



# MAGLUMI® H.pylori IgM (CLIA)

### INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the qualitative determination of H.pylori IgM in human serum and plasma using the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer and Biolumi series Integrated System, and the assay is used for an aid in the diagnosis of H.pylori infection.

### SUMMARY

*Helicobacter pylori* (*H.pylori*) is a gram negative, curved, spiral shaped rod (0.5-1.0 µm in width by 3.0-4.0 µm in length). *H.pylori* colonization is found in the deep portions of the mucous gel layer that coats the gastric mucosa, and between the mucous gel layer and apical surface of the gastric mucosal epithelial cells<sup>1-3</sup>. In some patients infected by *H.pylori*, *H.pylori* may also be located in the regions of the junctions between adjacent mucosal epithelial cells. It produces three enzymes in large amounts: urease, superoxide dismutase and catalases. Urease splits urea to produce ammonia, which provides conditions needed for the multiplication and sustenance of the organism in the gastric environment<sup>3</sup>. The colonization may induce the host's local and systemic immune response and may cause clinical signs and symptoms including neutrophil infiltration and the production of specific antibodies<sup>4-5</sup>. *H.pylori* is now accepted as a cause of gastritis, and *H.pylori* infections have also been associated with duodenal ulcer, gastric ulcer and nonulcer dyspepsia<sup>6</sup>.

The presence of *H.pylori* has been detected by using both invasive and non-invasive methods. Invasive methods include culture, histology, and the rapid urease test done on biopsy samples<sup>7</sup>. Many serological tests, mainly immune-globulin G (IgG) based, have been validated against invasive methods. *H.pylori* infection provokes both local and systemic antibody responses. The systemic response typically comprises a transient rise in IgM, followed by a rise in specific IgA and IgG maintained throughout infection<sup>4</sup>. IgM titer rises early in *H.pylori* infection and that the duration of its elevated level is brief<sup>8</sup>. Measurement of IgM antibodies to *H.pylori* may help early detection of the infection. Early detection of *H.pylori* infection may be useful for early treatment of individuals with acute infection<sup>9</sup>.

### TEST PRINCIPLE

Indirect chemiluminescence immunoassay.

The sample, buffer are mixed thoroughly and incubated, then add buffer and magnetic microbeads coated with H.pylori antigen, incubating and performing a wash cycle after a precipitation in a magnetic field. ABEI labeled with anti-human IgM monoclonal antibody are then added, reacting to form immune-complexes and incubating. After precipitation in a magnetic field, the supernatant is decanted and then a wash cycle is performed. Subsequently, the Starter 1+2 are added to initiate a chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLUs), which is proportional to the concentration of H.pylori IgM present in the sample.

### REAGENTS

#### Kit Contents

| Component                               | Description                                                                                                       | 100 tests/kit | 50 tests/kit | 30 tests/kit |
|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------|---------------|--------------|--------------|
| Magnetic Microbeads                     | Magnetic microbeads coated with H.pylori antigen (~5.33 µg/mL) in PBS buffer, NaNa <sub>3</sub> (<0.1%).          | 2.5 mL        | 1.5 mL       | 1.0 mL       |
| Calibrator Low                          | A low concentration of H.pylori IgM in PBS buffer, NaNa <sub>3</sub> (<0.1%).                                     | 1.0 mL        | 1.0 mL       | 1.0 mL       |
| Calibrator High                         | A high concentration of H.pylori IgM in PBS buffer, NaNa <sub>3</sub> (<0.1%).                                    | 1.0 mL        | 1.0 mL       | 1.0 mL       |
| Buffer                                  | PBS buffer, NaNa <sub>3</sub> (<0.1%).                                                                            | 23.5 mL       | 12.5 mL      | 8.1 mL       |
| ABEI Label                              | ABEI labeled with anti-human IgM monoclonal antibody (~10.0 ng/mL) in Tris-HCl buffer, NaNa <sub>3</sub> (<0.1%). | 22.5 mL       | 12.0 mL      | 7.8 mL       |
| Negative Control                        | PBS buffer, NaNa <sub>3</sub> (<0.1%).                                                                            | 1.0 mL        | 1.0 mL       | 1.0 mL       |
| Positive Control                        | A high concentration of H.pylori IgM (4.00 U/mL) in PBS buffer, NaNa <sub>3</sub> (<0.1%).                        | 1.0 mL        | 1.0 mL       | 1.0 mL       |
| All reagents are provided ready-to-use. |                                                                                                                   |               |              |              |

