

# H. pylori Rapid Test Device

## (Whole Blood/Serum/Plasma) Package Insert

A rapid test for the qualitative detection of IgG antibodies to *Helicobacter pylori* (*H. pylori*) in whole blood, serum and plasma.

For professional *in vitro* diagnostic use only.

### INTENDED USE

The *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma) is a rapid chromatographic immunoassay for the qualitative detection of IgG antibodies to *Helicobacter pylori* in whole blood, serum or plasma to aid in the diagnosis of *H. pylori* infection in adults 18 years of age and older.

### SUMMARY

*H. pylori* is a small, spiral-shaped bacterium that lives in the surface of the stomach and duodenum. It is implicated in the etiology of a variety of gastrointestinal diseases, including duodenal and gastric ulcer, non-ulcer dyspepsia and active and chronic gastritis.<sup>1,2</sup>

Both invasive and non-invasive methods are used to diagnose *H. pylori* infection in patients with symptoms of gastrointestinal disease. Sample-dependent and costly invasive diagnostic methods include gastric or duodenal biopsy followed by urease testing (presumptive), culture, and/or histologic staining.<sup>3</sup> Non-invasive techniques include the urea breath test, which requires expensive laboratory equipment and moderate radiation exposure, and serological methods.<sup>4,5</sup>

Individuals infected with *H. pylori* develop serum IgG antibodies which correlate strongly with histologically confirmed *H. pylori* infection.<sup>6,7,8</sup> The *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma) is a simple test that utilizes a combination of *H. pylori* antigen coated particles and anti-human IgG to qualitatively and selectively detect *H. pylori* IgG antibodies in whole blood, serum or plasma in just minutes.

### PRINCIPLE

The *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma) is a qualitative membrane strip based immunoassay for the detection of *H. pylori* IgG antibodies in whole blood, serum or plasma. In this test procedure, anti-human IgG is immobilized in the test line region of the device. The sample reacts with *H. pylori* antigen coated particles that have been applied to the label pad. This mixture migrates chromatographically along the length of the test strip and interacts with the immobilized anti-human IgG. If the sample contains *H. pylori* IgG antibodies, a colored line will appear in the test line region indicating a positive result. If the sample does not contain *H. pylori* IgG antibodies, a colored line will not appear in this region indicating a negative result. To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

### REAGENTS

The test device contains *H. pylori* antigen-coated particles and anti-human IgG coated membrane.

### PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after expiration date.
- Do not eat, drink or smoke in the area where the specimen samples and kits are handled.
- The positive and negative controls contain human plasma. Handle controls and all specimen samples as if they contain infectious agents. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimen samples.
- The positive and negative controls contain sodium azide as a preservative.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimen samples are assayed.
- Humidity and temperature can adversely affect results.
- The dispensing bulb used with the capillary tubes to add fingerstick whole blood to the device may contain trace amounts of latex which may cause an allergic reaction in some individuals.

### STORAGE AND STABILITY

The kit can be stored at room temperature or refrigerated (2-30°C). The test device is stable through the expiration date printed on the sealed pouch. The test device must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

### SAMPLE COLLECTION AND PREPARATION

- The *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma) can be performed using whole blood (from venipuncture or fingerstick), serum or plasma.
- To collect Venipuncture Whole Blood samples: Collect anti-coagulated blood sample (sodium or lithium heparin, potassium or sodium EDTA, sodium oxalate, sodium citrate) following standard laboratory procedures.
- To collect Fingerstick Whole Blood samples:
  - Wash the patient's hand with soap and warm water or clean with an alcohol swab. Allow to dry.
  - Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
  - Puncture the skin with a sterile lancet. Wipe away the first sign of blood.
  - Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
  - Touch the end of the capillary tube to the blood until filled to the red line; avoid air bubbles.
  - Place the bulb onto the top end of the capillary tube.
  - Squeeze the bulb to dispense the whole blood.
- Separate serum or plasma from blood as soon as possible to avoid hemolysis. Use only clear, non-hemolyzed samples.

