510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

K181464

B. Purpose for Submission:

To obtain a substantial equivalence determination for the detection of *Helicobacter pylori* antigens in human stool.

C. Measurand:

H. pylori antigen

D. Type of Test:

Chemiluminescence immunoassay

E. Applicant:

DiaSorin Inc.

F. Proprietary and Established Names:

LIAISON *Helicobacter* Antigen, LIAISON *Helicobacter* Antigen Control Set

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.3110 - *Campylobacter fetus* serological reagents

2. Classification:
   Class I

3. Product code(s):
   LYR; *Helicobacter pylori*
   JJX; single (specified) analyte controls (assayed and unassayed)
   JJF; analyzer, chemistry, micro, for clinical use

4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):

   The LIAISON *Helicobacter* Antigen assay is a chemiluminescent immunoassay (CLIA) intended for the qualitative determination of *Helicobacter pylori* (*H. pylori*) antigen in human stool. The test is an aid in the diagnosis of patients suspected of *H. pylori* infection and to measure post therapy response from patients who have discontinued therapy for at least 4 weeks. Assay results should be used in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.

   The test must be performed on the LIAISON XL Analyzer.

   The LIAISON *Helicobacter* Antigen Control Set is intended for use as assayed quality control samples to monitor the performance of the LIAISON *Helicobacter* Antigen assay. The performance characteristics of the LIAISON *Helicobacter* Antigen Control Set have not been established for any other assay or instrument platforms different from the LIAISON XL.

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   LIAISON XL Analyzer

I. Device Description:

The LIAISON *Helicobacter* Antigen assay is a delayed one-step sandwich assay for detection of *H. pylori* stool antigen. The assay uses a Reagent Integral (Table 1) that consists of Magnetic Particles, Conjugate monoclonal antibodies and Assay Buffer for detection of *H. pylori* stool antigen. The assay also uses additional reagents (Table 2) that are required but not provided with the assay. The reagents include calibrators and a stool extraction kit used to extract and homogenize 200 µL of sample. The processed sample consists of a mixture of extraction buffer and stool extracted *H. pylori* stool antigen which is then incubated with paramagnetic particles coated with a capture antibody for *H. pylori* stool antigen. Following incubation, an isoluminol conjugated antibody for *H. pylori* stool antigen is added to the reaction and incubated. After the second incubation, the unbound material is removed with a wash cycle. The starter reagents are then added and a flash chemiluminescence reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU).

The LIAISON *Helicobacter* Antigen Control Set, sold separately, is intended for use as assayed quality control samples to monitor the performance of the LIAISON *Helicobacter* Antigen assay. The control set consists of two controls (positive and negative). The positive control is provided lyophilized and the negative is provided as a liquid. The controls are evaluated each testing day or as required by specific laboratory guidelines.

Table 1. Reagent Integral

Magnetic Particles (2.4 mL)	[SORB]	Magnetic particles coated with mouse monoclonal antibody against *H. pylori* stool antigen in phosphate buffer, BSA, surfactant, 0.1% ProClin300 and 0.05% gentamicin sulfate
Conjugate (13.0 mL)	[CONJ]	Mouse monoclonal antibody conjugated to an isoluminol derivative in phosphate buffer, BSA, surfactant, 0.1% ProClin300 and 0.05% gentamicin sulfate
Assay Buffer (13.0 mL)	[BUF | AS].	Mouse IgG in phosphate buffer, BSA, surfactant, 0.1% ProClin300 and 0.05% gentamicin sulfate

