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

A. 510(k) Number:

K182559

B. Purpose for Submission:

To obtain a substantial equivalence determination for a modification of the PREMIER Platinum HpSA PLUS

C. Measurand:

Helicobacter pylori antigen

D. Type of Test:

Qualitative enzyme immunoassay (EIA)

E. Applicant:

Merdidian Bioscience, Inc.

F. Proprietary and Established Names:

PREMIER Platinum HpSA PLUS

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.3110; *Campylobacter fetus* serological reagents

2. Classification:

   Class I

3. Product code:

   LYR – *Campylobacter pylori*

4. Panel:

   83-Microbiology

H. Intended Use:

1. Intended use(s):

   The PREMIER Platinum HpSA PLUS enzyme immunoassay (EIA) is an *in vitro* qualitative procedure for the detection of *Helicobacter pylori* antigens in human stool. Test results are intended to aid in the diagnosis of *H. pylori* infection and to monitor response during and post-therapy in patients. Accepted medical practice recommends that testing by any current method, to confirm eradication, 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):

   For prescription use only.

4. Special instrument requirements:

   A spectrophotometric plate reader capable of reading the following wavelengths: 450 nm or 450/630 nm.

I. Device Description:

The PREMIER Platinum HpSA PLUS test is a microwell-based enzyme immunoassay that detects *H. pylori* antigens present in human stool. This version of the assay has several modifications compared to the earlier version, including a replacement capture/conjugate monoclonal minor antibody and capture/conjugate monoclonal major antibody propogated by different methods. Additionally, the positive control reagent final acceptance criteria have been modified, concurrent with the minor antibody change.

The test utilizes a plurality (mixture) of monoclonal anti-*H. pylori* capture antibodies adsorbed to microwells. Diluted patient samples and an enzyme conjugate reagent are added to the microwells and incubated for one hour at room temperature. A wash is performed to remove unbound material. Substrate is added and incubated for 10 minutes at room temperature. Color develops in the presence of bound enzyme. Stop solution is added and the results are interpreted visually or spectrophotometrically. No calculations are required and the visual color change makes the interpretation of results objective and simple. The color, if

positive, is a yellow color that may be read visually or by using a spectrophotometer at the following wavelengths: 450 nm or 450/630 nm.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   PREMIER Platinum HpSA PLUS

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

   K053335, K980076, K983255

3. Comparison with predicate:

Similarities		
Item	**Modified Device (K182559)**	**Predicate Device (K053335)**
Product Code	LYR	Same
Intended Use	The Premier Platinum HpSA PLUS enzyme immunoassay (EIA) is an *in vitro* qualitative procedure for the detection of *Helicobacter pylori* antigens in human stool. Test results are intended to aid in the diagnosis of *H. pylori* infection and to monitor response during and post-therapy in patients. Accepted medical practice recommends that testing by any current method, to confirm eradication, be done at least four weeks following completion of therapy.	Same
Technology	Qualitative Enzyme Immunoassay (EIA), Microwell Format	Same
Specimen Type	Human Stool (solid, liquid)	Same
Reagents and Components	• Antibody Coated Microwells • Positive Control • Sample Diluent/Negative Control • Premier 20X Buffer I • Enzyme Conjugate • Premier Substrate I • Premier Stop Solution 1 • Transfer pipettes • Microwell strip sealer • Wooden stick applicators	Same
Interpretation of Results	Results may be interpreted visually or using a spectrophotometer.	Same
LoD	4.66 ng/mL of stool	4.67 ng/mL of stool

Differences		
Item	**Modified Device (K182559)**	**Predicate Device (K053335)**
Antibody Coated Microwells	**Major Antibody:** Monoclonal anti-*H. pylori* capture antibody, derived from tissue culture. **Minor Antibody:** Replacment monoclonal anti-*H.pylori* capture antibody, derived from tissue culture.	**Major Antibody:** Monoclonal anti-*H. pylori* capture antibody, derived from ascites. **Minor Antibody:** Monoclonal anti-*H.pylori* capture antibody, derived from ascites.
Enzyme Conjugate	**Major Antibody:** Monoclonal anti-*H. pylori* conjugate antibody, derived from tissue culture. **Minor Antibody:** Replacment monoclonal anti-*H.pylori* conjugate antibody, sourced from cell culture.	**Major Antibody:** Monoclonal anti-*H. pylori* conjugate antibody, derived from ascites. **Minor Antibody:** Monoclonal anti-*H.pylori* conjugate antibody, derived from ascites.
Positive Control Acceptance Criteria	$A_{450/630}$ 1.8-2.3	$A_{450/630}$ 1.2-1.8

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

Not applicable

L. Test Principle:

Enzyme-linked immunosorbent assay

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 blinded specimens prior to testing. The specimen panels were tested according to the package insert method.

Contrived specimen panels were prepared by spiking *H. pylori* purified flaggelar antigen (*H. pylori* ATCC 43504) into negative pooled stool at antigen concentrations above, near and below the assay limit of detection for *H. pylori* antigen. Each panel consisted of one negative, three high negatives (0.1x LoD), three low positives (2x LoD), and three moderate positive (5x LoD) specimens, that were randomly sorted within each panel. Negative and positive controls were run on each day of testing. Three kit lots were used during the study. Results were interpreted using either single or dual wavelength spectrophotometric reads. The study results are summarized in **Table 1**. No differences were observed for single or dual wavelength spectrophotometric reads. The reproducibility performance was acceptable.