#### Warnings and Precautions

- For *in vitro* diagnostic use.
- For professional use only.
- Exercise the normal precautions required for handling all laboratory reagents.
- Personal protective measures should be taken to prevent any part of the human body from contacting samples, reagents, and controls, and should comply with local operating requirements for the assay.
- A skillful technique and strict adherence to the package insert are necessary to obtain reliable results.
- Do not use kit beyond the expiration date indicated on the label.
- Do not interchange reagent components from different reagents or lots.
- Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).
- All waste associated with biological samples, biological reagents and disposable materials used for the assay should be considered potentially infectious and should be disposed of in accordance with local guidelines.
- This product contains sodium azide. Sodium azide may react with lead or copper plumbing to form highly explosive metal azides. Immediately after disposal, flush with a large volume of water to prevent azide build-up. For additional information, see Safety Data Sheets available for professional user on request.

Note: If any serious incident has occurred in relation to the device, please report to Shenzhen New Industries Biomedical Engineering Co., Ltd. (Snibe) or our authorized representative and the competent authority of the Member State in which you are established.

#### Reagent Handling

- To avoid contamination, wear clean gloves when operating with a reagent kit and sample. When handling reagent kit, replace the gloves that have been in contact with samples, since introduction of samples will result in unreliable results.
- Do not use kit in malfunction conditions; e.g., the kit leaking at the sealing film or elsewhere, obviously turbid or precipitation is found in reagents (except for Magnetic Microbeads) or control value is out of the specified range repeatedly. When kit in malfunction conditions, please contact Snibe or our authorized distributor.
- To avoid evaporation of the liquid in the opened reagent kits in refrigerator, it is recommended that the opened reagent kits to be sealed with reagent seals contained within the packaging. The reagent seals are single use, and if more seals are needed, please contact Snibe or our authorized distributor.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.
- Use always the same analyzer for an opened reagent integral.
- For magnetic microbeads mixing instructions, refer to the Preparation of the Reagent section of this package insert.
- For further information about the reagent handling during system operation, please refer to Analyzer Operating Instructions.

#### Storage and Stability

- Do not freeze the integral reagents.
- Store the reagent kit upright to ensure complete availability of the magnetic microbeads.
- Protect from direct sunlight.

| Stability of the Reagents |                                  |
|---------------------------|----------------------------------|
| Unopened at 2-8°C         | until the stated expiration date |
| Opened at 2-8°C           | 6 weeks                          |
| On-board                  | 4 weeks                          |



130251027M: 100 tests/kit  
130651027M: 50 tests/kit  
130751027M: 30 tests/kit

| Stability of Controls    |                                  |
|--------------------------|----------------------------------|
| Unopened at 2-8°C        | until the stated expiration date |
| Opened at 10-30°C        | 6 hours                          |
| Opened at 2-8°C          | 6 weeks                          |
| Frozen at -20°C          | 3 months                         |
| Frozen and thawed cycles | no more than 3 times             |

### SPECIMEN COLLECTION AND PREPARATION

#### Specimen Types

Only the specimens listed below were tested and found acceptable.

| Specimen Types | Collection Tubes                            |
|----------------|---------------------------------------------|
| Serum          | Tubes without additive/accessory.           |
| Plasma         | K2-EDTA, Na2-EDTA, Li-heparin or Na-heparin |

- The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. Follow tube manufacturers' instructions carefully when using collection tubes.