Table 2. Additional components required but not provided with the assay kit

Calibrator 1 2 x 2.0 mL Lyophilized	[CAL | 1]	*H. pylori* stool antigen in phosphate buffer, BSA, surfactant, 0.1% ProClin300 and 0.05% gentamicin sulfate. Reconstitute with 2.0 mL distilled or deionized water.
Calibrator 2 2 x 2.0 mL Lyophilized	[CAL | 2]	*H. pylori* stool antigen in phosphate buffer, BSA, surfactant, 0.1% ProClin300 and 0.05% gentamicin sulfate. Reconstitute with 2.0 mL distilled or deionized water.
Sample Diluent 1 x 100 mL	[DIL | SPE]	Phosphate buffer, BSA, surfactant, 0.1% ProClin300 and 0.05% gentamicin sulfate After opening, Sample Diluent is stable for 8 weeks when stored at 2-8°C.
2 x 50 each	[PIPETTOR]	Liquid Stool Pipettors ([REF]X0031)
LIAISON Stool Extraction Device* 2 x 50 each part	[TUBES] [FILTERS] [CAPS]	Polypropylene mixing tube, conical tube and blue cap, with high-density polyethylene (HDPE) blue filter unit.

*Device does not contain Bisphenol A (BPA), latex or Di (2-eithylhexyl) phthalate (DEHP).

The assay is only intended to be read on the LIAISON XL Analyzer. Standardization of the LIAISON XL Analyzer is performed using Calibrator 1 and Calibrator 2 which are then referenced to an in-house standard preparation.

Materials required by not provided (system related)
LIAISON XL Analyzer
LIAISON Wash/System Liquid ([REF]319100)
LIAISON XL Waste Bags ([REF]X0025)
LIAISON XL Cuvettes ([REF]X0016)
LIAISON XL Starter Kit ([REF]319200)
LIAISON XL Disposable Tips ([REF]X0015)

Additional required materials:
LIAISON Helicobacter Antigen Control Set ([REF]318201)

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Premier Platinum HpSA

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

   K053335

3. Comparison with predicate:

Similarities		
Item	**Device: LIAISON *Helicobacter* Antigen (K181464)**	**Predicate: Premier Platinum HpSA PLUS (K053335)**
Product Code	LYR	Same
Intended Use	The LIAISON Helicobacter Antigen assay is a chemiluminescent immunoassay (CLIA) intended for the qualitative determination of *Helicobacter pylori* (H. pylori) antigen in human stool. The test is an aid in the diagnosis of patients suspected of *H. pylori* infection and to measure post therapy response from patients who have discontinued therapy for at least 4 weeks. Assay results should be used in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.	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.

Similarities		
Item	**Device: LIAISON *Helicobacter* Antigen (K181464)**	**Predicate: Premier Platinum HpSA PLUS (K053335)**
	The test must be performed on the LIAISON XL Analyzer. The LIAISON *Helicobacter* Antigen Control Set is intended for use as assayed quality control samples to monitor the performance of the LIAISON *Helicobacter* Antigen assay. The performance characteristics of the LIAISON *Helicobacter* Antigen Control Set have not been established for any other assay or instrument platforms different from the LIAISON XL.	
Results	Qualitative	Same
Measurand	*H. pylori* antigen	Same
Specimen Required	Stool	Same

Differences		
Item	**Device: LIAISON *Helicobacter* Antigen (K181464)**	**Predicate: Premier Platinum HpSA PLUS (K053335)**
Limit of Detection	4 ng/mL	≥ 4.67 ng/mL in stool
Technology	Automated Chemiluminescent Immunoassay (CLIA)	Manual/Semiautomated Enzyme Immunoassay (EIA)
Cutoff	1.1 Index (for positive)	0.100 at $OD_{450/630}$
Interpretation	Negative <0.90 Index Equivocal zone (≥ 0.90 Index and < 1.10 Index) Positive ≥ 1.10 Index	Negative <0.100 $OD_{450/630}$ Positive ≥ 0.100 $OD_{450/630}$

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

- EP05-A2, Evaluation of Precision Performance of Quality Measurement Methods; Approved Guideline - Second Edition 2004
- Clinical and Laboratory Standards Institute (CLSI) EP15-A3, Vol .28, No.3, User Verification of Precision and Estimation of Bias; Approved Guideline - Third Edition
- EP07-A2, Interference Testing in Clinical Chemistry – Approved Guideline – Second Edition 2005

