sites of the prospective study are presented in the tables below.

The samples that produced discrepant results between **BioSign® Flu A+B** and viral culture were further analyzed with *pro*FLU *plus* by Prodesse (real time RT-PCR, PCR hereafter). These results are presented in the footnote below each table.

Nasopharyngeal Aspirate Sample

	Reference (Virus Culture) Results			
BioSign Flu A+ B	Flu A Positive	Flu A Negative	Total	Performance
Flu A Positive	41	30*	71	Sensitivity: 95.3% 95% CI: 92.1-98.5%
Flu A Negative	2**	180	182	Specificity: 85.7% 95% CI: 83.3-88.1%
Total	43	210	253	

	Reference (Virus Culture) Results			
BioSign Flu A+ B	Flu B Positive	Flu B Negative	Total	Performance
Flu B Positive	11	6*	17	Sensitivity: 91.6% 95% CI: 83.6-99.6%
Flu B Negative	1**	235	236	Specificity: 97.5% 95% CI: 96.5-98.5%
Total	12	241	253	

*Of 30 discrepant results, 22 were positive by both BioSign and PCR
** Of 2 discrepant results, 1 was negative by both BioSign and PCR

*Of 6 discrepant results, all 6 were positive by BioSign and by PCR
** The discrepant sample was positive by PCR

Nasopharyngeal Sample

BioSign Flu A+ B	Reference (Virus Culture) Results: Flu A Positive	Flu A Negative	Total	Performance
Flu A Positive	26	51*	77	Sensitivity: 89.6% 95% CI: 84.0-95.2%
Flu A Negative	3**	171	174	Specificity: 77.0% 95% CI: 74.2-79.8%
Total	29	222	251	

*Of 51 discrepant results, 41 were positive by both BioSign and PCR
** Of 3 discrepant results, 1 was negative by both BioSign and PCR

BioSign Flu A+ B	Reference (Virus Culture) Results: Flu B Positive	Flu B Negative	Total	Performance
Flu B Positive	33	15*	48	Sensitivity: 86.8% 95% CI: 81.4-92.2%
Flu B Negative	5**	198	203	Specificity: 92.9% 95% CI: 91.2-94.6%
Total	38	213	251	

*Of the 15 discrepant results, 8 were positive by both BioSign and PCR
** Of the 5 discrepant results, 2 were negative by both BioSign and PCR

Nasal Swab Sample

BioSign Flu A+ B	Reference (Virus Culture) Results: Flu A Positive	Flu A Negative	Total	Performance
Flu A Positive	33	80*	113	Sensitivity: 91.7% 95% CI: 78.2-97.1%
Flu A Negative	3**	242	245	Specificity: 75.2% 95% CI: 70.2-79.6%
Total	36	322	358	

*Of 80 discrepant results, 65 were positive by both BioSign and PCR
** Of 3 discrepant results, all 3 were positive by PCR

BioSign Flu A+ B	Reference (Virus Culture) Results: Flu B Positive	Flu B Negative	Total	Performance
Flu B Positive	14	40*	54	Sensitivity: 82.4% 95% CI: 59.0-93.8%
Flu B Negative	3**	301	304	Specificity: 88.3% 95% CI: 84.4-91.3%
Total	17	341	358	

*Of 40 discrepant results, 18 were positive by both BioSign and PCR
** Of 3 discrepant results, 1 was negative by both BioSign and PCR

As further verification of the PCR test results shown from the samples with discrepant results between BioSign and viral culture, available archived remnant samples from the clinical studies with concordant results were also tested by PCR. The specificity for both Flu A and Flu B was 100%, while the sensitivity for Flu A was 90% and the sensitivity for Flu B was 91.7%.

Archived Sample Test

Eighty (80) frozen archived samples originally obtained from influenza positive patients visiting Columbia NY Presbyterian Hospital and confirmed as positive for either influenza A or Influenza B by viral culture were tested with BioSign Flu A+B.

The tables below present test results with archived samples.