#### Specimen Conditions

- Do not use heat-inactivated samples or grossly hemolyzed/hyperlipidaemia specimens and specimens with obvious microbial contamination.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some serum specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the serum specimen is centrifuged before a complete clotting, the presence of fibrin may cause erroneous results.
- Samples must be free of fibrin and other particulate matter.
- To prevent cross contamination, use of disposable pipettes or pipette tips are recommended.

#### Preparation for Analysis

- Inspect all specimens for foam. Remove foam with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.
- Frozen specimens must be completely thawed before mixing. Mix thawed specimens thoroughly by low speed vortexing or by gently inverting. Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous. If specimens are not mixed thoroughly, inconsistent results may be obtained.
- Specimens should be free of fibrin, red blood cells, or other particulate matter. Such specimens may give reliable results and must be centrifuged prior to testing. Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- The sample volume required for a single determination of this assay is 10 µL.

#### Specimen Storage

Specimens removed from the separator, red blood cells or clot may be stored up to 8 hours at 10-30°C or 72 hours at 2-8°C, or 3 months frozen at -20°C. Frozen specimens subjected to up to 2 freeze/thaw cycles have been evaluated.

#### Specimen Shipping

- Package and label specimens in compliance with applicable local regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

### PROCEDURE

#### Materials Provided

H.pylori IgM (CLIA) assay, control barcode labels.

#### Materials Required (But Not Provided)

- General laboratory equipment.
- Fully-auto chemiluminescence immunoassay analyzer Maglumi 600, Maglumi 800, Maglumi 1000, Maglumi 2000, Maglumi 2000 Plus, Maglumi 4000, Maglumi 4000 Plus, MAGLUMI X8, MAGLUMI X3, MAGLUMI X6, or Integrated System Biolumi 8000, Biolumi CX8.
- Additional accessories of test required for the above analyzers include Reaction Module, Starter 1+2, Wash Concentrate, Light Check, Tip, and Reaction Cup. Specific accessories and accessories' specification for each model refer to corresponding Analyzer Operating Instructions.
- Please use accessories specified by Snibe to ensure the reliability of the test results.

#### Assay Procedure

##### Preparation of the Reagent

- Take the reagent kit out of the box and visually inspect the integral vials for leaking at the sealing film or elsewhere. If there is no leakage, please tear off the sealing film carefully.
- Open the reagent area door; hold the reagent handle to get the RFID label close to the RFID reader (for about 2s); the buzzer will beep; one beep sound indicates successful sensing.
- Keeping the reagent straight insert to the bottom along the blank reagent track.
- Observe whether the reagent information is displayed successfully in the software interface, otherwise repeat the above two steps.
- Resuspension of the magnetic microbeads takes place automatically when the kit is loaded successfully, ensuring the magnetic microbeads are totally resuspended homogenous prior to use.

##### Assay Calibration

- Select the assay to be calibrated and execute calibration operation in reagent area interface. For specific information on ordering calibrations, refer to the calibration section of Analyzer Operating Instructions.
- Execute recalibration according to the calibration interval required in this package insert.

##### Quality Control

- When new lot used, check or edit the quality control information.
- Scan the control barcode, choose corresponding quality control information and execute testing. For specific information on ordering quality controls, refer to the quality control section of the Analyzer Operating Instructions.

##### Sample Testing

After successfully loading the sample, select the sample in interface and edit the assay for the sample to be tested and execute testing. For specific information on ordering patient specimens, refer to the sample ordering section of the Analyzer Operating Instructions.

To ensure proper test performance, strictly adhere to Analyzer Operating Instructions.

#### Calibration

Traceability: This method has been standardized against the Snibe internal reference standard.

Test of assay specific calibrators allows the detected relative light unit (RLU) values to adjust the master curve.