L. Test Principle:

This test uses chemiluminescence immunoassay (CLIA) technology based on the emission of light as a result of a chemical reaction. During the first incubation, paramagnetic particles coated with a capture antibody for *H. pylori* stool antigen are mixed with calibrators, extracted samples or controls. During the second incubation, the conjugate antibody reacts with *H. pylori* antigen that is bound to the solid phase. After each incubation, unbound material is removed with a wash cycle. The starter reagents are then added to initiate a flash chemiluminescence reaction. The resulting light signals are measured by a photomultiplier as RLUs and are indicative of the presence of *H. pylori* antigen in calibrators, samples or controls.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision was assessed by measuring repeatability at one site using two kit lots, two positive controls, two negative control and six clinically negative stool matrix samples that were spiked with recombinant *H. pylori* antigen at three different concentrations (two each) as follows: high negative < 1 X LoD (samples #1 and #2), low positive 2-3 X LoD (samples #3 and #4) and moderate positive 3-4 X LoD (samples #5 and #6). Samples and kit controls were assayed in duplicate in two runs per day over 12 days (48 data points for each panel member). Multiple operators participated in the study. Mean, standard deviation, and coefficient of variation (%CV) were calculated using multiple sources of variability that included within-run, within-day, between-day, and total variability. The study showed acceptable results which are summarized in Table 3.

Table 3 Precision Study Results.

Sample ID N=48	Mean Index Value	Within Run		Within Day		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Ctrl	0.06	0.00	7.8%	0.00	0.0%	0.00	4.6%	0.00	7.8%
Neg Ctrl	0.06	0.00	7.6%	0.00	0.0%	0.00	5.6%	0.01	8.8%
Pos Ctrl	2.72	0.05	1.9%	0.04	1.5%	0.03	1.2%	0.07	2.6%
Pos Ctrl	2.70	0.06	2.4%	0.03	1.2%	0.01	0.2%	0.07	2.7%
Sample #1	0.80	0.02	2.6%	0.02	2.3%	0.03	3.1%	0.04	4.7%
Sample #2	0.84	0.02	2.9%	0.01	1.0%	0.03	3.8%	0.04	4.9%
Sample #3	1.84	0.06	3.1%	0.02	1.2%	0.04	2.4%	0.08	4.1%
Sample #4	1.99	0.04	2.1%	0.07	3.5%	0.02	1.0%	0.08	4.2%
Sample #5	3.03	0.08	2.7%	0.00	0.0%	0.07	2.2%	0.10	3.3%
Sample #6	3.00	0.08	2.6%	0.06	2.1%	0.06	2.0%	0.12	3.9%

Reproducibility was assessed across three testing sites (one internal) using two kit controls in duplicate (positive and negative) and six samples containing antigen spiked into matrix as described for the precision study. High negative (samples #3 and #4), low positive (samples #5 and #6), and moderate positive (samples #1 and #2) concentrations of *H. pylori* stool antigen were assayed in replicates of three, in two runs per day over five operating days with two technicians at each site performing the test every day, totaling 90 observations for each panel member. Mean, standard deviation, and coefficient of variation (%CV) were calculated using multiple sources of variability that include within run, within day, between-day, site to site, and total variability. The study showed acceptable results which are summarized in Table 4.

Table 4. Reproducibility Study Results

Sample ID	Mean Index Value	Within Run		Run to Run Within Day		Day to Day Within Site		Site to Site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Ctrl	0.07	0.004	5.1%	0.002	2.4%	0.002	2.1%	0.009	12.5%	0.010	13.9%
Neg Ctrl	0.07	0.003	4.0%	0.003	4.0%	0.001	1.4%	0.007	10.0%	0.009	11.5%
Pos Ctrl	4.80	0.076	1.6%	0.050	1.0%	0.063	1.3%	0.105	2.2%	0.153	3.1%
Pos Ctrl	4.78	0.070	1.5%	0.050	1.0%	0.068	1.4%	0.113	2.4%	0.157	3.3%
Sample #1	2.12	0.034	1.6%	0.038	1.8%	0.108	5.1%	0.119	5.6%	0.168	8.0%
Sample #2	2.37	0.049	2.1%	0.046	1.9%	0.156	6.6%	0.226	9.5%	0.283	11.9%
Sample #3	0.69	0.024	3.5%	0.021	3.0%	0.037	5.4%	0.065	9.4%	0.081	11.8%
Sample #4	0.69	0.023	3.3%	0.026	3.8%	0.019	2.7%	0.065	9.4%	0.077	11.0%
Sample #5	1.21	0.031	2.5%	0.037	3.1%	0.029	2.4%	0.093	7.7%	0.109	9.0%
Sample #6	1.20	0.021	1.7%	0.030	2.5%	0.056	4.7%	0.120	10.1%	0.138	11.5%

