

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

A. 510(k) Number:

K053335

B. Purpose for Submission:

Change from polyclonal to monoclonal antibody technology

C. Measurand:

Helicobacter pylori antigen

D. Type of Test:

Qualitative enzyme immunoassay (EIA)

E. Applicant:

Meridian Bioscience Inc.

F. Proprietary and Established Names:

Premier Platinum HpSA PLUS

G. Regulatory Information:

1. Regulation section:

21 CFR 866.3110

2. Classification:

Class I

3. Product code:

LYR – Campylobacter pylori

4. Panel:

Microbiology (83)

H. Intended Use:

1. 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.

2. Indication for 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.

3. Special conditions for use statement:

For prescription use

4. Special instrument requirements:

Results may be read with a single or dual wavelength spectrophotometer

I. Device Description:

The device is a kit consisting of microwells coated with antibodies specific for *H. pylori*, positive and negative controls, wash buffer, enzyme conjugate, substrate and stop solution.

J. Substantial Equivalence Information:

1. Predicate device name:

Premier Platinum HpSA

2. Predicate 510(k) numbers:

K980076 & K983255

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Same	Same
Stool matrix	Same	Same

Differences		
Item	Device	Predicate
Limit of detection	≥ 4.67 ng/mL stool	≥ 184 ng/mL in stool
Assay cut off	0.100 at OD _{450/630}	0.120 at OD _{450/630}

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

FDA Draft Guidance :Review Criteria for Assessment of Laboratory Tests for the detection of antibodies to *Helicobacter pylori*. Sep. 1992

L. Test Principle:

The Premier Platinum HpSA PLUS test utilizes a mixture of monoclonal anti-*H. pylori* capture antibodies adsorbed to microwells. Diluted patient samples and a conjugate (peroxidase conjugated to monoclonal antibodies) are added to the wells and incubated for one hour at room temperature. A wash is performed to remove unbound material. Substrate is added and incubated for ten minutes at room temperature. Color develops in the presence of bound enzyme. Stop Solution is added and the results are interpreted visually or spectrophotometrically

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Assay precision, intra-assay variability and inter-assay variability were assessed with a reference panel prepared from high positive samples (n = 2), low negative samples (n = 2), and low positive and high negative specimens (n = 1 each). The latter were diluted to near the assay limit of sensitivity. Nine replicates each of the low positive and high negative samples were included in the panel to bring the total cohort to 22 reference specimens. 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 (OD value just below 0.100) produced weakly positive results (OD values just above 0.100) in 42 out of 162 tests. It is expected that high negative samples prepared at the cut-off will produce weakly positive results 50% of the time. (See EP12-A, User protocol for evaluation of qualitative performance; approved guideline;

NCCLS/CLSI, Vol. 22, no.14, 2002.) Low positive, high positive and low negative samples produced the correct results 100% of the time. 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:

N/A

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

N/A

d. Detection limit:

Serial dilutions of purified *H. pylori* flagellar antigen and a *H. pylori* bacterial strain (ATCC 43504) were prepared in stool or Sample Diluent and used to determine the lowest concentration of antigen that would still yield a definitive positive result ($A_{450/630} \geq 0.100$ on Premier Platinum HpSA PLUS). Final concentrations were calculated from the data points using linear regression analysis. The analytical limit for *H. pylori* flagellar antigen is 4.67 ng/mL in stool and 0.69 ng/mL in sample diluent. The limit for *H. pylori* bacterial strain is 1.0×10^6 organisms/mL in stool and 4.4×10^4 organisms/mL in Sample Diluent.

e. Analytical specificity:

The specificity of Premier Platinum HpSA PLUS was tested by utilizing the following bacterial, yeast or viral strains. Positive and negative stools were spiked with $\geq 1.2 \times 10^9$ bacterial or yeast organisms/mL and tested by Premier Platinum HpSA PLUS. The concentration of viral organisms was not calculated. None of the organisms affected positive or negative test results.

Microorganism or virus

<i>Adenovirus</i>	<i>Aeromonas hydrophila</i>	<i>Campylobacter lari</i>	<i>Campylobacter fetus</i>
<i>Campylobacter jejuni</i>	<i>Campylobacter</i> ni 2	<i>Campylobacter jejuni</i> solution	<i>Campylobacter lari</i>
<i>Candida albicans</i>	<i>Citrobacter freundii</i>	<i>Clostridium difficile</i>	<i>Clostridium perfringens</i>
<i>Enterobacter cloacae</i>	<i>Enterococcus faecalis</i>	<i>Escherichia coli</i> 0157:H7	<i>Escherichia coli</i> 8739
<i>Escherichia coli</i> 9637	<i>Escherichia fergusonii</i>	<i>Escherichia hermannii</i>	<i>Escherichia hermannii</i> EMDi-64
<i>Helicobacter pylori</i>	<i>Klebsiella pneumoniae</i>	<i>Lactobacillus lactis</i>	<i>Listeria monocytogenes</i>
<i>Peptostreptococcus</i>	<i>Proteus vulgaris</i>	<i>Pseudomonas</i>	<i>Pseudomonas</i>