Table 1. Reproduciblity Testing Results Obtained with the Modified Device by Single or Dual Wavelength Spectrophotometric Read

Sampe Type	**Clinical Site 1 Percent Agreement**		**Clinical Site 2 Percent Agreement**		**Clinical Site 3 Percent Agreement**		**Total**	
							Percent Agreement	**95% CI**
Negative	30/30	100%	30/30	100%	30/30	100%	90/90 (100%)	95.9%-100%
High Negative	30/30	100%	30/30	100%	30/30	100%	90/90 (100%)	95.9%-100%
Low Positive	30/30	100%	30/30	100%	30/30	100%	90/90 (100%)	95.9%-100%
Moderate Positive	30/30	100%	30/30	100%	30/30	100%	90/90 (100%)	95.9%-100%
Negative Control	10/10	100%	10/10	100%	10/10	100%	30/30 (100%)	88.6%- 100%
Positive Control	10/10	100%	10/10	100%	10/10	100%	30/30 (100%)	88.6%- 100%

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 4.66 ng/mL, measured by dual wavelength, for unpreserved, pooled negative human stool.

e. Analytical specificity:

Cross-reactivity
The specificity of the modified PREMIER Platinum HpSA PLUS was tested with the bacterial, viral, and fungal strains listed in **Table 2**, below. Positive and negative stools (unpreserved pooled negative human stool, previously screened by the

modified and predicate device) were spiked with $1.0x10^7$ CFU/mL bacteria and fungi. Viruses were spiked at a final concentration greater than $1x10^5$ $TCID_{50}$/mL. None of the microorganisms tested yielded a positive result in the negative stool or interfered with detection of *H. pylori* antigen in positive stool.

Table 2. Microorganisms Tested for Cross-Reactivity

Adenovirus 41	*Klebsiella pneumoniae*
Aeromonas hydrophila	*Lactococcus lactis*
Bacillus subtilis	*Listeria monocytogenes*
Borrelia burgdorferi	*Peptostreptococcus anaerobius*
Campylobacter coli	*Proteus vulgaris*
Campylobacter fetus	*Pseudomonas aeruginosa*
Campylobacter jejuni	*Pseudomonas fluorescens*
Campylobacter jejuni (2)	Rotavirus
Campylobacter lari	*Salmonella enterica subsp. enterica serovar dublin*
Candida albicans	*Salmonella enterica subsp. enterica serovar hilversum*
Citrobacter freundii	*Salmonella enterica subsp. enterica serovar heidelberg* (Group B)
Clostridium difficile	*Salmonella enterica subsp. enterica serovar minnesota*
Clostridium perfringens	*Salmonella enterica subsp. enterica serovar typhimurium*
Enterobacter cloacae	*Serratia liquefaciens*
Enterococcus faecalis	*Serratia marcescens*
Escherichia coli O157:H7	*Shigella boydii*
Escherichia coli	*Shigella dysenteriae*
Escherichia coli 8739	*Shigella flexneri*
Escherichia coli 9637	*Shigella sonnei*
Escherichia fergusonii	*Staphylococcus aureus*
Escherichia hermanii	*Staphylococcus aureus* (Cowan Strain I)
Escherichia hermanii EMDI-64	*Staphylococcus epidermidis*
Haemophilus influenza	*Yersinia enterocolitica*

Interfering substances

The following substances, that may be present in human stool, do not interfere with positive or negative test results at the stated concentrations per 500 uL human stool: Barium sulfate – 25 mg, Mylanta – 11.5 mg, Pepto-Bismol – 0.44 mg, Prilosec (omeprazole) – 1 mg, Tagamet (cimetidine) – 1 mg, TUMS – 10 mg, Hemoglobin – 62.5 mg, Mucin – 17 mg, NSAID Ibuprofen – 0.250 mg, Stearic acid – 5.3 mg, Paltmitic acid – 2.65 mg, White blood cells – 250 uL, Whole blood – 250 uL.

Assay cut-off:

Not applicable

f. Prozone/Hook Effect:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison testing was done to compare performance of the modified PREMIER Platinum HpSA PLUS, using a replacement capture/conjugate monoclonal minor antibody and capture/conjugate monoclonal major antibody propogated by different methods, to that of the predicate device.

Testing was performed on 159 archived, unpreserved clinical stool specimens. The specimens were collected from individuals with signs and symptoms of *H. pylori* infection (from the Intended Use Population). Three lots of the modified device were tested. When compared to results obtained with the predicate, the percent positive and percent negative agreements were 100%. The results are summarized in **Table 3** below.

Table 3. Performance Comparison between the Modified Device and Predicate Device

	PP HpSA PLUS Predicate		
PP HpSA PLUS Modified	**Positive**	**Negative**	**Total**
Positive	57	0	57
Negative	0	102	102
Total	57	102	159
			95% CI
Positive Percent Agreement	100% (57/57)		93.7-100%
Negative Percent Agreement	100% (102/102)		96.4-100%

The percent positive and negative agreements compared to the predicate device were 100% (57/57, CI = 93.7% - 100%) and 100% (102/102, CI = 96.4% -100%), respectively. These results are acceptable.

b. Matrix comparison:

Not applicable

3. Clinical studies:

   a. Clinical Sensitivity:

   Not applicable

   b. Clinical specificity:

   See section M3a. above.

   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:

   Studies on the epidemiology of *H. pylori* have shown that this organism is present worldwide. Gastritis caused by *H. pylori* has been shown to correlate with age, ethnic background, family size and socioeconomic class. The prevalence of *H. pylori* infection 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%. Currently recommended eradication treatments have an efficacy rate between 75% and 90%.

   The modified Premier Platinum HpSA PLUS test detects the prescence of *H. pylori* antigens in human stool. Expected values for a given population should be determined for each laboratory. The rate of positivity may vary depending on geographic location, method of specimen collection, handling and transportation, test employed and general health environment of the patient population under study.

N. Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

O. Conclusion:

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