SPECIAL 510(k): Device Modification
OIR Review Memorandum

To: Princeton BioMeditech Corporation **RE:** K132465

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II, Class III or Class I devices requiring 510(k). The following items are present and acceptable (delete/add items as necessary):

1. The name and 510(k) number of the SUBMITTER'S previously cleared device:

   BioSign Flu A+B

   510(k) number: K083746

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

3. Description of the device **MODIFICATION(S):**

The modification presented in this special 510(k) consisted of expanded reactivity table to include reactivity information for one H7N9 influenza A virus (A/Anhui/1/2013), four (4) H3N2v viruses (A/Indiana/10/2011, A/Indiana/08/2011, A/Minnesota/10/2011, A/Minnesota/10/2011 X-203), and an influenza B virus (B/Texas/39/2006). The firm tested the ability of the BioSign Flu A+B test to detect the six aforementioned viruses. The viruses used were obtained from the Centers for Disease Control and Prevention as non-infectious beta-propiolactone inactivated virus. A LoD study was performed with each of the viruses using the same procedure employed in the original submission. Each titered virus was diluted until the minimal visual signal intensity appeared on the test line. This was defined as the lowest reacting level of the virus. Each virus was then tested in triplicate at that dilution. All virus strains tested were detected in 3 out of 3 tests at the lowest reacting level. The empirically determined LoD's for each virus are listed below:

- A/Anhui/1/2013 (H7N9) 7.94×10^6 EID_{50}/mL
- A/Indiana/10/2011 (H3N2v) 2.34×10^3 $TCID_{50}$/mL
- A/Indiana/08/2011 (H3N2v) 2.87×10^6 $TCID_{50}$/mL
- A/Minnesota/10/2011 (H3N2v) 2.13×10^6 $TCID_{50}$/mL
- A/Minnesota/10/2011 X-203 (H3N2v) 2.28×10^3 $TCID_{50}$/mL
- B/Texas/39/2006 2.34×10^4 $TCID_{50}$/mL

The BioSign Flu A+B test and Status Flu A&B test package inserts have been updated to include the additional analytical reactivity information. Status Flu A&B is the name of the same device being sold by LifeSign LLC under agreement with Princeton BioMeditech Corporation.

4. The **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed.**

5. **Comparison Information**

Similarities

	Modified Device	**Predicate Device**
Features	BioSign Flu A+B test	BioSign Flu A+B test
Intended Use	The BioSign Flu A+B test is an *in vitro* rapid qualitative test that detects influenza type A and type B nucleoprotein antigens directly from nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens obtained from 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. Negative test results are 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 patient management decisions. The test is intended for professional and laboratory use. Performance characteristics for influenza were established during the 2007-2009 influenza seasons when influenza A viruses A/New Caledonia/20/99 (H1N1), A/Solomon Islands/3/2006 (H1N1), A/Brisbane/59/2007 (H1N1), A/California/07/2009 (H1N1), A/Wisconsin/67/2005 (H3N2), A/Brisbane/10/2007 (H3N2), and influenza B viruses B/Ohio/01/2005, B/Florida/4/2006, B/Brisbane/60/2008 were the predominant influenza viruses in circulation according to the Flu Activity & Surveillance report by CDC. Performance characteristics may vary against other emerging influenza viruses. If infection with a novel Influenza 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.	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 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. Negative test results are 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 patient management decisions. The test is intended for professional and laboratory use. Performance characteristics for influenza were established during the 2007-2009 influenza seasons when influenza A viruses New Caledonia/20/99 (H1N1), Solomon Islands/3/2006 (H1N1), Brisbane/59/2007 (H1N1), California/07/2009 (H1N1), A/Wisconsin/67/2005 (H3N2), A/Brisbane/10/2007 (H3N2), and influenza B viruses Ohio/01/2005, Florida/4/2006, Brisbane/60/2008 were the predominant influenza viruses in circulation according to the Flu Activity & Surveillance report by CDC. Performance characteristics may vary against other emerging influenza viruses. If infection with a novel Influenza 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