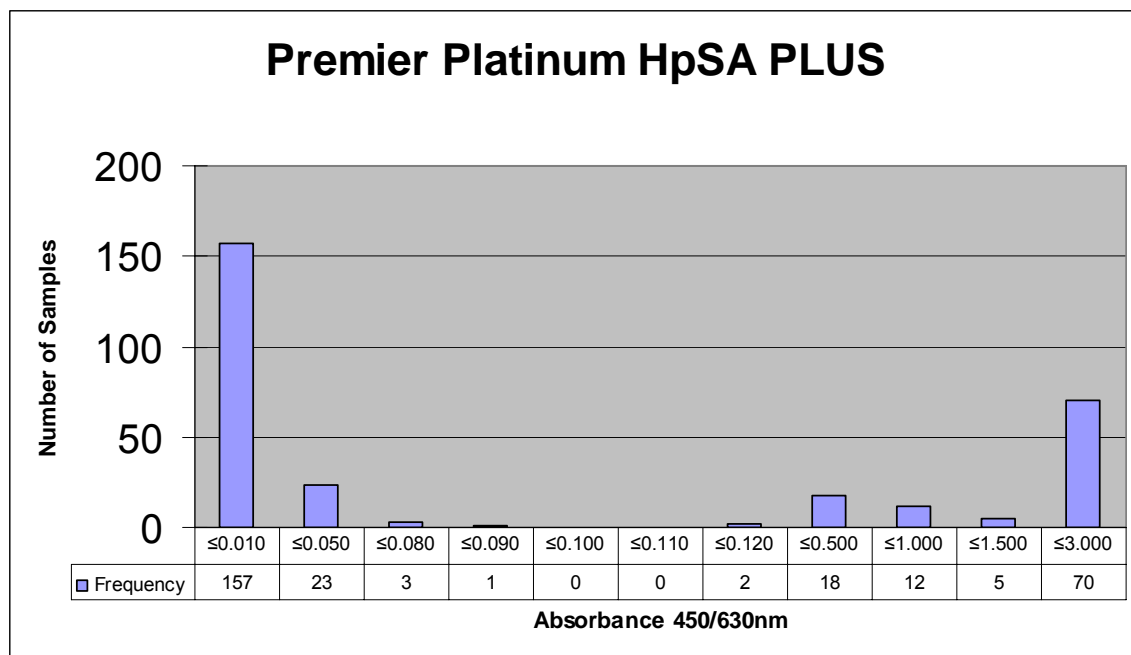
<i>anaerobius</i>		<i>aeruginosa</i>	<i>fluorescens</i>
<i>Salmonella Group B</i>	<i>Salmonella typhimurium</i>	<i>Serratia liquefaciens</i>	<i>Serratia liquefaciens</i>
<i>Serratia marcescens</i>	<i>Shigella boydii</i>	<i>Shigella flexneri</i>	<i>Shigella dysenteriae</i>
<i>Shigella sonnei</i>	<i>Staphylococcus aureus</i>	<i>Staphylococcus aureus (Cowans 1)</i>	<i>Staphylococcus epidermidis</i>
<i>Streptococcus faecalis</i>	<i>Yersinia enterocolitica</i>	<i>Yersinia enterocolitica</i>	<i>Rotavirus</i>
<i>Salmonella enterica serovar Hilversum</i>	<i>Salmonella enterica subsp. Enterica serovar Hilversum</i>	<i>Salmonella enterica subsp. Enterica serovar Minnesota</i>	

TESTS FOR 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: TUMS - 10 mg, Mylanta - 0.84 mg, Pepto Bismol - 0.35 mg, Tagamet - 1 mg, Prilosec OTC - 1 mg, barium sulfate - 10 mg, whole blood - 100 uL, mucin - 6.7 mg, human hemoglobin (ie, dark stool) – 15 mg steric + palmitic acids (ie, fatty stool) – 7.9 mg.

f. Assay cut-off:

The cut-off value of 0.100 was established on a lot-to-lot basis with specific procedures for optimizing solid phase and conjugate reagents. The validity of selection of this cut-off was proven in verification studies and clinical studies performed on three lots of fully manufactured product. The histogram provided below plots the values of samples tested during the clinical studies. The histogram shows that most samples consistently produce values that fall well above the cut-off, or well below that value.



2. Comparison studies:

a. *Method comparison with predicate device:*

Tests with 291 samples from symptomatic patients collected either prior to or following treatment were used to demonstrate that Premier Platinum HpSA PLUS performed similarly to Premier Platinum HpSA. Thirty three of these samples were originally evaluated in an earlier trial to demonstrate the effectiveness of Premier Platinum HpSA. Test performance is detailed in the following table.

PP HpSA PLUS	PP HpSA (Predicate)		
	Positive	Negative	Indeterminate
Positive	94	10	3
Negative	0	183	1
Agreement	Positive test	94/94 = 100%	
	Negative Test	183/193 = 94.8%	
	Overall	277/287 = 96.5%	

Eight of the ten samples that were positive by Premier Platinum HpSA PLUS, but negative by Premier Platinum HpSA, were positive by CLO, histology or UBT testing. The three samples that were positive by Premier Platinum HpSA PLUS but indeterminate by Premier Platinum HpSA were positive by CLO, histology or UBT testing. The one sample, that was negative by Premier Platinum HpSA PLUS but indeterminate by Premier Platinum HpSA, was negative by CLO, histology or UBT testing.

O. Conclusion:

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