

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number:

k071657

B. Purpose for Submission:

New Device Clearance

C. Measurand:

Influenza A and B nucleoprotein antigens

D. Type of Test:

Qualitative, *in vitro* immunochromatographic assay

E. Applicant:

Meridian Bioscience, Inc

F. Proprietary and Established Names:

TRU FLU

G. Regulatory Information:

a) Regulation section:

21CFR 866.3330; Influenza Virus Serological Reagents

b) Classification:

Class I

Product Code:

GNX, Antigens, CF, including CF controls, Influenza A, B, and C.

c) Panel:

83 Microbiology

H. Intended Use:

a) Intended use(s):

TRU FLU is a rapid, qualitative, lateral-flow immunochromatographic assay for detecting both influenza A and influenza B viral nucleoprotein antigens in human nasal wash, nasopharyngeal aspirate and nasal and nasopharyngeal swab samples in symptomatic patients. This test is not intended for the detection of influenza C viruses. A negative test is presumptive and it is recommended these results be confirmed by cell culture. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other clinical management decisions.

b) Indication(s) for use:

Same as intended use.

c) Special condition for use statement(s):

The device is for prescription use only

d) Special instrument Requirements:

NA

I. Device Description:

In vitro immunochromatographic immunoassay

J. Predicate device name(s):

Viral cell culture, ImmunoCard STAT! Flu A&B PLUS

2. Predicate 510(k) number(s): K041626Comparison with predicate:**Table 1: Summary of Device Similarities and Differences**

<i>Characteristics</i>	<i>TRU FLU</i>	<i>ImmunoCard STAT! Flu A&B PLUS (prior format)</i>
<i>Device Type</i>		
Technology	Single use, rapid, lateral flow immunoassay	Single use, rapid, lateral flow immunoassay
In vitro diagnostic device	Yes	Yes
Control	Purchased separately	Purchased separately
Calibrator	No	No
<i>Intended Use</i>		
Detection of influenza A antigen	Yes	Yes
Detection of influenza B antigen	Yes	Yes
Screening test	No	No
Diagnostic test	Yes	Yes
Identification test	No	No
Monitoring therapy	No	No
<i>Acceptable Samples</i>		
Swab -- Nasal	Yes	Yes
Swab -- Nasopharyngeal	Yes	Yes
Wash -- Nasal	Yes	Yes
Wash -- Nasopharyngeal	Yes	Yes
Aspirate -- Nasopharyngeal	Yes	Yes
Reagents/Components Provided		
Nitrocellulose test strip	Yes (attached to plastic holder/tube closure)	Yes (enclosed in plastic frame)
Conjugate reagent	Yes (supplied as dried bead in Conjugate Tube)	Yes (supplied in conjugate pad attached to test strip)
Reading Guide	Yes (part of plastic holder/tube)	Yes (part of plastic frame)

Table 1 Continued

<i>Characteristics</i>	<i>TRU FLU</i>	<i>ImmunoCard STAT! Flu A&B PLUS (prior format)</i>
Sample Diluent/Negative Control (external)	Yes	Yes
Internal procedural control	Yes	Yes
External positive control	No (Purchased separately -- FLU/RSV Positive Control, Catalogue 751110)	No (Purchased separately -- FLU/RSV Positive Control, Catalogue 751110)
Source of influenza A antibodies	Monoclonal M2110169, IVF8	Monoclonal M2110169, IVF8
Source of influenza B antibodies	Monoclonal 2/3, M2110171	Monoclonal 2/3, M2110171

K. Standard/Guidance Document Referenced (if applicable):

N/A

L. Test Principle:

TRU FLU is a single use immunochromatographic assay that consists of a Conjugate Tube, a Test Strip, and Sample Diluent. The Conjugate Tube contains a lyophilized bead of colloidal gold-linked monoclonal antibodies to influenza A and influenza B (detector antibodies). The Test Strip carries a nitrocellulose membrane with dried capture antibodies at separate lines for influenza A and influenza B. The Test Strip holder caps the Conjugate Tube during testing and subsequent disposal to reduce exposure to potential pathogens. The conjugate bead is first rehydrated in the Conjugate Tube with Sample Diluent, prior to the addition of patient specimen. The contents are mixed before the Test Strip is added. As the test is incubated at 20-25°C, influenza A or influenza B antigens, if present in the diluted sample, bind to the corresponding monoclonal antibody-colloidal gold conjugate as the sample moves up the Test Strip. The influenza A capture monoclonal antibody is bound to the Test Strip at the test-FLU A position of the device. When it binds the antigen-influenza A antibody-colloidal gold complex, it yields a visible pink-red line. Similarly, the influenza B capture monoclonal antibody bound to the assay membrane at the test-FLU B position will result in a pink-red line when it captures antigen-influenza B antibody-colloidal gold complexes. When no antigen is present, no complexes are formed and no pink-red line will appear at either the test FLU A or the test FLU B position of the Test Strip. An internal control line helps determine whether adequate flow has occurred through the Test Strip during a test run. A visible pink-red line at the Control position of the Test Strip should be present each time a specimen or control is tested. If no pink-red control line is seen, the test is considered invalid.

