

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

A. 510(k) Number:

K052716

B. Purpose for Submission:

For substantial equivalence determination

C. Measurand:

IgG Antibodies against Helicobacter pylori

D. Type of Test:

Rapid qualitative immunochromatographic assay

E. Applicant:

Otsuka Pharmaceutical Co., Ltd.

F. Proprietary and Established Names:

RAPIRUN H. pylori antibody detection kit

G. Regulatory Information:

1. Regulation section:

Regulated under 21 CFR section 866.3110, Campylobacter fetus serological reagents

2. Classification:

I

3. Product code:

LYR – Campylobacter pylori

4. Panel:

H. Intended Use:

1. Intended use:

The RAPIRUN H. pylori antibody Detection kit is a rapid immunochromatographic assay intended for the qualitative detection of antibodies against Helicobacter pylori (H. pylori) in urine to aid in the diagnosis of H. pylori infection. The RAPIRUN kit is suitable for use in both point-of-care and clinical laboratory settings.

2. Indication(s) for use:

The RAPIRUN H. pylori antibody Detection kit is a rapid immunochromatographic assay intended for the qualitative detection of antibodies against Helicobacter pylori (H. pylori) in urine to aid in the diagnosis of H. pylori infection. The RAPIRUN kit is suitable for use in both point-of-care and clinical laboratory settings.

3. Special conditions for use statement(s):

Prescription use and point-of-care use

4. Special instrument requirements:

N/A

I. Device Description:

The RAPIRUN H. pylori antibody detection kit consists of a nitrocellulose membrane test device, sample diluent and disposable pipettes. The test device consists of Helicobacter pylori extracted protein, colloidal gold-conjugated anti-human IgG (Fc) polyclonal antibody (goat). The sample diluent is buffer containing sodium azide. The test device includes a sample window (S) in which the test specimen is placed and an evaluation window in which a test line (T) and a control line (C) are visible. Colloidal gold conjugated anti-human IgG (Fc) polyclonal antibody (goat) is present between the sample window and the evaluation window. The test line and control line in the evaluation window are immobilized with H. pylori antigen and with anti-human IgG polyclonal antibodies (goat) respectively.

Each kit is sufficient for ten tests and is provided ready for use with no further preparation necessary. Within the kit, each test device is individually packaged.

J. Substantial Equivalence Information:

1. Predicate device name(s):

HM-CAP H. pylori EIA test

Instant view H. pylori Rapid Test

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

K984544, K955085, K944159

K024360

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Detection of H. pylori antibodies as an aid in the diagnosis of H. pylori infection	Same
Type of test	Qualitative	Same
Analyte	IgG antibodies to H.pylori	Same
Methodology	Immunoassay	Same
User setting	Point of care or clinical lab	Clinical lab – HM CAP Point of care- Instant View

Differences		
Item	Device	Predicate
Matrix	Urine	Serum or plasma - HM CAP Whole blood or serum – Instant view
Detection method	Visual inspection	Absorbance – HM CAP

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

Review Criteria for Assessment of Lab Tests for the detection of antibodies to

L. Test Principle:

When a urine sample diluted with the sample diluent is added dropwise to the sample window, the IgG in the diluted sample reacts with the conjugated antibodies. Immunocomplexes are formed and flow into the nitrocellulose membrane. If anti H. pylori IgG antibody complexes are present in these immunocomplexes, they react with the H. pylori antigen immobilizing on the test line and are captured producing a red band. On the other hand, immunocomplexes without anti H. pylori IgG antibodies pass the test line and are captured by the anti-human IgG polyclonal antibodies (goat) immobilizing on the control line producing a red band. If red colored bands appear in both test and control zones, the test can be considered positive. A red colored band only in the control zone is a negative test result. The test result is invalid if no red colored band appears in the control zone.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Two studies were performed to assess the reproducibility of the RAPIRUN kit. Control samples for both studies were prepared from pooled sera which were negative and positive respectively, for anti-H. pylori antibodies. Three levels of controls were tested: negative, weakly positive and highly positive. In the first study, three lots of kits were tested on the same day. For each lot, 3 replicates of each of the three control samples were tested. The expected negative and positive results were obtained in all cases. In the second study, intra-day, inter-day, inter-operator and inter-lot reproducibility were evaluated as follows

Intra-day One operator tested one lot at 3 different times on the same day

Inter-day One operator tested one lot on 3 different days

Inter-operator Three operators tested one lot on the same day

Inter-lot Three operators tested 3 different lots on 3 different days

The expected negative and positive results were obtained in all cases.