Recalibration is recommended as follows:

- Whenever a new lot of Reagent or Starter 1+2 is used.
- Every 7 days.
- The analyzer has been serviced.
- Control values lie outside the specified range.

#### Quality Control

Controls are recommended for the determination of quality control requirements for this assay and should be run in singlicate to monitor the assay performance. Refer to published guidelines for general quality control recommendations, for example Clinical and Laboratory Standards Institute (CLSI) Guideline C24 or other published guidelines<sup>8</sup>.

Quality control is recommended once per day of use, or in accordance with local regulations or accreditation requirements and your laboratory's quality control procedures, quality control could be performed by running the H.pylori IgM assay:

- Whenever the kit is calibrated.
- Whenever a new lot of Starter 1+2 or Wash Concentrate is used.

Controls are only applicable with MAGLUMI and Biolumi systems and only used matching with the same top eight LOT numbers of corresponding reagents. For each target value and range refer to the label.

The performance of other controls should be evaluated for compatibility with this assay before they are used. Appropriate value ranges should be established for all quality control materials used.

Control values must lie within the specified range, whenever one of the controls lies outside the specified range, calibration should be repeated and controls retested. If control values lie repeatedly outside the predefined ranges after successful calibration, patient results must not be reported and take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the package insert.
- If necessary, contact Snibe or our authorized distributors for assistance.

If the controls in kit are not enough for use, please order H.pylori IgM (CLIA) Controls (REF: 1602011015MT) from Snibe or our authorized distributors for more.

RESULTS

Calculation

The analyzer automatically calculates the H.pylori IgM concentration in each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are expressed in U/mL. For further information please refer to the Analyzer Operating Instructions.

Interpretation of Results

The expected range for the H.pylori IgM assay was obtained by testing 128 H.pylori IgM positive patients and 344 H.pylori IgM negative people in China, gave the following expected value by ROC curve:

- Non-reactive: A result less than 1.00 U/mL (<1.00 U/mL) is considered to be negative.
- Reactive: A result greater than or equal to 1.00 U/mL (≥1.00 U/mL) is considered to be positive.

Results may differ between laboratories due to variations in population and test method. It is recommended that each laboratory establish its own reference interval.

LIMITATIONS

- Results should be used in conjunction with patient's medical history, clinical examination and other findings.
- If the H.pylori IgM results are inconsistent with clinical evidence, additional testing is needed to confirm the result.
- The assay is mainly used to aid in the diagnosis of individuals with suspected or confirmed H.pylori infection.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies<sup>9,10</sup>. Additional information may be required for diagnosis.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or animal serum products can be prone to this interference and anomalous values may be observed<sup>11</sup>.
- Bacterial contamination or heat inactivation of the specimens may affect the test results.

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

Precision

Precision was determined using the assay, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): duplicates at two independent runs per day for 5 days at three different sites using three lots of reagent kits (n = 180). The following results were obtained:

| Sample           | Mean (U/mL)<br>(n=180) | Within-Run |      | Between-Run |      | Reproducibility |      |
|------------------|------------------------|------------|------|-------------|------|-----------------|------|
|                  |                        | SD (U/mL)  | %CV  | SD (U/mL)   | %CV  | SD (U/mL)       | %CV  |
| Serum Pool 1     | 0.669                  | NA         | NA   | NA          | NA   | NA              | NA   |
| Serum Pool 2     | 1.147                  | 0.039      | 3.40 | 0.020       | 1.74 | 0.052           | 4.53 |
| Serum Pool 3     | 3.591                  | 0.105      | 2.92 | 0.077       | 2.14 | 0.175           | 4.87 |
| Plasma Pool 1    | 0.662                  | NA         | NA   | NA          | NA   | NA              | NA   |
| Plasma Pool 2    | 1.109                  | 0.038      | 3.43 | 0.025       | 2.25 | 0.053           | 4.78 |
| Plasma Pool 3    | 3.550                  | 0.111      | 3.13 | 0.060       | 1.69 | 0.159           | 4.48 |
| Negative Control | 0.197                  | NA         | NA   | NA          | NA   | NA              | NA   |
| Positive Control | 3.998                  | 0.136      | 3.40 | 0.064       | 1.60 | 0.206           | 5.15 |