M. Performance Characteristics (if/when applicable):Analytical performance:***Precision/Reproducibility:***

Assay precision, intra-assay variability and inter-assay variability were assessed with a reference panel prepared from pools of negative samples spiked with specific virus. The reproducibility panel consisted of high positive (n = 2), low negative (n = 1), and low positive (n = 4) and high negative specimens (n = 4). The latter were prepared near the assay limit of sensitivity. Each reference specimen was coded to prevent its identification during testing. Each was evaluated twice per day for three consecutive days by three different laboratories. High negative samples (viral load just below LOD) produced weakly positive results in 8 out of 72 high negative replicate tests performed with the samples prepared near the cutoff (See EP12-A, User protocol for evaluation of qualitative performance; approved guideline; NCCLS/CLSI, Vol. 22, no.14, 2002.) Low positive samples (viral concentration near the LOD) produced 1 negative result in 72 replicate tests. The high positive and low negative samples produced correct results 100% of the time.

a. **Linearity/assay reportable range:**

NA

b. **Traceability, Stability, Expected values (controls, calibrators, or method):**

NA

c. **Detection limit:**

The analytical sensitivity was assessed using two-fold serial dilutions of selected influenza A and influenza B virus stocks. The organisms tested are listed in the Table below. The sensitivity was the highest dilution that produced a definitive positive reaction.

Strain ID	Influenza Strain	Limit of Detection (LOD) in pfu/mL
Influenza A/Puerto Rico/8/34	A (H1N1)	9.8 X 10 ³
Influenza A/Hong Kong/8/68	A (H3N2)	7.3 X 10 ⁴
Influenza B/Lee/40	B	1.7 X 10 ⁴

d. **Analytical specificity:**

The specificity of TRU FLU was tested utilizing the following bacterial, viral and yeast strains. Positive and negative respiratory specimens were spiked with $\geq 4 \times 10^7$ /mL bacteria or yeast. Virus inoculations were performed at $\geq 6.7 \times 10^4$ TCID₅₀/mL. None of the microorganisms tested yielded a positive result with the influenza-negative samples or interfered with detection of the influenza A and/or B positive samples. Both the negative and positive respiratory samples were positive when spiked with influenza A strain VR-100 or influenza B strain VR-295.

Adenovirus Types 1, 5 and 7A, Coxsackie Type A9, Human Coronavirus Types 229E and OC43, Cytomegalovirus, Measles, Human metapneumovirus, Parainfluenza Types 1, 2 and 3, Rhinovirus Type 39, RSV (2 strains), *Bacillus cereus*, *Bacillus subtilis*, *Bordetella parapertussis*, *Bordetella pertussis*, *Branhamella catarrhalis*, *Candida albicans*, *Candida glabrata*, *Citrobacter freundii*, *Enterobacter cloacae*, *Escherichia coli*, *Enterococcus faecalis*, *Haemophilus influenzae*, *Klebsiella oxytoca*, *Klebsiella*

pneumoniae, *Listeria monocytogenes*, *Legionella pneumophila*, *Neisseria cinerea*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Serratia liquifaciens*, *Staphylococcus aureus*, *Staphylococcus aureus* (Cowan I), *Staphylococcus epidermidis*, *Streptococcus* (not typed), *Streptococcus* Groups A, B, D, F, and G, *Streptococcus pneumoniae*, *Yersinia enterocolitica*. A clinical sample containing Epstein Barr virus at 3.48×10^9 genome equivalents/mL was nonreactive with TRU FLU.