An additional study was performed using a panel of 8 urine specimens tested with varying concentrations of H. pylori antibodies (2 each of negative, weakly positive, positive and highly positive). 3 levels of control samples were also tested. Evaluation was as follows:

Inter-lot	One operator tested 3 different lots on the same day
Inter-day	One operator tested one lot on 3 different days
Intra-day	One operator tested one lot at three different times on the same day
Inter-operator	Three operators tested one lot on the same day

The expected negative and positive results were obtained in all cases.

b. Linearity/assay reportable range:

N/A

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

N/A

d. Detection limit:

Three control samples that were negative, weakly positive and highly positive for anti- *H. pylori* antibody were selected from pooled negative and pooled positive sera respectively. The negative and positive samples were diluted 4000-fold with a 2 mmol/L Borax buffer solution containing 0.5% bovine serum albumin. The highly positive Control sample was diluted 6-fold by the negative sample to create a weakly positive control sample. The titer of anti- *H. pylori* antibody contained in the weakly positive control sample corresponds to that of the highly positive sample diluted 24000-fold.

e. Analytical specificity:

A cross reactivity study was performed to investigate the effects of proteins extracted from the following bacteria on the test results obtained using the RAPIRUN kit:

Enterococcus faecalis, *Enterococcus faecium*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Staphylococcus aureus*.

Test samples were prepared by adding proteins extracted from the bacteria to two urine samples negative for anti *H. pylori* antibodies and three urine samples positive for anti *H. pylori* antibodies. All test samples were run in triplicate. None of the proteins extracted from the 6 bacteria had any effect on the expected test results.

Interference Studies

An interference study was performed to investigate the effects of 26 substances on samples using the RAPIRUN kit. Each substance was added individually to 2 urine samples negative for anti-H. pylori antibodies and to 2 urine samples positive for anti-H. pylori antibodies. Substances tested included proteins, drugs and other metabolites considered to be possibly present in urine. Interference was observed for human gamma-globulin, human serum, and bilirubin F. No interference was observed for the remaining 23 substances namely :

Human serum albumin, mucoprotein, glucose, hemoglobin, bilirubin C, vitamin C, acetylsalicylic acid, caffeine, acetaminophen, atrophine, norephedrine, uric acid, urea, creatine, creatinine, calcium oxalate, 5-aminolevulinic acid, myoglobin, 3-hydroxybutyric acid, β_2 -microglobulin, L-Leucine, L-Cystine and acetone.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A multi-center prospective study was conducted at four Physicians Office Labs (POL)/Point-of-Care (POC) settings. Subjects between the ages of 18 and 75 yrs who were either asymptomatic or experiencing dyspepsia were recruited from the investigational sites. Specific inclusion and exclusion criteria were listed. A urine specimen was collected from each of the 188 evaluable patients and tested with the RAPIRUN kit at the investigational sites. A blood specimen was also collected from all subjects and tested with the HM-CAP EIA test at a central testing laboratory. Additionally all patients underwent a standard urea breath test (UBT) and the breath samples were analyzed using the UBiT-IR300 Infrared Spectrophotometer method at the investigational sites. The urine, serum and breath specimens for each patient were collected on the same day. There were no deviations from the protocol. No device malfunctions nor adverse events were reported. Results from the RAPIRUN for the qualitative detection of antibodies to H. pylori in urine were compared to results from the HM-CAP EIA for the detection of antibodies to H. pylori in serum and to the UBiT-IR 300 Infrared Spectrophotometer for measuring $^{13}\text{CO}_2$ enrichment in breath.

Results of RAPIRUN vs. HM-CAP:

% Overall Agreement: 87.23% (81.97 – 91.39 % C.I.)

% Positive agreement: 84.71% (75.82 – 91.30% C.I.)

% Negative Agreement: 89.32% (81.96 – 94.31% C.I.)

Results of RAPIRUN vs. UBiT-IR300

% Overall Agreement: 93.09% (88.51 – 96.27% C.I.)

% Positive Agreement: 86.46% (78.53 – 92.40 % C.I.)

% Negative Agreement: 100.00% (96.17 – 100.00% C.I.)

b. Matrix comparison:

Urine, serum and breath samples for each patient were collected on the same day. Results from the RAPIRUN (urine matrix) were compared to those from the HM-CAP EIA (serum matrix) and to the UBiT-IR 300 Infrared spectrophotometer for measuring ¹³CO₂ enrichment in breath. See 2(a) above.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

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:

Prevalence of *H. pylori* infection varies widely across the USA and is associated with age, ethnic and socioeconomic factors. Prevalence has been shown to increase with age at about 1% per year for the overall population. Overall frequency of *H. pylori* infection has been reported as 33% with higher rates in some ethnic groups. One hundred and eighty eight subjects symptomatic and asymptomatic, ranging from 18 – 73 years were enrolled at 4 POC/POL settings. Urine specimens from 83 subjects (44%) tested positive and 105 (56%) tested negative with the RAPIRUN kit.

N. Proposed Labeling:

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

O. Conclusion:

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