	Viral culture should not be attempted in these cases unless a BSL+3 facility is available to receive and culture specimens.	in these cases unless a BSL+3 facility is available to receive and culture specimens.
Sample Type	Same as predicate device	Nasal swab Nasopharyngeal swab Nasopharyngeal aspirate/wash
Analytical Principle	Same as predicate device	Solid phase chromatographic immunoassay
Extraction	Same as predicate device	Incubated 1 minute in extraction reagent
Read Result Time	Same as predicate device	10 Minutes
Test Line	Same as predicate device	Colloidal gold
Internal Control	Same as predicate device	Reddish-purple line
Control Samples	Same as predicate device	Positive Control Swab: Influenza A and B antigens (non-infective recombinant nucleoprotein) Negative Control Swab: Inactivated Group B Streptococcus antigen (non-infective)

Differences

The package insert has been updated to include detection of the A/Anhui/1/2013, A/Indiana/10/2011, A/Indiana/08/2011, A/Minnesota/10/2011, A/Minnesota/10/2011 X-203, and B/Texas/39/2006 viruses at the following limits of detection:

- A/Anhui/1/2013 (H7N9) 7.94 x 10^6 EID_{50}/mL
- A/Indiana/10/2011 (H3N2v) 2.34 x 10^3 $TCID_{50}$/mL
- A/Indiana/08/2011 (H3N2v) 2.87 x 10^6 $TCID_{50}$/mL
- A/Minnesota/10/2011 (H3N2v) 2.13 x 10^6 $TCID_{50}$/mL
- A/Minnesota/10/2011 X-203 (H3N2v) 2.28 x 10^3 $TCID_{50}$/mL
- B/Texas/39/2006 2.34 x 10^4 $TCID_{50}$/mL

Although this test has been shown to detect these H7N9, H3N2v, and type B/Texas/39/2006 viruses cultured from positive human respiratory specimens, the performance characteristics of this device with clinical specimens that are positive for these influenza viruses have not been established.

Two minor grammatical changes were made within the Intended Use, but those changes do not alter the meaning of the IU.

6. **Design Control Activities Summary**:

Analytical reactivity testing was conducted for the H7N9 virus, four H3N2v viruses, and the influenza B virus using identical methods employed in the original submission for the unmodified device.

The risk analysis method used to assess the impact of the modification, adding additional viruses to the analytical sensitivity section of the package insert, was Failure Modes and Effects Analysis (FMEA). Based on the result of the risk analysis, the verification activities required and acceptance criteria were

identified. Since the change is adding detection levels of additional strains without changing anything in the test device, including fundamental scientific technology or indications for use, no risk is involved for this change except as listed below:

Change	Hazard	Resolution of Risk	Testing Performed	Test Method	Acceptance Criteria	Acceptance Criteria Met?
Addition of new virus strains to package insert	Non-detection of the virus strain added	Confirm Analytical Sensitivity for all additional strains	Analytical Sensitivity Testing conducted for each of the added strains	Tested in triplicate for each dilution of each additional strain	Positive Results at 10 minutes for each virus at the determined analytical sensitivity	* Yes
	Misinterpretation of test use: test used for detection of the additional strains from human specimen	Labeling: Limitation of test added as a footnote below the inclusivity table for all additional strains	n/a	n/a	n/a	n/a

* This was indicated after all experiments were completed.

A "Declaration of Conformity" statement was submitted for the manufacturing facility and validation activities and signed by the Regulatory Affairs manager and the Quality Assurance manager. The statements indicate that:

1. The manufacturing facility is in conformance with design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.
2. The validation activities, as required by the risk analysis, for the modification were performed by the designated individuals and the results demonstrated that the predetermined acceptance criteria were met.

In conclusion, based on the results of the analytical reactivity testing the modified labeling is truthful and accurate. The changes do not affect the performance of the test and it is therefore substantially equivalent to the current cleared test.

7. Truthful and Accurate Statement, a **510(k) Summary or Statement** and the **Indications for Use Enclosure.**

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared device.