

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY**

**A. 510(k) Number:**

K071101

**B. Purpose for Submission:**

This device is a modification of ImmunoCard STAT! RSV PLUS (K041445).

**C. Measurand:**

Respiratory Syncytial Virus antigens

**D. Type of Test:**

Rapid, qualitative, lateral-flow immunoassay for the detection of Respiratory Syncytial Virus (RSV) antigens (fusion protein or nucleoprotein) in human nasal wash, nasopharyngeal aspirate and nasal and nasopharyngeal swab samples.

**E. Applicant:**

Meridian Bioscience, Inc.

**F. Proprietary and Established Names:**

TRU RSV

**G. Regulatory Information:**

1. Regulation section:

21 CFR section 866.3480, Respiratory syncytial virus serological reagents.

2. Classification:

Class I

3. Product code:

GQG

4. Panel:

Microbiology (83)

## **H. Intended Use:**

1. Intended use(s):

TRU RSV is a rapid, qualitative, lateral-flow immunoassay for the detection of Respiratory Syncytial Virus (RSV) antigens (fusion protein or nucleoprotein) in human nasal wash, nasopharyngeal aspirate, and nasal and nasopharyngeal swab samples. It is designed to test specimens from symptomatic patients aged 5 years or less. A negative result does not preclude RSV infection. It is recommended that all negative test results be confirmed by cell culture.

2. Indication(s) for use:

Same as intended use.

3. Special conditions for use statement(s):

For prescription use.

4. Special instrument requirements:

Not applicable.

## **I. Device Description:**

TRU RSV is a single use capture immunoassay to detect RSV antigen in human respiratory samples. The test 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 RSV fusion protein and nucleoprotein (detector antibodies). Test Strip carries a nitrocellulose membrane with dried capture antibodies placed at a designated Test Line for RSV. The Test Strip holder caps the Conjugate Tube during testing and subsequent disposal to reduce exposure to potential pathogens.

## **J. Substantial Equivalence Information:**

1. Predicate device name(s):

ImmunoCard STAT! RSV PLUS.

2. Predicate K number(s):

(K041445)

3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
	<b><i>TRU RSV</i></b>	<b><i>ImmunoCard STAT! RSV PLUS</i></b>
<b>Device Type</b>		
Technology	Single use, rapid, lateral flow immunoassay	Single use, rapid, lateral flow immunoassay
In vitro diagnostic device	Yes	Yes
Control	Excludes external control reagent (purchased separately)	Excludes external control reagent (purchased separately)
Calibrator	No	No
<b>Intended Use</b>		
Detection of RSV antigens	Yes	Yes
Screening test	No	No
Diagnostic test	Yes	Yes
Identification test	No	No
Monitoring therapy	No	No
<b>Acceptable Samples</b>		
Swab -- Nasal	Yes	Yes
Swab -- Nasopharyngeal	Yes	Yes
Wash -- Nasal	Yes	Yes
Aspirate -- Nasopharyngeal	Yes	Yes
<b>Reagents/Components</b>		
Nitrocellulose test strip	Yes	Yes
Conjugate reagent	Yes	Yes
Reading Guide	Yes	Yes
Sample Diluent/Negative Control (external)	Yes	Yes
Internal procedural control	Yes	Yes
External positive control	No (purchased separately)	No (purchased separately)

<b>Similarities (continued)</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
	<b><i>TRU RSV</i></b>	<b><i>ImmunoCard STAT! RSV PLUS</i></b>
Source of RSV antibodies	Capture: Murine monoclonal anti-RSV (antibodies to fusion protein and nucleoprotein) Detector: Murine monoclonal anti-RSV (antibodies to fusion protein and nucleoprotein)	Capture: Murine monoclonal anti-RSV (antibodies to fusion and internal proteins) Detector: Murine monoclonal anti-RSV (antibodies to fusion and internal proteins)
<b>Assay steps</b>		

Equipment Required	No	No
End Point	Appearance of pink-red color at Test and/or Control lines	Appearance of pink-red color at Test and/or Control lines
Interpretation of Test Result	RSV Positive = appearance of pink-red lines at Test and Control Line positions (indicates presence of RSV antigens) RSV Negative = no test line color with pink-red Control Line (indicates absence of RSV antigens)	RSV Positive = appearance of pink-red lines at Test and Control Line positions (indicates presence of RSV antigens) RSV Negative = no test line color with pink-red Control Line (indicates absence of RSV antigens)