- **Testing should ideally be performed immediately after the samples have been collected.** Do not leave the samples at room temperature for prolonged periods. Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 2 days of collection. Whole blood collected by fingerstick should be tested immediately. Do not freeze whole blood samples. Serum or plasma samples may be stored at 2-8°C for up to 3 days. For long term storage, samples should be kept below -20°C.
- Bring samples to room temperature prior to testing. Frozen samples must be completely thawed and mixed well prior to testing. Samples should not be frozen and thawed repeatedly.
- If samples are to be shipped, they should be packed in compliance with federal regulations covering the transportation of etiologic agents.

## MATERIALS

### Materials Provided

- Test devices
- Disposable sample droppers
- Disposable heparinized capillary tubes and dispensing bulb
- Positive control (Diluted human plasma containing *H. pylori*-specific IgG, 0.09% sodium azide)
- Negative control (Diluted human plasma, 0.09% sodium azide)
- Sample Buffer
- Procedure card
- Package insert

### Materials Required But Not Provided

- Sample collection container (for venipuncture whole blood)
- Lancet (for fingerstick whole blood only)
- Centrifuge (for serum and plasma only)
- Timer

## DIRECTIONS FOR USE

Allow the test device, sample, buffer and controls to reach room temperature (15-30°C) before testing.

1. Remove the test device from the foil pouch and use it as soon as possible. For best results, perform the test immediately after opening the foil pouch.
2. Place the test device on a clean and level surface.
  - For **Whole Blood (Venipuncture)** samples: Hold the dropper upright and add **2 drops of whole blood** (about 50 µl) to the sample well (S) of the test device. Then add **1 drop of Sample Buffer** to the sample well. Start the timer.

- For **Whole Blood (Fingerstick)** samples: Add **one capillary tube of blood** (about 50 µl) to the sample well (S) of the test device. Then add **1 drop of Sample Buffer** to the sample well. Start the timer.
  - For **Serum or Plasma** samples: Hold the dropper upright and add **2 drops of serum or plasma** (about 50 µl) to the sample well (S) of the test device. Then add **1 drop of Sample Buffer** to the sample well. Start the timer. Avoid trapping air bubbles in the sample well. See the illustration below.
3. Wait for the red line(s) to appear. The result should be read at 10 minutes. The background should be clear before the result is read.

Note: Low levels of *H. pylori* IgG specific antibodies might result in a weak line in the test region (T) after a long period of time. Do not read the result after 15 minutes.

## INTERPRETATION OF RESULTS

(Please refer to the illustration above)

**POSITIVE:** Two distinct red lines appear. One line should be in the control region (C) and another line should be in the test region (T). A positive result means that *H. pylori* IgG specific antibodies were detected in the sample.

**\*NOTE:** The shade of the red color in the test line region (T) will vary based on the amount of *H. pylori* IgG specific antibodies in the sample. Any shade of red in the test region (T) should be considered positive.

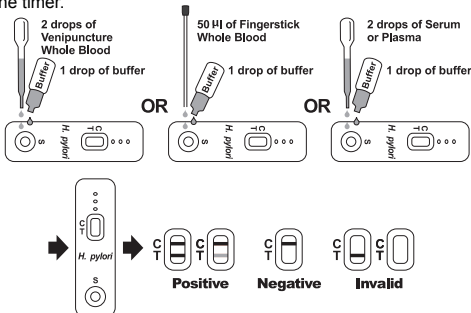
**NEGATIVE:** One red line appears in the control region (C). No apparent red or pink line appears in the test region (T). A negative result means that *H. pylori* IgG specific antibodies were not found in the sample or are below the detection limit of the test.

**INVALID:** No line appears in the control region (C). If this occurs, read the directions again and repeat the test with a new test strip. If the result is still invalid, stop using the test kit and contact your distributor.

## QUALITY CONTROL

### Internal Quality Control

Internal procedural controls are included in the test. A red line appearing in the control region (C) is an internal positive procedural control. It confirms sufficient sample volume and correct procedural technique. A clear background is an internal negative background control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.



## External Quality Control

It is recommended that a positive and negative external control be run every 20 tests, and as deemed necessary by your internal laboratory procedures. External positive and negative controls are supplied in the kit. If controls do not perform as expected, assay results are invalid.