g. *Interfering Substances:*

The following substances were found to have no effect on results when present in respiratory samples at the concentrations indicated: Acetylsalicylic Acid (20 mg/mL), Acetaminophen (10 mg/mL), Halls® Throat Drops (20 mg/mL), Ludens® Throat Drops (20 mg/mL), Ricola® Throat Drops (20 mg/mL), Diphenhydramine (5 mg/mL), Dextromethorphan (9% v/v), Phenylephrine hydrochloride (9% v/v), Oxymetazoline hydrochloride (9% v/v), Chlorpheniramine maleate (5 mg/mL), Ibuprofen (10 mg/mL), Clemastine fumarate (5 mg/mL), Naproxen sodium (10 mg/mL), Loratadine (5 mg/mL), Pseudoephedrine (20 mg/mL), Listerine® Mouthwash (9% v/v), Scope® Mouthwash (9% v/v), Cepacol® Mouthwash (9% v/v), Whole blood (0.5%), Guaifenesin (9% v/v), Albuterol (9% v/v).

a. Comparison studies:

a. *Method comparison with predicate device:*

N/A

b. *Matrix comparison:*

NA

b. Clinical studies:

Clinical sensitivity:

Nine independent laboratories and the manufacturer, (located in distinct geographic regions), evaluated TRU FLU in parallel with tissue culture. Six hundred and ninety seven fresh and 63 frozen samples, collected prospectively during the 2006-7 influenza season were tested. In the case of frozen samples tissue culture tests were performed while they were fresh and before they were frozen. Twenty seven percent (185/697) of the prospective samples were from patients 22 years of age or older, 64% (447/697) from patients 12 years of age or less and 8% (59/697) from patients 13 to 21 years of age. The age of six patients donating samples was not recorded. Of the 63 samples tested only in the frozen state, the majority (33/63 or 52%) were from patients aged 2 months to 2 years. The patient ages for the remaining retrospective samples were 14% (9/63) for patients aged 1 month or less, 22% (14/63) for patients aged 3-12 years, and 11% (7/63) for patients aged 13-21 years. Fifty three percent of the prospective and 51% retrospective samples were from males while 47% prospective and 49% retrospective samples were from females. The gender of five patients donating samples was not recorded. No differences in performance were observed based on patient gender or patient age. The results of trials based on sample type are given in Tables 2-4. Of the

697 prospective samples tested, 11 were not classified with respect to sample type and 1 produced invalid culture results. These 12 samples were excluded from the calculations.

Table 2. Results with prospective wash/aspirate samples

	TRU FLU Flu A			TRU FLU Flu B		
Tissue Culture	Positive	Negative	Total	Positive	Negative	Total
Positive	34	5	39	21	12	33
Negative	35*	291	326	2	330	332
Total	69	296	365	23	342	365
			95% CI			95% CI
Sensitivity	34/39	87.2%	72.6-95.7%	21/33	63.6%	45.1-79.6%
Specificity	291/326	89.3%	85.9-92.6%	330/332	99.4%	97.8 – 99.9%

*NOTE: 2 samples were TRU FLU A+B+, tissue culture negative samples; another 3 were TRU FLU A+B+ and positive for influenza B by tissue culture. TRU FLU A+B+ tests were not repeated during the clinical trials. TRU FLU A+B+ tests are considered suspect without repeat testing.

Table 3. Results with prospectively frozen wash/aspirate samples

	TRU FLU Flu A			TRU FLU Flu B		
Tissue Culture	Positive	Negative	Total	Positive	Negative	Total
Positive	17	3	20	1	1	2
Negative	3	40	43	0	61	61
Total	20	43	63	1	62	63
			95% CI			95% CI
Sensitivity	17/20	85.0%	62.1-96.8%	1/2	50.0%	1.3-98.7%
Specificity	40/43	93.0%	80.9-98.5%	61/61	100%	94.1-100%

Table 4. Results with prospective swab samples

	TRU FLU Flu A			TRU FLU Flu B		
Tissue Culture	Positive	Negative	Total	Positive	Negative	Total
Positive	63	10	73	38	27	65
Negative	18*	229	247	1	254	255
Total	81	239	320	39	281	320
			95% CI			95% CI
Sensitivity	63/73	86.3%	76.3 – 93.2%	38/65	58.5%	45.6 – 70.6%
Specificity	229/247	92.7%	88.7 – 95.6%	254/255	99.6%	97.8 - 100%

- NOTE: 7 samples were TRU FLU A+B+ and positive for influenza B by tissue culture. TRU FLU A+B+ tests were not repeated during the clinical trials. TRU FLU A+B+ tests are considered suspect without repeat testing.

N. Proposed labeling: The labeling is sufficient and it satisfies the requirement of 21 CFR Part 809.10.

O. Conclusion: The submitted material in this premarket notification is complete and supports a substantial equivalence decision.