b. Linearity/assay reportable range:

Not applicable

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

Each Reagent Integral requires calibration to an onboard 10 point standard preparation Master Curve that was previously loaded on to the LIASON XL ANALYZER when manufactured. Calibration is performed using the two calibrators included with each Reagent Integral.

Stability

Reagent Stability:

Reagent Integral Stability

Reagent Integral stability testing included four internal controls, one negative stool sample, one low positive spiked antigen stool sample, one moderative positive spiked antigen stool sample, and one high positive spiked antigen stool sample. Testing was performed weekly. Three Reagent Integral lots were used to establish stability conditions for opened and unopened reagents. All testing results were acceptable for up to eight weeks. The data supports a labeling claim for an open use stability of eight weeks at 2-8°C. Open use stability on board the LIAISON Analyzer was performed using one Reagent Integral Lot at specified intervals. All testing results were acceptable for up to eight weeks (see Table 5a).

Table 5a. Reagent stability

Unopened stored @ 2-8°C	Up to stated expiration date
Opened stored @ 2-8°C	8 weeks
Opened stored on analyzer	8 weeks

Calibrators Stability:

Calibrators were stored at 2-8°C and tested weekly. The Calibrators were found to be stable up to the stated expiration date if unopened, up to 28 days if opened and reconstituted, or up to 16 weeks if aliquoted and stored at -20°C (see Table 5b).

Table 5b. Calibrator stability

Unopened stored @ 2-8°C	Up to stated expiration date
Opened, reconstituted, stored @ 2-8°C	28 days
Aliquoted, stored @ -20°C	16 weeks
Freeze/Thaw	Up to 3 freeze/thaw cycles

Sample Stability:

A sample stability study was performed using ten (10) contrived stool samples spiked to the following levels: three high negatives, four low positive, and three moderate positive samples. Stool samples were spiked, extracted, and then stored until testing in triplicate (see Table 5c). Additional fresh stools samples were spiked with antigen then extracted at time of testing, these fresh samples should be tested within 72 hours if stored at 2-8°C and should be frozen at -20°C in not tested within the first 72 hours. All of the positives remained positive and all the negatives remained negative. Stability testing was acceptable.

Table 5c. Sample stability

Storage @ 18-25°C	8 hours
Storage @ 2-8°C	3 days
Storage @ -20°C	12 weeks
Freeze/Thaw	Up to 3 freeze/thaw cycles

Expected Calibrator values:

Calibrator 1 is manufactured to have a target concentration range of 1.2 – 1.8 Index value.

Calibrator 2 is manufactured to have a target concentration range of 8.0 – 12.0 Index value.

The negative control is manufactured to a target value less than 0.70 Index value. The positive control is manufactured to a have a target value of 5.0 Index value.

d. Detection limit:

The preliminary limit of Detection (LoD) testing was established by testing nine dilutions of stool samples of known *H. pylori* concentrations near the index value of 1.0. Samples were prepared by spiking stool with purified recombinant *H. pylori* antigen. Initial testing was performed in triplicate with the LIAISON *Helicobacter* Antigen assay. Confirmatory LoD was defined as the concentration of samples that gave a ≥ 95% positivity detection rate. The LoD was confirmed by evaluating sixty (60) additional replicates at the preliminary LoD concentration. The limit of detection for *H. pylori* stool antigen was determined to be at 4.0 ng/mL.

e. Analytical specificity:

Cross reactivity:
Studies were performed on the LIAISON *Helicobacter* antigen assay using potentially cross-reacting microorganisms that may cause symptoms similar to an *H. pylori* infection. Clinically negative stool matrix samples were spiked with recombinant *H. pylori* antigen at two levels: < 1 X LoD and 2-3 X LoD. Each concentration was then run with or without the potentially cross-reactive microorganism spiked at 1.2 x 10^8 CFU/mL (bacteria, fungi) and 1x10^5 $TCID_{50}$/mL (viruses) to determine the impact on the expected *H. pylori* result. None of the organisms affected positive or negative test results. Table 6 lists the organisms tested.