## Procedure for External Quality Control Testing

Using the positive or negative external controls in place of a patient sample, add 2 drops of positive or negative control solution to the sample well (S) of a new test device, then add 1 drop of Sample Buffer. Start the timer. Continue with Step 3 in the Directions For Use section.

## LIMITATIONS

1. The *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma) should be used only to evaluate patients with clinical signs and symptoms suggestive of gastrointestinal disease and is not intended for use with asymptomatic patients.
2. The *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma) is for *in vitro* diagnostic use only. The test should be used for the detection of *H. pylori* IgG antibodies in whole blood, serum or plasma samples only. Neither the quantitative value nor the rate of increase in *H. pylori* antibody concentration can be determined by this qualitative test.
3. The *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma) will only indicate the presence of *H. pylori* IgG antibodies in the sample and should not be used as the sole criteria for the diagnosis of *H. pylori* infection.
4. Grossly hemolysed samples will yield invalid results. Strictly follow the Package Insert instructions to obtain accurate results.
5. A positive result does not allow one to distinguish between active infection and colonization by *H. pylori*.
6. A positive result only indicates the presence of IgG antibody to *H. pylori* and does not necessarily indicate that gastrointestinal disease is present.
7. A negative result indicates that IgG antibody to *H. pylori* is not present or is below the detection limit of the test.
8. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
9. Literature references have suggested cross reactivity of IgG antibody with a closely related organism, *Borrelia burgdorferi*. Performance of this assay has not been evaluated with this organism. Therefore, the specificity of this test device is not known if this organism is encountered.
10. Literature references have suggested that high triglyceride levels interfere with IgG antibody. However, performance of this assay has not been evaluated with this substance. Therefore, test results of these devices are not known if high levels of this substance are encountered.
11. This assay has not been established for patients under 18 years of age.

## EXPECTED VALUES

*H. pylori* infection is present worldwide and has been shown to correlate with age, ethnic background, family size, and socioeconomic class.<sup>9</sup> In the United States, the incidence of infection may increase 1-2% annually.<sup>10</sup> Eighty to 100% of individuals with signs and symptoms of other gastrointestinal conditions such as duodenal ulcers are reported to be positive for *H. pylori* infection.<sup>11</sup>

## PERFORMANCE CHARACTERISTICS

### Clinical Sensitivity, Specificity and Accuracy

Using two independent sites, a total of 484 clinical samples were obtained from a population of symptomatic individuals who presented for endoscopic examination for the detection of *H. pylori* infection. Culture and/or histology of biopsy specimens served as the reference method for the study done in Site A while histology and/or rapid urease test of the biopsy specimens served as the reference method for the study done in Site B. Whole blood (venous and fingerstick), serum and plasma were also collected for the detection of *H. pylori* specific IgG antibody by the *H. pylori* Rapid Test Device.

Of the 321 fresh clinical samples collected in Site A, 136 were considered biopsy positive and 185 clinical specimens were considered biopsy negative. Biopsy "positive" was defined as either or both culture and histology are positive and biopsy "negative" was defined as both culture and histology are negative. The results for each sample matrix are summarized below.