Aspirate Sample

	Reference (Virus Culture) Results			
BioSign Flu A+ B	Flu A Positive	Flu A Negative	Total	Agreement
Flu A Positive	50	0	50	100%
Flu A Negative	0	30	30	100%
Total	50	30	80	

	Reference (Virus Culture) Results			
BioSign Flu A+ B	Flu B Positive	Flu B Negative	Total	Agreement
Flu B Positive	30	0	30	100%
Flu B Negative	0	50	50	100%
Total	30	50	80	

Swab Sample

T	Reference (Virus Culture) Results			
BioSign Flu A+ B	Flu A Positive	Flu A Negative	Total	Agreement
Flu A Positive	50	0	50	100%
Flu A Negative	0	30	30	100%
Total	50	30	80	

	Reference (Virus Culture) Results			
BioSign Flu A+ B	Flu B Positive	Flu B Negative	Total	Agreement
Flu B Positive	30	0	30	100%
Flu B Negative	0	50	50	100%
Total	30	50	80	

Reproducibility Study

The reproducibility study for the BioSign® Flu A+B test was conducted at two Physicians' Offices and one laboratory using a panel of 180 coded specimens for each site. Testing was performed by two people for five days at each site following the same test protocol as would be used for fresh patient sample. The panel contained high negative, low positive and moderate positive specimens. Each specimen level was tested at each site in replicates of 15 over a period of five days.

The results obtained at each site agreed 100% with the expected results. No differences were observed within run (15 replicates), between runs (three different days), or between sites (three POL sites and one lab).

Analytical Sensitivity

Limit of Detection (LOD)

The LODs were determined for each of the two strains selected from the influenza type A and type B strains. The sensitivity level of each selected viral strain was tested 60 times to confirm the sensitivity level as LOD level, which gives 95% detection rate.
All four viral strains tested were detected 96.7% of the time in 60 replicates at the level listed in the table below.

Influenza Type	Viral Strain	$TCID_{50}$/mL	#Positive/#Total	% Positive
A	A/PR/8/34(H1N1)	1.05×10^2	58/60	96.7
A	A/Victoria/3/75(H3N2)	9.95×10^1	58/60	96.7
B	B/Taiwan/2/62	1.58×10^3	58/60	96.7
B	B/Maryland/1/59	1.99×10^1	58/60	96.7

Analytical Inclusivity

The analytical inclusivity was established for a total of 21 influenza strains: 11 strains of influenza A type and 10 strains of influenza B type. The results are shown in the table below.

Influenza Type	Viral Strain	$TCID_{50}$/mL	Influenza Type	Viral Strain	$TCID_{50}$/mL
A	A/PR/8/34(H1N1)	1.05×10^2	B	B/Lee/40	5.00×10^0
A	A/FM/1/47(H1N1)	1.73×10^1	B	B/Allen/45	1.58×10^0
A	A/NWS/33(H1N1)	4.10×10^3	B	B/GL/1739/54	9.95×10^2
A	A/Hong Kong/8/68(H3N2)	8.5×10^2	B	B/Taiwan/2/62	1.58×10^3
A	A/Denver/1/57(H1N1)	7.20×10^0	B	B/Maryland/1/59	1.99×10^1
A	A/Aichi/2/68(H3N2)	9.95×10^0	B	B/Mass/3/66	5.00×10^1
A	A/Port Chalmers/1/73	1.99×10^2	B	B/R22 Barbara	1.6×10^{-1}
A	A/Victoria/3/75(H3N2)	9.95×10^1	B	B/R75	2.94×10^3
A	A/New Jersey/8/76(H1N1)	9.95×10^1	B	B/Russia/69	3.16×10^3
A	A/WS/33(H1N1)	5.00×10^1	B	B/Hong Kong/5/72	2.88×10^1
A	A/Swine/1976/31	1.58×10^2			
A	2009 H1N1 Clinical Isolate* (Swine Origin Influenza A)	1.00×10^3			

A	2009 H1N1 Clinical Isolate* (Swine Origin Influenza A)	1.00×10^3			
A	A/CA/07/2009(H1N1)	6.15×10^3			
A	A/CA/08/2009(H1N1)	9.31×10^3			
A	A/NY/18/2009(H1N1)	2.5×10^3			
A	A/Mexico/4108/2009(H1N1)	8.51×10^3			
A	A/CA/07/2009 NYC, X-179A (H1N1)	1.08×10^3			
A	A/Virginia/ATCC2/2009(H1 N1)	2.32×10^3			
A	A/Virginia/ATCC3/2009(H1 N1)	5.00×10^4			

*Clinical Isolate cultured and tittered. Culture confirmed positive for 2009 H1N1 Influenza A strain using *pro*FLU *Influenza A Subtyping*

The performance of BioSign® Flu A+B was evaluated with nasal and nasopharyngeal swab samples obtained from patients infected with the 2009 H1N1 influenza virus consisting of sixty six (66) frozen clinical Nasal and Nasopharyngeal samples that had previously tested positive for 2009 H1N1 by the cleared CDC RT-PCR test. The BioSign® Flu A+B test detected 71% (47/66) of the CDC RT-PCR test positive specimens. The detection rate was 91% with the higher tittered specimens and 38% with the lower tittered specimens.