Table 6. Microorganisms Tested for Cross-reactivity

Organism	Organism	Organism
Aeromonas hydrophila	*Escherichia coli*	*Serratia liquefaciens*
Bacillus subtilis	*Escherichia fergusonii*	*Shigella boydii*
Borrelia burgdorferi	*Escherichia hermannii*	*Shigella flexneri*
Campylobacter coli	*Haemophilus influenzae*	*Shigella sonnei*
Campylobacter fetus	*Klebsiella pneumoniae*	*Staphyloccocus epidermis*
Campylobacter jejuni	*Lactobacillus lactis*	*Vibrio parahaemolyticus*
Campylobacter upsaliensis	*Listeria monocytogenes*	*Yersinia enterocolitica*
Campylobacter hyointestinalis	*Peptostreptococcus anaerobius*	Adenovirus Type 2
Candida albicans	*Plesiomonas shigelloides*	Adenovirus Type 40
Citrobacter freundii	*Proteus vulgaris*	Adenovirus Type 41
Clostridioides difficile	*Pseudomonas aeruginosa*	Coxsackievirus B1
Clostridium perfringens	*Pseudomonas fluorescens*	Coxsackievirus B6
Clostridium sordellii	*Salmonella Group B*	Echovirus
Enterobacter cloacae	*Salmonella Group C*	Rotavirus
Enterobacter cloacae	*Salmonella Group D*	
Enterococcus faecalis	*Salmonella Group E*	

Interference:

Testing was performed to determine interference in the presence of potentially interfering exogenous substances and commonly used medications relevant to digestive complications and endogenous substances that may be found in stool. Two matched stool sample pools containing *Helicobacter* antigen at concentrations near the 1-2 X LoD and < 1 X LoD (low positive and high negative) were spiked with the test substances and tested in triplicate. Mean Index values were calculated for each sample. The Index values were averaged and the matched pairs were then compared to determine if any of the substances affected test performance.

Acceptance criteria required that the spiked sample comparison to vehicle control did not exhibit a change in classification from positive to negative or negative to positive. No interference was observed in the LIAISON *Helicobacter* Antigen assay at the highest concentration for each substance listed in Table 7.

Table 7. Substances Tested for Interference.

Substance	Concentration Tested
Barium Sulfate	5.0 mg/mL
Stearic Acid	2.65 mg/mL
Palmitic Acid	1.3 mg/mL
Hemoglobin	3.2 mg/mL
Imodium AD	0.00667 mg/mL
Kaopectate	0.87 mg/mL
Metronidazole	12.5 mg/mL
Mucin	3.33 mg/mL

Mylanta (Maalox)	4.2 mg/mL
Pepto Bismol	0.87 mg/mL
MiraLAX (PEG 3350)	79.05 mg/mL
Prilosec	0.5 mg/mL
Gas X/Simethicone	0.625 mg/mL
Tagamet	0.5 mg/mL
Tums	0.5 mg/mL
Vancomycin Hydrochloride	2.5 mg/mL
White Blood Cells	5%
Whole Blood	25%

f. Assay cut-off:

The cut-off value discriminating between the presence and the absence of *H. pylori* stool antigen is described in Table 8.