### Serum

#### Culture/ Histology

		+		-	
<i>H. pylori</i> Rapid Test Device	+	121	21		
	-	15	164		

Sensitivity = 121/136 = 89% (82% - 94%)\*

Specificity = 164/185 = 89% (83% - 93%)\*

Accuracy = 285/321 = 89% (85% - 92%)\*

### Plasma

#### Culture/ Histology

		+		-	
<i>H. pylori</i> Rapid Test Device	+	120	21		
	-	16	164		

Sensitivity = 120/136 = 88% (81% - 93%)\*

Specificity = 164/185 = 89% (83% - 93%)\*

Accuracy = 284/321 = 88% (84% - 92%)\*

### Fingerstick

#### Culture/ Histology

		+		-	
<i>H. pylori</i> Rapid Test Device	+	54	12		
	-	8	76		

Sensitivity = 54/62 = 87% (76% - 94%)\*

Specificity = 76/88 = 86% (77% - 93%)\*

Accuracy = 130/150 = 87% (80% - 92%)\*

### Venous Whole Blood

#### Culture/ Histology

		+		-	
<i>H. pylori</i> Rapid Test Device	+	119	22		
	-	17	163		

Sensitivity = 119/136 = 88% (81% - 93%)\*

Specificity = 163/185 = 88% (83% - 92%)\*

Accuracy = 282/321 = 88% (84% - 91%)\*

\*Denotes 95% Confidence Interval

Of the 163 archived clinical serum samples collected and tested in Site B, 71 were deemed biopsy positive and 92 were deemed biopsy negative. Biopsy "positive" was defined as either or both histology and rapid urease test are positive and biopsy "negative" was defined as both histology and rapid urease test are negative.

#### Histology/Rapid Urease Test

		+		-	
		52	16	19	76
<b>H. pylori Rapid Test Device</b>	+				
	-				

Sensitivity = 52/71 = 73% (61% - 83%)\*

Specificity = 76/92 = 83% (73% - 90%)\*

Accuracy = 128/163 = 78% (71% - 84%)\*

\*Denotes 95% Confidence Interval

Similarly, the matching archived plasma samples were also tested yielding a sensitivity of 65% (52-76)\*, a specificity of 89% (81-95)\* and an accuracy of 78% (71-84)\*. Using Fisher's exact test, a statistical comparison was made between the results obtained with the archived serum and plasma samples. The resultant P value is 1.0, indicating that there is no significant difference between the results obtained from the two sample matrices tested. The discrepant samples were checked with a commercially available EIA to confirm the presence of *H. pylori* specific IgG antibody in the samples. Of the 35 discrepant samples, 3 were equivocal, 14 out of 16 positive samples were shown to have *H. pylori* specific IgG antibody, and 10 out of the 19 negative samples did not contain the *H. pylori* specific IgG antibody. In addition, the above archived clinical samples were tested with two commercially available rapid diagnostic test kits, sample volume permitting. One hundred sixty-two (162) plasma specimens were used to compare the *H. pylori* Rapid Test Device to Comparator A; while 163 serum specimens were used to compare the product to Comparator B. The correlation between the *H. pylori* Rapid Test Device and the comparator rapid diagnostic test kits are summarized below.

#### Comparator A

		+		-	
		54	2	15	91
<b>H. pylori Rapid Test Device</b>	+				
	-				

Positive Agreement = 54/69 = 78% (67% - 87%)\*

Negative Agreement = 91/93 = 98% (92% - 100%)\*

Overall Agreement = 145/162 = 90% (84% - 94%)\*

#### Comparator B

		+		-	
		67	1	1	94
<b>H. pylori Rapid Test Device</b>	+				
	-				

Positive Agreement = 67/68 = 98% (92% - 100%)\*

Negative Agreement = 94/95 = 99% (94% - 100%)\*

Overall Agreement = 161/163 = 99% (96% - 100%)\*

\*Denotes 95% Confidence Interval

#### POL Studies

Three physicians' offices were used to conduct an evaluation of the *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma). Personnel with various educational backgrounds performed the testing. Each physician's office tested a randomly coded panel of samples consisting of negative (20), low positive (20) and medium positive (20) for three days. The results obtained had a >99% correlation with the expected results.

#### Cross-Reactivity

Sera containing known amounts of IgG antibodies to *H. pylori* have been tested with *C. jejuni*, *C. fetus*, *C. coli*, *P. aeruginosa* and *E. coli*. No cross-reactivity was observed, indicating that the *H. pylori* Rapid Test Device (Whole Blood/ Serum/ Plasma) has a high degree of specificity for human serum IgG antibodies to *H. pylori*.

#### Interference Studies

No interference with the *H. pylori* Rapid Test Device (Whole Blood/Serum/ Plasma) results was observed in samples containing high levels of hemoglobin (up to 1000 mg/dL), bilirubin (up to 1000 mg/dL) and human serum albumin (up to 2000 mg/mL). The test results were also unaffected when the hematocrit was altered ranging from 20% to 67%.

