

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

A. 510(k) Number:

K153661

B. Purpose for Submission:

To seek clearance for a modification of the ImmunoCard STAT! HpSA

C. Measurand:

H. pylori antigen

D. Type of Test:

Lateral flow immunoassay

E. Applicant:

Meridian Bioscience Inc.

F. Proprietary and Established Names:

ImmunoCard STAT! HpSA

G. Regulatory Information:

1. Regulation section:

21 CFR Part 866.3110 *Campylobacter fetus* serological reagents

2. Classification:

Class I

3. Product code:

LYR

4. Panel:

83, (Microbiology)

H. Intended Use:

1. Intended use(s):

The ImmunoCard STAT! HpSA is a rapid in vitro qualitative procedure for the detection of *Helicobacter pylori* antigens in human stool. The stool antigen detection is intended to aid in the diagnosis of *H. pylori* infection and to demonstrate loss of *H. pylori* stool antigen following treatment. Conventional medical practice recommends that testing by any method to confirm loss of antigen be done at least four weeks following completion of therapy.

2. Indication(s) for use:

Same as the Intended Use.

3. Special conditions for use statement(s):

Not applicable

4. Special instrument requirements:

Not applicable

I. Device Description:

The ImmunoCard STAT! HpSA is a rapid lateral flow immunoassay. It consists of chromatography strips impregnated with dissociated monoclonal anti-*H. pylori* antibody as the capture antibody, red latex-conjugated detector antibody and blue latex-conjugated anti-protein as the detector antibodies for tests and controls respectively. Each strip is enclosed in a plastic frame with a window. The kit also contains a positive control which is a dilute suspension of inactivated *H. pylori* in a buffered solution containing <0.1% sodium azide as a preservative, and a specimen diluent which is a buffered salt solution. This device contained modifications in the monoclonal antibodies (dissociated monoclonal capture antibody) used on the capture and detector sides of the assay and the formulation of the sample and internal control diluent.

J. Substantial Equivalence Information:

1. Predicate device name(s):

ImmunoCard STAT! HpSA

2. Predicate 510(k) number(s):

K032222

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	K153661	K032222
Intended Use	The ImmunoCard STAT! HpSA is a rapid in vitro qualitative procedure for the detection of <i>Helicobacter pylori</i> antigens in human stool. The stool antigen detection is intended to aid in the diagnosis of <i>H. pylori</i> infection and to demonstrate loss of <i>H. pylori</i> stool antigen following treatment. Conventional medical practice recommends that testing by any method to confirm loss of antigen be done at least four weeks following completion of therapy.	Same
Sample Type	Human stool samples (solid, semisolid, and liquid)	Same
Assay	Qualitative	Same
Assay Target	<i>Helicobacter pylori</i> antigens in human stool	Same
Reading Method	Visual interpretation of test results	Same
Fundamental Scientific Technology	Rapid immunochromatographic assay	Same
Reagents Provided	ICS HpSA Test Device Sample Diluent Positive Control	Same

Differences		
Item	Device	Predicate
	K153661	K032222
Capture Antibody	Modified monoclonal anti- <i>H. pylori</i> antibody	Monoclonal anti- <i>H. pylori</i> antibody

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

Not applicable

L. Test Principle:

ImmunoCard STAT! HpSA uses capture solid phase technology to detect the presence of antigen in test specimens. To perform the test, patient stool is added to the Sample Diluent using the applicator stick that is part of the Sample Diluent Vial. The diluted stool sample (approximately a 1 in 10 dilution) is dispensed through the tip of the Sample Diluent Vial into the round sample window of the device. *H. pylori* antigen, if present in the diluted sample, binds to the detector antibody-latex conjugate as the sample moves through the device. The capture, dissociated monoclonal, antibody which is bound to the assay membrane at the reading window, binds the antigen-antibody latex complex. The result is a visible pink/red line. When no antigen is present, no complex is formed and no pink/red line will appear at the test position of the central window.

A control line, appearing at the control position in the test window, shows whether adequate flow has occurred through the device during a test run. The control line is derived from protein of non-mammalian origin. Blue latex particles are conjugated with a monoclonal antibody to this non-mammalian animal protein. Together they migrate as the monoclonal antibody/blue latex complex during the incubation step. A blue line at the control position on the device should be present each time a specimen or control is tested. If no blue control line is seen, the test is considered invalid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Studies were performed to demonstrate the inter-laboratory and intra-laboratory reproducibility of the modified device. Testing was performed by two technologists in three separate laboratories over the course of five days. Each technologist was supplied with a panel of coded specimens prior to testing. The specimens were diluted and tested according to the package insert method.

Contrived specimen panels were prepared by spiking *H. pylori* into negative pooled fecal specimens at antigen concentrations above, near and below the assay limit of detection for *H. pylori* antigen ATCC 43504. Each panel consisted of ten specimens: three moderately positive (6x LoD), three low positive (2x LoD), three high negative, and one natural negative specimen, that were randomly sorted within each panel. Two test kits were used during the study. The study results are summarized in Table 1. The reproducibility performance was acceptable.