Table 8. Interpretation of Results

Index	Result	Interpretation
<0.90	Negative	Indicates the absence of *H. pylori* stool antigen, (or the level of antigen is below that which can be detected by the assay)
≥0.90 and <1.10	Equivocal	Equivocal samples should be retested using a new extraction from the original sample in order to confirm the initial result. Samples that are positive (≥1.10) by the second test should be considered positive. Samples that are negative (<0.90) by the second test should be considered negative. For samples that are equivocal on retesting, a new specimen should be collected and tested.
≥1.10	Positive	Indicates the presence of detectable *H. pylori* stool antigen

g Prozone/Hook Effect:

<u>High Dose Hook Effect (false negative):</u>

A study was conducted to demonstrate that a high concentration of *H. pylori* antigen does not interfere with a positive reaction in the LIAISON *Helicobacter* Antigen assay. High concentration samples were prepared by spiking negative fecal matrix with *H. pylori* antigen at 1.8 µg/mL (i.e., eight-fold higher than the highest concentration observed in a positive clinical sample). A total of 16 different dilutions were prepared from the contrived sample. Samples were prepared by spiking three

concentrations above the clinical range and 13 samples across the clinical range. Testing was performed in triplicate according to the package insert instructions. The results demonstrated that there was no hook effect, and that elevated levels of *H. pylori* antigen did not affect the test results.

2. Comparison studies:

   a. Method comparison with predicate device:

   Not applicable

   b. Matrix comparison:

   Not applicable

3. Clinical studies:

   a. Clinical Sensitivity:

   Prospective study

   Initial Diagnosis
   The performance of the LIAISON *Helicobacter* antigen assay was evaluated by conducting a multi-site prospective clinical study. Twelve (12) independent sites performed biopsies and collected stool specimens from patients suspected of *H. pylori* infection. These specimens were collected from 11 sites within the US and one site from outside the US (Italy).

   The stool specimens were divided between three clinical sites, different from those conducting biopsy, for testing. The three sites that performed the clinical testing with the LIAISON *Helicobacter* antigen assay were ARUP Utah, Northwell Health Core Laboratories New York, and DiaSorin Inc., Minnesota. Technicians at these three sites were blinded to the biopsy (composite reference method, CRM) results obtained from the collection sites.

   The CRM for diagnosis of *H. pylori* infection is based on endoscopy obtained gastric biopsy. The biopsied tissue was tested for the presence of *H. pylori* by histology and rapid urease test. The sensitivity and specificity for the LIAISON *Helicobacter* antigen assay was determined using the CRM.

   Prospective testing consisted of 481 stool specimens collected from the patients with symptoms gastritis or *H. pylori* infection who were scheduled to undergo endoscopy with gastric biopsy as part of routine care (Initial Diagnosis Group). Of these, 204 patients were excluded either because they were on a treatment regimen [i.e., proton-pump inhibitors (PPIs), or antibiotics] or had samples with CRM results that were inconclusive, incomplete or were not readable. The remaining 277 patients who were

not taking PPIs or antibiotics at the time of specimen collection were considered for final analysis.

The ages of patients ranged from 22 years to 87 years old. Of the 277 patients tested, 69% were female and 31% were male. No difference in test performance was observed based on patient age or gender. The results are provided in Table 9 which shows the clinical performance of the LIAISON *Helicobacter* antigen assay test at all three of the test sites combined. The results of the study show that the LIAISON *Helicobacter* antigen assay test exhibited a sensitivity of 95.5%, and a specificity of 98.6% compared to the CRM. The results are summarized in Table 9.

Table 9. Clinical Performance of the LIAISON *Helicobacter* Antigen assay- Initial Diagnosis

Initial diagnosis	CRM Positive	CRM Negative
LIAISON *Helicobacter* antigen assay Positive	**64**	**3**
LIAISON *Helicobacter* antigen assay Negative	**3**	**207**

Sensitivity (95% C.I.)	95.5% (87.6% - 98.5%)
Specificity (95% C.I.)	98.6%(95.9% - 99.5%)

Post Therapy Diagnosis

Eradication (post therapy) evaluation was conducted on patients enrolled prospectively at two sites. A total of 8 specimens were collected at least 4 weeks after completion of the treatment regimen. Post therapy evaluation was conducted using a two-step algorithm of patient analysis. First, patients were screened for the continued presence of *H. pylori* using an FDA-cleared stool antigen test. Positive patients were reflexed to a follow-up endoscopy and biopsy analysis by rapid urease test and histology. The results of the study show that the LIAISON *Helicobacter* antigen assay exhibited a sensitivity of 100.0% compared to the CRM. The results are summarized in Table 10.