#### Reproducibility Studies

Three lots were used to perform reproducibility studies of the *H. pylori* Rapid Test Device (Whole Blood/ Serum/Plasma). Three sample matrices (serum, plasma and whole blood) were tested with replicates of ten tests each using four levels for each sample matrix (negative, low positive, medium positive and high positive). The results demonstrated that the *H. pylori* Rapid Test Device has relatively high levels of precision when tested within run, between runs and between days.

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#### CLIA Category

Whole Blood  
Serum/Plasma

Waived  
Moderately Complex

# H. pylori Rapid Test Device (Whole Blood ONLY) Package Insert

A rapid test for the qualitative detection of IgG antibodies to *Helicobacter pylori* (*H. pylori*) in whole blood.

For professional *in vitro* diagnostic use only.

## INTENDED USE

The *H. pylori* Rapid Test Device (Whole Blood) is a rapid chromatographic immunoassay for the qualitative detection of IgG antibodies to *Helicobacter pylori* in whole blood to aid in the diagnosis of *H. pylori* infection in adults 18 years of age and older.

## SUMMARY

*H. pylori* is a small, spiral-shaped bacterium that lives in the surface of the stomach and duodenum. It is implicated in the etiology of a variety of gastrointestinal diseases, including duodenal and gastric ulcer, non-ulcer dyspepsia and active and chronic gastritis.<sup>1,2</sup>

Both invasive and non-invasive methods are used to diagnose *H. pylori* infection in patients with symptoms of gastrointestinal disease. Sample-dependent and costly invasive diagnostic methods include gastric or duodenal biopsy followed by urease testing (presumptive), culture, and/or histologic staining.<sup>3</sup> Non-invasive techniques include the urea breath test, which requires expensive laboratory equipment and moderate radiation exposure, and serological methods.<sup>4,5</sup>

Individuals infected with *H. pylori* develop serum IgG antibodies which correlate strongly with histologically confirmed *H. pylori* infection.<sup>6,7,8</sup> The *H. pylori* Rapid Test Device (Whole Blood) is a simple test that utilizes a combination of *H. pylori* antigen coated particles and anti-human IgG to qualitatively and selectively detect *H. pylori* IgG antibodies in whole blood in just minutes.

## PRINCIPLE

The *H. pylori* Rapid Test Device (Whole Blood) is a qualitative membrane strip based immunoassay for the detection of *H. pylori* IgG antibodies in whole blood. In this test procedure, anti-human IgG is immobilized in the test line region of the device. The sample reacts with *H. pylori* antigen coated particles that have been applied to the label pad. This mixture migrates chromatographically along the length of the test strip and interacts with the immobilized anti-human IgG. If the sample contains *H. pylori* IgG antibodies, a colored line will appear in the test line region indicating a positive result. If the sample does not contain *H. pylori* IgG antibodies, a colored line will not appear in this region indicating a negative result. To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

## REAGENTS

The test device contains *H. pylori* antigen-coated particles and anti-human IgG coated membrane.

## PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after expiration date.

- Do not eat, drink or smoke in the area where the specimen samples and kits are handled.
- The positive and negative controls contain human plasma. Handle controls and all specimen samples as if they contain infectious agents. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimen samples.
- The positive and negative controls contain sodium azide as a preservative.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimen samples are assayed.
- Humidity and temperature can adversely affect results.
- The dispensing bulb used with the capillary tubes to add fingerstick whole blood to the device may contain trace amounts of latex which may cause an allergic reaction in some individuals.

## STORAGE AND STABILITY

The kit can be stored at room temperature or refrigerated (2-30°C). The test device is stable through the expiration date printed on the sealed pouch. The test device must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