Analytical Specificity

Interference

Interference was determined using the assay, three samples containing different concentrations of analyte were spiked with potential endogenous and exogenous interferences in a protocol (EP7-A2) of the CLSI. The measurement deviation of the interference substance is within ±10%. The following results were obtained:

| Interference      | No interference up to | Interference              | No interference up to |
|-------------------|-----------------------|---------------------------|-----------------------|
| Bilirubin         | 20 mg/dL              | Tetracycline              | 120 mg/dL             |
| Hemoglobin        | 800 mg/dL             | Furazolidone              | 12 mg/dL              |
| Intralipid        | 1000 mg/dL            | Metronidazole             | 96 mg/dL              |
| HAMA              | 30 ng/mL              | Esomeprazole              | 3 mg/dL               |
| Rheumatoid factor | 1500 IU/mL            | Omeprazole                | 3 mg/dL               |
| ANA               | 398 AU/mL             | Rabeprazole               | 3 mg/dL               |
| Total cholesterol | 500 mg/dL             | Lansoprazole              | 4 mg/dL               |
| Total IgG         | 4086 mg/dL            | Pantoprazole              | 5 mg/dL               |
| Total IgM         | 364 mg/dL             | Ilaprazole                | 1 mg/dL               |
| Levofloxacin      | 30 mg/dL              | Potassium bismuth citrate | 27 mg/dL              |
| Clarithromycin    | 60 mg/dL              | Ibuprofen                 | 144 mg/dL             |
| Amoxicillin       | 120 mg/dL             |                           |                       |

Cross-Reactivity

The assay is highly specific for H. pylori IgM antibodies, with no observed crossreactivity to Campylobacter jejuni IgM, Bacillus cereus IgM, Escherichia coli IgM, Enterobacter cloacae IgM, Proteus vulgaris IgM, Candida albicans IgM, Enterococcus faecalis IgM, Klebsiella pneumoniae IgM, Helicobacter heilmannii IgM, Staphylococcus aureus IgM, Streptococcus pneumoniae IgM, Fusobacterium nucleatum IgM, Clostridium IgM, Pseudomonas aeruginosa IgM, H.pylori IgG, HAV IgM, HBV IgM, HCV IgM, CMV IgM, Toxo IgM, Rubella IgM, HIV IgM, Treponema pallidum IgM and HSV IgM.

High-Dose Hook

No high-dose hook effect was seen for H.pylori IgM concentrations up to 1000 U/mL.

Clinical Sensitivity

The clinical sensitivity of the H.pylori IgM assay was determined in China by testing 193 samples collected from expected positive population with commercial assay confirmation of H.pylori IgM positive result.

| N of samples | Reactive | Sensitivity | 95% CI         |
|--------------|----------|-------------|----------------|
| 193          | 193      | 100.00%     | 99.85%-100.00% |

Clinical Specificity

The clinical specificity of the H.pylori IgM assay was determined in China by testing 163 samples collected from expected negative population with commercial assay confirmation of H.pylori IgM negative result.

| N of samples | Non-reactive | Specificity | 95% CI         |
|--------------|--------------|-------------|----------------|
| 164          | 163          | 99.39%      | 98.20%-100.00% |

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SYMBOLS EXPLANATIONS



Consult instructions for use



Temperature limit  
(Store at 2-8°C)



Contains sufficient for<n> tests



This way up



*In vitro* diagnostic medical device



Catalogue number



CE marking with notified body ID number



Manufacturer



Use-by date



Keep away from sunlight



Authorized representative in the European Community



Kit component



Batch code

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