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
	<b><i>TRU RSV</i></b>	<b><i>ImmunoCard STAT! RSV PLUS</i></b>
<b>Reagents/Components Provided</b>		
Nitrocellulose test strip	Attached to plastic holder/tube closure	Enclosed in plastic frame
Conjugate reagent	Supplied as dried bead in Conjugate Tube	Supplied in conjugate pad attached to test strip
Reading Guide	Part of plastic holder/tube closure	Part of plastic frame
<b>Test Device</b>	Nitrocellulose membrane with immobilized capture antibody. Top end is inserted into plastic frame or holder. Conjugate Tube containing antibody- colloidal gold conjugate (lyophilized bead)	Test Card with nitrocellulose membrane with immobilized capture antibody, conjugate pad with colloidal gold particle-linked detector antibody, plastic frame with reading/reaction window and sample port.
<b>Level of skill required</b>	Moderate	CLIA Waived

<b>Assay steps</b>	<ol style="list-style-type: none"> <li>1. Add 100 µL Sample Diluent to the Conjugate Tube.</li> <li>2. Add 100 µL sample to the Conjugate Tube and mix.</li> <li>3. Insert Test Strip to Conjugate Tube.</li> <li>4. Press down on cap of Test Strip to seal Conjugate Tube.</li> <li>5. Incubate 15 min, 20-25 C.</li> <li>6. Read at end of incubation using guide on holder.</li> </ol>	<ol style="list-style-type: none"> <li>1. Add 4 drops Sample Diluent to a test tube.</li> <li>2. Add 150 µL sample and mix.</li> <li>3. Add 150 µL diluted specimen to Test Device.</li> <li>4. Incubate 15 min, 20-25 C.</li> <li>5. Read at end of incubation using guide at reaction window.</li> </ol>
--------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

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

Not applicable.

**L. Test Principle:**

The conjugate bead is first re-hydrated in the Conjugate Tube with Sample Diluent. Patient sample is then added, the contents mixed and the Test Strip added. If RSV antigens are present, they first bind to the monoclonal antibody-colloidal gold conjugate. When the sample migrates up the Test Strip to the Test Line, the antigen-conjugate complex is bound to the capture antibody, yielding a pink-red line. When no antigen is present, no complexes are formed and no pink-red line appears at the Test Line. 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):**

1. Analytical performance:

a. *Precision/Reproducibility:*

- i. 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=2), and low positive (n=3) and high negative specimens (n=3). The latter were prepared near the assay limit of sensitivity. Each sample was evaluated twice per day for three consecutive days by three different laboratories.

- ii. Reproducibility was 100% with no intra-assay and inter-assay variability for samples prepared above or below the limit of analytical sensitivity.

b. *Linearity/assay reportable range:*

Not applicable.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Not applicable.

d. *Detection limit:*

The analytical sensitivity of this assay was established in tests with dilutions of RSV strains VR-26 (RSV A), VR-1302 (RSV A), VR-1540 (RSV A), VR-955 (RSV B), VR-1400 (RSV B) and VR-1401 (RSV B). The lower limit of detection is dependent on factors such as the cell culture lines used, the number of passages performed and the efficiencies of the isolation methods. For this reason, assay limit of detection levels may vary if other strains or samples are tested.

Strain ID	Strain Type	Limit of Detection (LOD) TCID <sub>50</sub> /ml
VR-26	A	2.49 x 10 <sup>2</sup>
VR-1302	A	4.47
VR-1540	A	5.52 x 10 <sup>1</sup>
VR-955	B	4.47
VR-1400	B	1.10 x 10 <sup>1</sup>
VR-1401	B	2.47

e. *Analytical specificity:*

The specificity of TRU RSV was tested utilizing the following bacterial, viral and yeast strains. Adenovirus Types 1, 5 and 7A, Coxsackie Type A9, Human Coronavirus Types 229E and OC43, Cytomegalovirus, Influenza A (2 strains), Influenza B (1 strain), Human metapneumovirus, Measles, Parainfluenza Types 1, 2 and 3, Rhinovirus Type 39, *Bacillus cereus*, *Bacillus subtilis*, *Bordetella parapertussis*, *Bordetella pertussis*, *Branhamella catarrhalis*, *Candida albicans*, *Candida glabrata*, *Citrobacter freundii*, *Enterobacter cloacae*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Legionella pneumophila*, *Neisseria cinerea*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*,

*Serratia liquifaciens*, *Staphylococcus aureus*, *Staphylococcus aureus* (Cowan I), *Staphylococcus epidermidis*, *Streptococcus* (not typed), *Streptococcus* Groups A, B, D, F, and G, *Streptococcus pneumoniae*.