Table 1. Reproducibility Testing with the Modified Device

Sample Type	Clinical Site 1 Percent Agreement		Clinical Site 2 Percent Agreement		Clinical Site 3 Percent Agreement		Total		
	Percent Agreement	95% CI	Percent Agreement	95% CI	Percent Agreement	95% CI	Percent Agreement	95% CI	
High Negative	30/30	100.0	30/30	100.0	30/30	100.0	90/90	100.0	95.9 – 100.0
Low Positive	30/30	100.0	30/30	100.0	30/30	100.0	90/90	100.0	95.9 – 100.0
Moderate Positive	30/30	100.0	29/30	96.7	30/30	100.0	89/90	98.9	94.0 – 99.8
Negative	10/10	100.0	9/10	90.0	10/10	100.0	29/30	96.7	83.3 – 99.4
Negative Control	10/10	100.0	10/10	100.0	10/10	100.0	30/30	100.0	88.6 - 100.0
Positive Control	10/10	100.0	10/10	100.0	10/10	100.0	30/30	100.0	88.6 - 100.0

b. *Linearity/assay reportable range:*

Not applicable

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

Not applicable

d. *Detection limit:*

The lower limit of detection of this assay is 64 ng/mL in tests with sonicated antigen prepared from *H. pylori* strain TV1970. This limit does not vary from formed (solid) to semi-solid stool.

e. *Analytical specificity:*

Cross reactivity

The specificity of *ImmunoCard* STAT! HpSA was tested with the following bacterial, viral and yeast strains. Positive and negative stools were spiked with $\geq 1 \times 10^7$ bacteria or yeast. Viruses were spiked at 10^5 TCID₅₀/mL. None of the microorganisms tested yielded a positive result in the negative stool or interfered with detection of the positive stool. Both the negative and positive stool were positive when spiked with *H. pylori* strain 43504.

- Adenovirus Type 2
- Adenovirus Type 40
- Coxsackie Type B 1
- Coxsackie Type B6
- Echovirus Type 22
- Feline calicivirus
- Rotavirus

Aeromonas hydrophila
Bacillus sp.
Campylobacter coli
Campylobacter jejuni
Candida albicans
Citrobacter freundii
Clostridium perfringens
Clostridium difficile (2)
Enterobacter cloacae
Enterococcus faecalis (2)
E. coli (2)
E. coli 0157:H7 (2)
E. fergusonii
Haemophilus influenzae
Helicobacter felis
Klebsiella pneumoniae
Proteus vulgaris
Pseudomonas aeruginosa
Salmonella dublin
Salmonella (Group B)
Salmonella hilversum
Salmonella minnesota
Salmonella typhimurium
Staphylococcus aureus
Staphylococcus aureus (Cowan I)
Staphylococcus epidermidis
Serratia liquifaciens
Shigella boydii
Shigella dysenteriae
Shigella flexneri
Shigella sonnei
Yersinia enterocolitica
Borrelia burgdorferi (Stool inoculated with antigen protein to a final conc. of 32 ug/mL)

Interfering substances

The following substances were found to have no effect on results when present in stool at the concentrations indicated.

Tums® Antacid (5 mg/mL)
Tagamet® (5 mg/mL)
Prilosec® (5 mg/mL)
Mylanta® Antacid (1:20)
Pepto-Bismol® (1:20)
Barium sulfate (5%)
Whole Blood (50%)
Leukocytes (50%)
Mucin (3.4%)
Stearic acid/Palmitic acid (fecal fat) (4%)

Hemoglobin (tarry stool) (12.5%)

f. Assay cut-off:

The assay cut off is 64 ng/mL of *H. pylori* antigen.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison testing was done to compare performance of the subject device using the modified dissociated monoclonal capture antibody to that of the predicate device using the unmodified monoclonal antibody.

The testing was performed with two operators who were blinded to the 150 prospectively collected and archived specimens. The specimens were collected from the intended use population. When tested with the predicate, the results were 57 positive and 93 negative. The results are summarized in Table 2 below.

Table 2. Performance Comparison between Modified Device and Predicate Device

	ICS HpSA Predicate		
ICS HpSA Modified	Positive	Negative	Total
Positive	56	1	57
Negative	1	92	93
Total	57	93	150
			95% CI
Positive Agreement	56/57(98.3%)		90.7-99.7%
Negative Agreement	92/93(98.9%)		94.1-99.8%

The percent positive and negative agreements compared to the predicate device were 98.3% (56/57, CI = 90.7 - 99.7%) and 98.9% (92/93, CI 94.1 - 99.8%), respectively. These results are acceptable.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data:

Not applicable

4. Clinical cut-off:

See assay cut off above.

5. Expected values/Reference range:

Studies on the epidemiology of *H. pylori* have shown that this organism is present worldwide. The prevalence of *H. pylori* infection by various test methods in a given population can vary from 20% to 90%. In patients diagnosed with duodenal ulcers, however, it has been shown in every age group to be approximately 80%. The *ImmunoCard* STAT! HpSA test detects the presence of *H. pylori* antigens in human stool.

Expected values for a given population should be determined for each laboratory. The rate of positives may vary depending on geographic location, method of specimen collection, handling and transportation, test employed and general health environment of patient population under study.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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