Table 10. Clinical Performance of the LIAISON *Helicobacter* Antigen assay- Post Therapy

Initial diagnosis	CRM Positive	CRM Negative
LIAISON *Helicobacter* antigen assay Positive	**8**	**0**
LIAISON *Helicobacter* antigen assay Negative	**0**	**0**

Sensitivity (95% C.I.)	100% (67.6% - 100%)

b. Clinical specificity:

See section M.3a. above.

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

See section M.3a. above.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

N. Instrument Name:

LIAISON XL Analyzer

O. System Descriptions:

1. Modes of Operation:

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes _____ or No ____X____

Does the applicant's device transmit data to a computer, webserver, or mobile device

using wireless transmission?

Yes _____ or No _____X___

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes _____X___ or No _____

3. Specimen Identification:

   Specimens are identified by unique barcodes

4. Specimen Sampling and Handling:

   See section M.1.c. above.

5. Calibration:
   DiaSorin's LIAISON *Helicobacter* antigen assay generates a continuous response (relative light units, RLU) which is used in sample grading to provide a qualitative (positive, negative, or equivocal) reportable result. The sample grading is based on the use of a 10 point calibration curve (Master Curve) that was generated at the manufacturer (In-house) when the analyzer was manufactured. Calibration of each Reagent Integral is achieved by comparing the two calibrators (Calibrator 1 and Calibrator 2) provided in the Reagent Integral in the Master Curve.

   The Master Curve is stored on the LIAISON® XL Analyzer and specifically matched to the kit in use via the instructions encoded in the RFID tag attached to the Reagent Integral. Each 10 point Master Curve has been generated by a mathematical elaboration of the data resulting from multiple testing (a minimum of 10 runs) of Master Standards when the analyzer is manufactured.

   The Master Standards are prepared from purified recombinant antigen also referred to as the 'in house' Primary Standard Reference Preparation provided by the manufacturer.

   The kit calibrators are manufactured by diluting stock solutions consisting of purified recombinant antigen manufactured to an established Index value. The kit calibrators are tested with a specific Integral lot against the Master Calibrators to assess the concentration. They are subsequently corrected by dilution or concentration if the result (Index value) is out of the target range.

   Calibrator 1 is manufactured to have a target *H. pylori* antigen level of 1.5 Index value. Calibrator 2 is manufactured to have a target *H. pylori* antigen level of 10.0 Index value.

The Calibrators are assayed by the user with a specific Reagent Integral lot to transform the Master Curve (10 point) into a Working Curve (2 point) and further used to calculate sample results. The LIAISON XL Analyzer Working Curve is obtained by the user during assay calibration by assigning a curve to the two point kit calibrators based upon the Master Curve. This Working Curve is used to calculate the patient sample results. The Analyzer is calibrated in triplicate whenever one of the following conditions occurs:

- Quality Control results are out of the acceptable range.
- With each new lot of reagents (Reagent Integral or Starter Reagents)
- After each servicing of the LIAISON XL Analyzer
- The previous calibration was performed more than four weeks before

6. Quality Control:

   LIAISON *Helicobacter* Antigen Control Set ([REF] 318201) is intended to monitor for substantial reagent failure. LIAISON controls should be run in singlet to monitor the assay performance. Quality control is required to be performed once per day of use, or according to the guidelines or requirements of local regulations or accredited organizations. It is recommended that the user refer to CLSI C24-A35 and 42 CFR 493.1256(c) for guidance on appropriate quality control practices.

   The expected range of control concentrations is provided on the certificate of analysis, the test is valid. If control values lie outside the expected ranges, the test is invalid and patient results cannot be reported. Assay calibration should be performed if a control failure is observed and controls and patient specimens must be repeated.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not Applicable

Q. Proposed Labeling:

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

R. Conclusion:

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