RSV positive and negative respiratory specimens were spiked with  $\geq 4 \times 10^7$ /mL bacteria or yeast. Virus inoculations were performed at  $\geq 6.7 \times 10^4$  TCID<sub>50</sub>/mL. None of the microorganisms tested yielded a positive result in the RSV-negative sample or interfered with detection of the RSV-positive sample. The RSV-negative respiratory sample was positive when spiked with RSV strain VR-26.

A clinical sample containing Epstein Barr virus at  $2.32 \times 10^8$  genome equivalents/mL was non-reactive with TRU RSV.

*f. Assay cut-off:*

Not applicable.

*g. Interfering Substances:*

The following substances, when introduced directly into nasal samples, do not interfere with testing at the concentrations identified: Acetaminophen (10 mg/mL), Acetylsalicylic acid (20 mg/mL), Albuterol (9.1% v/v), Halls® Throat Drops (20mg/mL), Ludens® Throat Drops (20 mg/mL), Chlorpheniramine maleate (1.7 mg/mL), Clemastine fumarate (5mg/mL), Diphenhydramine HCl (5 mg/mL), Dextromethorphan (9.1% v/v), Naproxen sodium (10 mg/mL), Phenylephrine hydrochloride (9.1% v/v), Oxymetazoline (9.1% v/v), Guaifenesin (9.1% v/v), Pseudoephedrine HCl (20 mg/mL), Listerine® Mouthwash (9.1% v/v).

Whole blood at concentrations greater than 2.9% interfered with test interpretation. Chlorpheniramine maleate at concentrations greater than 1.7 mg/mL may cause false-positive test results.

2. Comparison studies:

*a. Method comparison with predicate device:*

Not applicable.

*b. Matrix comparison:*

Not applicable.

3. Clinical studies:

a. b. *Clinical Sensitivity and specificity*

Clinical studies were performed during the 2006-07 season to evaluate the performance of TRU RSV against tissue culture in the laboratory setting. Four independent laboratories (in three different geographic regions of the US) and the manufacturer's laboratory tested a total of 625 samples submitted for RSV testing. 304 of the samples were tested prospectively, while 321 were tested as frozen/thawed samples. Samples were equally distributed between male and female patients.

<b>Fresh Wash/Aspirate</b>	<b>TRU RSV</b>		
<b>Tissue Culture</b>	<b>Positive</b>	<b>Negative</b>	<b>Total</b>
<b>Positive</b>	64	8	72
<b>Negative</b>	21	90	111
<b>Total</b>	85	98	183
			<b>95% CI</b>
<b>Sensitivity</b>	64/72	88.9%	79.3-95.1%
<b>Specificity</b>	90/111	81.1%	73.8-88.4%
<b>Correlation</b>	154/183	84.2%	78.9-89.4%

<b>Fresh Swab</b>	<b>TRU RSV</b>		
<b>Tissue Culture</b>	<b>Positive</b>	<b>Negative</b>	<b>Total</b>
<b>Positive</b>	12	1	13
<b>Negative</b>	7	100	107
<b>Total</b>	19	101	120
			<b>95% CI</b>
<b>Sensitivity</b>	12/13	92.3%	64.0-99.8%
<b>Specificity</b>	100/107	93.5%	87.0-97.3%
<b>Correlation</b>	112/120	93.3%	87.3-97.1%

<b>Frozen Wash/ Aspirate</b>	<b>TRU RSV</b>		
<b>Tissue Culture</b>	<b>Positive</b>	<b>Negative</b>	<b>Total</b>
<b>Positive</b>	79	9	88
<b>Negative</b>	12	149	161
<b>Total</b>	91	158	249
			<b>95% CI</b>
<b>Sensitivity</b>	79/88	89.8%	81.5-95.2%
<b>Specificity</b>	149/161	92.5%	87.3-96.1%
<b>Correlation</b>	228/249	91.6%	87.4-94.7%

<b>Frozen Swab</b>	<b>TRU RSV</b>		
<b>Tissue Culture</b>	<b>Positive</b>	<b>Negative</b>	<b>Total</b>
<b>Positive</b>	33	13	46
<b>Negative</b>	1	25	26
<b>Total</b>	34	38	72
			<b>95% CI</b>
<b>Sensitivity</b>	33/46	71.7%	56.5-84.0%
<b>Specificity</b>	25/26	96.2%	80.4-99.9%
<b>Correlation</b>	58/72	80.6%	69.5-88.9%

c. *Other clinical supportive data (when a. and b. are not applicable):*

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

**N. Proposed Labeling:**

Labeling is sufficient and it satisfies the requirements of 21 CFR section 809.10.

**O. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.