## SAMPLE COLLECTION AND PREPARATION

- The *H. pylori* Rapid Test Device (Whole Blood) can be performed using whole blood from venipuncture or fingerstick.
- To collect Venipuncture Whole Blood samples: Collect anti-coagulated blood sample (sodium or lithium heparin, potassium or sodium EDTA, sodium oxalate, sodium citrate) following standard laboratory procedures.
- To collect Fingerstick Whole Blood samples:
  - Wash the patient's hand with soap and warm water or clean with an alcohol swab. Allow to dry.
  - Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
  - Puncture the skin with a sterile lancet. Wipe away the first sign of blood.
  - Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
  - Touch the end of the capillary tube to the blood until filled to the red line; avoid air bubbles.
  - Place the bulb onto the top end of the capillary tube.
  - Squeeze the bulb to dispense the whole blood.
- **Testing should ideally be performed immediately after the samples have been collected.** Do not leave the samples at room temperature for prolonged periods. Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 2 days of collection. Whole blood collected by fingerstick should be tested immediately. Do not freeze whole blood samples.
- If samples are to be shipped, they should be packed in compliance with federal regulations covering the transportation of etiologic agents.

## MATERIALS

### Materials Provided

- Test devices
- Disposable sample droppers
- Disposable heparinized capillary tubes and dispensing bulb
- Positive control (Diluted human plasma containing *H. pylori*-specific IgG, 0.09% sodium azide)
- Negative control (Diluted human plasma, 0.09% sodium azide)
- Sample Buffer
- Procedure card
- Package insert

### Materials Required But Not Provided

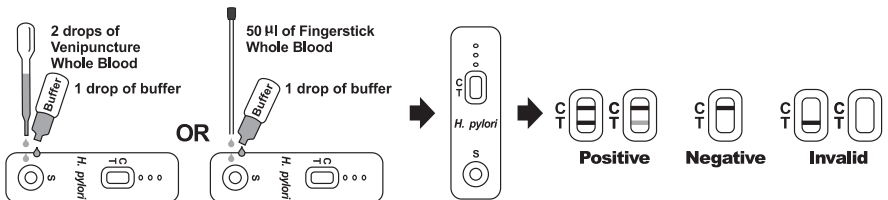
- Sample collection container (for venipuncture whole blood)
- Lancet (for fingerstick whole blood only)
- Centrifuge (for serum and plasma only)
- Timer

## DIRECTIONS FOR USE

Allow the test device, sample, buffer and controls to reach room temperature (15-30°C) before testing.

1. Remove the test device from the foil pouch and use it as soon as possible. For best results, perform the test immediately after opening the foil pouch.
2. Place the test device on a clean and level surface.
  - For **Whole Blood (Venipuncture)** samples: Hold the dropper upright and add **2 drops of whole blood** (about 50  $\mu$ l) to the sample well (S) of the test device. Then add **1 drop of Sample Buffer** to the sample well. Start the timer.
  - For **Whole Blood (Fingerstick)** samples: Add **one capillary tube of blood** (about 50  $\mu$ l) to the sample well (S) of the test device. Then add **1 drop of Sample Buffer** to the sample well. Start the timer.
3. Wait for the red line(s) to appear. The result should be read at 10 minutes. The background should be clear before the result is read.

Note: Low levels of *H. pylori* IgG specific antibodies might result in a weak line in the test region (T) after a long period of time. Do not read the result after 15 minutes.



## INTERPRETATION OF RESULTS

(Please refer to the illustration above)

**POSITIVE\*:** Two distinct red lines appear. One line should be in the control region (C) and another line should be in the test region (T). A positive result means that *H. pylori* IgG specific antibodies were detected in the sample.

\*NOTE: The shade of the red color in the test line region (T) will vary based on the amount of *H. pylori* IgG specific antibodies in the sample. Any shade of red in the test region (T) should be considered positive.

**NEGATIVE:** One red line appears in the control region (C). No apparent red or pink line appears in the test region (T). A negative result means that *H. pylori* IgG specific antibodies were not found in the sample or are below the detection limit of the test.

**INVALID:** No line appears in the control region (C). If this occurs, read the directions again and repeat the test with a new test strip. If the result is still invalid, stop using the test kit and contact your distributor.

## QUALITY CONTROL

### Internal Quality Control

Internal procedural controls are included in the test. A red line appearing in the control region (C) is an internal positive procedural control. It confirms sufficient sample volume and correct procedural technique. A clear background is an internal negative background control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.