NOTE:

The performance characteristics of the test with cultured avian influenza A subtype H5N1 virus, or with specimens from human infected with H5N1 or other avian influenza viruses has not been established.

Analytical Specificity

Cross-reactivity

The potential cross-reactivity of the non-influenza respiratory pathogens and other microorganisms with which the majority of the population may be infected was tested on the BioSign® Flu A+B test at medically relevant levels, 10^6 cfu/mL for bacteria and 10^5 pfu/mL for non-flu viruses. None of the organisms or viruses listed in the table below gave a positive result with BioSign® Flu A+B at the tested concentration.

Viruses Tested	
Adenovirus*	Measles**
Human coronavirus**	Human metapneumovirus**
Cytomegalovirus**	Mumps virus**
Enterovirus**	Respiratory syncytial virus; Type B*
Epstein Barr Virus**	Rhinovirus; Type 1A**
Human parainfluenza;Type 1, 2 and 3*	

**In the study the virus was confirmed using commercially available PCR (not approved by FDA).

* In the study the virus was confirmed using FDA approved immuno-fluorecence assay.

Bacteria Tested	
Bordetella pertussis	*Neisseria sp.*
Chlamydia pneumoniae	*Pseudomonas aeruginosa*
Corynebacterium sp.	*Staphylococcus aureus: Protein A Producer*
Escherichia coli	*Staphylococcus epidermidis*
Hemophilus influenzae	*Streptococcus pneumoniae*
Lactobacillus sp.	*Streptococcus pyogenes*
Legionella spp	*Streptococcus salivarius*
Moraxella catarrhalis	
Mycobacterium tuberculosis avirulent	
Mycoplasma pneumoniae	
Neisseria meningitides	

Interference

The interference study was conducted using medically relevant concentrations of the potentially interfering substances listed below with two strains each of influenza type A and type B to assess the potential interference of the substances on the performance of the **BioSign® Flu A+B** test.

The test was conducted by spiking each substance into samples containing the lowest detectable virus level of influenza Type A or Type B for the positive interference testing and into samples without influenza virus for the negative interference testing. Each substance had no inhibitory effect on the **BioSign® Flu A+B** test at the concentration listed in the table below.

Substances Tested	Concentration Tested
Mucin	1 mg/ml
Whole Blood	1%
Phenylephrine	10 mg/mL
Oxymetazoline	10 mg/mL
Sodium Chloride with preservative	20%
Beclomethasone	1 mg/mL
Dexamethasone	1 mg/mL
Flunisolide	1 mg/mL
Triamcinolone	1 mg/mL
Budesonide	1 mg/mL
Mometasone	1 mg/mL
Fluticasone	0.5 mg/mL
Luffa opperculata, sulfur	1%
Galphimia glauca	1%
Histaminum hydrochloricum	1%
Live intranasal influenza virus vaccine	1%
Benzocaine	1 mg/mL
Menthol	1 mg/mL
Zanamivir	1 mg/mL
Mupirocin	1 mg/mL
Tobramycin	1 mg/mL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
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Silver Spring, MD 20993-0002

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Monmouth Junction, NJ 08852-1905

NOV 10 2010

Re: k083746
Trade/Device Name: BioSign Flu A+B Test
Regulation Number: 21 CFR 866.3330
Regulation Name: Influenza Virus Serological Reagents
Regulatory Class: Class I
Product Code: GNX
Dated: November 8, 2010
Received: November 9, 2010

Dear Dr. Kyung-ah Kim:

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 class II (Special Controls), 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); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); 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 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 Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety 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,

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

K083746

Indications for Use

510(k) Number (if known): K083746

NOV 10 2010

Device Name: BioSign® Flu A+B, Status Flu A & B

Indications For Use:

The **BioSign® Flu A+B** test is an *in vitro* rapid qualitative test that detects influenza type A and type B antigens directly from nasal swab, nasopharyngeal swab, nasopharyngeal aspirate/wash specimens of patients with signs and symptoms of respiratory infection. It is intended to aid in the rapid differential diagnosis of influenza A and B viral infections. A negative test result is presumptive and it is recommended these results be confirmed by viral culture. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other management decisions. The test is intended for professional and laboratory use.

Prescription Use √ AND/OR Over-The-Counter Use
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K083746