### External Quality Control

It is recommended that a positive and negative external control be run every 20 tests, and as deemed necessary by your internal laboratory procedures. External positive and negative controls are supplied in the kit. If controls do not perform as expected, assay results are invalid.

### Procedure for External Quality Control Testing

Using the positive or negative external controls in place of a patient sample, add 2 drops of positive or negative control solution to the sample well (S) of a new test device, then add 1 drop of Sample Buffer. Start the timer. Continue with Step 3 in the Directions For Use section.

## LIMITATIONS

1. The *H. pylori* Rapid Test Device (Whole Blood) should be used only to evaluate patients with clinical signs and symptoms suggestive of gastrointestinal disease and is not intended for use with asymptomatic patients.
2. The *H. pylori* Rapid Test Device (Whole Blood) is for *in vitro* diagnostic use only. The test should be used for the detection of *H. pylori* IgG antibodies in whole blood samples only. Neither the quantitative value nor the rate of increase in *H. pylori* antibody concentration can be determined by this qualitative test.
3. The *H. pylori* Rapid Test Device (Whole Blood) will only indicate the presence of *H. pylori* IgG antibodies in the sample and should not be used as the sole criteria for the diagnosis of *H. pylori* infection.
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10. Literature references have suggested that high triglyceride levels interfere with IgG antibody. However, performance of this assay has not been evaluated with this substance. Therefore, test results of these devices are not known if high levels of this substance are encountered.
11. This assay has not been established for patients under 18 years of age.

## EXPECTED VALUES

*H. pylori* infection is present worldwide and has been shown to correlate with age, ethnic background, family size, and socioeconomic class.<sup>9</sup> In the United States, the incidence of infection may increase 1-2% annually.<sup>10</sup> Eighty to 100% of individuals with signs and symptoms of other gastrointestinal conditions such as duodenal ulcers are reported to be positive for *H. pylori* infection.<sup>11</sup>

## PERFORMANCE CHARACTERISTICS

### Clinical Sensitivity, Specificity and Accuracy

Using two independent sites, a total of 484 clinical samples were obtained from a population of symptomatic individuals who presented for endoscopic examination for the detection of *H. pylori* infection. Culture and/or histology of biopsy specimens served as the reference method for the study done in Site A while

histology and/or rapid urease test of the biopsy specimens served as the reference method for the study done in Site B. Whole blood (venous and fingerstick), serum and plasma were also collected for the detection of *H. pylori* specific IgG antibody by the *H. pylori* Rapid Test Device.

Of the 321 fresh clinical samples collected in Site A, 136 were considered biopsy positive and 185 clinical specimens were considered biopsy negative. Biopsy "positive" was defined as either or both culture and histology are positive and biopsy "negative" was defined as both culture and histology are negative. The results for each sample matrix are summarized below.

Serum		Culture/ Histology	
		+	-
<i>H. pylori</i> Rapid Test Device	+	121	21
	-	15	164

Sensitivity = 121/136 = 89% (82% - 94%)\*

Specificity = 164/185 = 89% (83% - 93%)\*

Accuracy = 285/321 = 89% (85% - 92%)\*

Plasma		Culture/ Histology	
		+	-
<i>H. pylori</i> Rapid Test Device	+	120	21
	-	16	164

Sensitivity = 120/136 = 88% (81% - 93%)\*

Specificity = 164/185 = 89% (83% - 93%)\*

Accuracy = 284/321 = 88% (84% - 92%)\*

Fingerstick		Culture/ Histology	
		+	-
<i>H. pylori</i> Rapid Test Device	+	54	12
	-	8	76

Sensitivity = 54/62 = 87% (76% - 94%)\*

Specificity = 76/88 = 86% (77% - 93%)\*

Accuracy = 130/150 = 87% (80% - 92%)\*

Venous Whole Blood		Culture/ Histology	
		+	-
<i>H. pylori</i> Rapid Test Device	+	119	22
	-	17	163

Sensitivity = 119/136 = 88% (81% - 93%)\*

Specificity = 163/185 = 88% (83% - 92%)\*

Accuracy = 282/321 = 88% (84% - 91%)\*

\*Denotes 95% Confidence Interval

Of the 163 archived clinical serum samples collected and tested in Site B, 71 were deemed biopsy positive and 92 were deemed biopsy negative. Biopsy "positive" was defined as either or both histology and rapid urease test are positive and biopsy "negative" was defined as both histology and rapid urease test are negative.

<i>H. pylori</i> Rapid Test Device		Histology/Rapid Urease Test	
		+	-
+	52	16	
-	19	76	

Sensitivity = 52/71 = 73% (61% - 83%)\*

Specificity = 76/92 = 83% (73% - 90%)\*

Accuracy = 128/163 = 78% (71% - 84%)\*

\*Denotes 95% Confidence Interval

Similarly, the matching archived plasma samples were also tested yielding a sensitivity of 65% (52-76)\*, a specificity of 89% (81-95)\* and an accuracy of 78% (71-84)\*. Using Fisher's exact test, a statistical comparison was made between the results obtained with the archived serum and plasma samples. The resultant P value is 1.0, indicating that there is no significant difference between the results obtained from the two sample matrices tested.

The discrepant samples were checked with a commercially available EIA to confirm the presence of *H. pylori* specific IgG antibody in the samples. Of the 35 discrepant samples, 3 were equivocal, 14 out of 16 positive samples were shown to have *H. pylori* specific IgG antibody, and 10 out of the 19 negative samples did not contain the *H. pylori* specific IgG antibody.

In addition, the above archived clinical samples were tested with two commercially available rapid diagnostic test kits, sample volume permitting. One hundred sixty-two (162) plasma specimens were used to compare the *H. pylori* Rapid Test Device to Comparator A; while 163 serum specimens were used to compare the product to Comparator B. The correlation between the *H. pylori* Rapid Test Device and the comparator rapid diagnostic test kits are summarized below.

		Comparator A	
		+	-
<i>H. pylori</i> Rapid Test Device	+	54	2
	-	15	91

Positive Agreement = 54/69 = 78% (67% – 87%)\*

Negative Agreement = 91/93 = 98% (92% – 100%)\*

Overall Agreement = 145/162 = 90% (84% – 94%)\*

		Comparator B	
		+	-
<i>H. pylori</i> Rapid Test Device	+	67	1
	-	1	94

Positive Agreement = 67/68 = 98% (92% – 100%)\*

Negative Agreement = 94/95 = 99% (94% – 100%)\*

Overall Agreement = 161/163 = 99% (96% – 100%)\*

\*Denotes 95% Confidence Interval

### **POL Studies**

Three physicians' offices were used to conduct an evaluation of the *H. pylori* Rapid Test Device (Whole Blood/Serum/Plasma). Personnel with various educational backgrounds performed the testing. Each physician's office tested a randomly coded panel of samples consisting of negative (20), low positive (20) and medium positive (20) for three days. The results obtained had a >99% correlation with the expected results.

### **Cross-Reactivity**

Sera containing known amounts of IgG antibodies to *H. pylori* have been tested with *C. jejuni*, *C. fetus*, *C. coli*, *P. aeruginosa* and *E. coli*. No cross-reactivity was observed, indicating that the *H. pylori* Rapid Test Device (Whole Blood/ Serum/ Plasma) has a high degree of specificity for human serum IgG antibodies to *H. pylori*.

### **Interference Studies**

No interference with the *H. pylori* Rapid Test Device (Whole Blood/Serum/ Plasma) results was observed in samples containing high levels of hemoglobin (up to 1000 mg/dL), bilirubin (up to 1000 mg/dL) and human serum albumin (up to 2000 mg/mL). The test results were also unaffected when the hematocrit was altered ranging from 20% to 67%.

### **Reproducibility Studies**

Three lots were used to perform reproducibility studies of the *H. pylori* Rapid Test Device (Whole Blood/ Serum/Plasma). Three sample matrices (serum, plasma and whole blood) were tested with replicates of ten tests each using four levels for each sample matrix (negative, low positive, medium positive and high positive). The results demonstrated that the *H. pylori* Rapid Test Device has relatively high levels of precision when tested within run, between runs and between days.

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### **CLIA Category**

Whole Blood

Waived