Snibe Diagnostic

CE REF 130219016M: 100 tests

MAGLUMI™ 2019-nCoV IgM (CLIA)

INTENDED USE
The kit is an *In Vitro* chemiluminescence immunoassay for the qualitative determination of IgM antibodies to novel coronavirus (2019-nCoV IgM) in human serum or plasma using the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.

SUMMARY AND EXPLANATION OF THE TEST
The novel coronavirus (2019-nCoV) causes an epidemic of acute respiratory syndrome in humans in Wuhan[1], belonging to the genus Betacoronavirus. It has an envelope, particles are round or oval, often polymorphic, and the diameter is 60 ~ 140nm. Its genetic characteristics are significantly different from SARSr-CoV and MERSr-CoV. Current research shows that it has more than 85% homology with bat SARS-like coronavirus (bat-SL-CoVZC45)[2].
2019-nCoV is mainly transmitted through respiratory droplets and can also be transmitted through contact. The sources of infection seen so far are mainly patients with pneumonia infected by the novel coronavirus[2].
Research has shown that detection of IgM and IgG antiviral antibodies in the serum samples from a patient[3]. After human infection in 2019-nCoV, its antigen stimulates the immune system to produce an immune response, and corresponding antibodies appear in the blood. Among them, 2019-nCoV IgM appears earlier, which are mostly positive after 3-5 days of onset[2],and then 2019-nCoV IgM titers decrease, the 2019-nCoV IgG potency rose rapidly. The titer of IgG antibody during the recovery phase may increase 4 times or more compared to the acute phase[2].
This kit is mainly used for the assisted diagnosis of the novel coronavirus (2019-nCoV) infection.
2019-nCoV, named by the World Health Organization on January 7, 2020, is announced the official name: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV) on February 11, 2020. On the same day, the Director-General of the World Health Organization (WHO) Tedros Adhanom Ghebreyesus announced that pneumonia infected with SARS-CoV-2 will be officially named "COVID-19".

PRINCIPLE OF THE TEST
The MAGLUMI 2019-nCoV IgM (CLIA) assay is a capture chemiluminescence immunoassay.
The sample, buffer, magnetic microbeads coated with anti-human IgM monoclonal antibody are mixed thoroughly and incubated, forming immune-complexes. After precipitation in a magnetic field, decant the supernatant, and perform a wash cycle. Then add 2019-nCoV recombinant antigen labeled with ABEI and incubate to form complexes. After precipitation in a magnetic field, decant the supernatant, and then perform another wash cycle. 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 2019-nCoV IgM present in the sample.

KIT COMPONENTS
Material Provided

Component	Contents	100 tests (REF: 130219016M)
Magnetic Microbeads	Magnetic microbeads coated with anti-human IgM monoclonal antibody, PBS buffer and BSA, NaN_3 (<0.1%).	2.5 mL
Calibrator Low	2019-nCoV IgM, PBS buffer and BSA, NaN_3 (<0.1%).	1.0 mL
Calibrator High	2019-nCoV IgM, PBS buffer, and BSA, NaN_3 (<0.1%).	1.0 mL
Buffer	PBS buffer, Goat anti-Human IgG, Goat anti-Human IgA Mouse IgG, Goat IgG and BSA, NaN_3 (<0.1%).	23.5 mL
ABEI Label	2019-nCoV recombinant antigen labeled with ABEI, Tris-HCl buffer, Mouse IgG, Goat IgG, and BSA, NaN_3 (<0.1%).	23.5 mL
Diluent	PBS buffer, Goat anti-Human IgG, Goat anti-Human IgA Mouse IgG, Goat IgG and BSA, NaN_3 (<0.1%).	23.5 mL
Negative Control	PBS buffer, containing BSA, NaN_3 (<0.1%).	1.0 mL
Positive Control	2019-nCoV IgM, PBS buffer, containing BSA and NaN_3 (<0.1%).	1.0 mL
All reagents are provided ready-to-use.		

Accessories Required But Not Provided
MAGLUMI Series:

Reaction Module	REF: 630003
Starter 1+2	REF: 130299004M;130299012M; 130299027M
Wash Concentrate	REF: 130299005M
Light Check	REF: 130299006M
Reaction Cup	REF: 130105000101
Maglumi 600	REF: 23020018
Maglumi 800	REF: 23020003
Maglumi 1000	REF: 23020009
Maglumi 2000	REF: 23020006
Maglumi 2000 Plus	REF: 23020007
Maglumi 4000	REF: 23020014
Maglumi 4000 Plus	REF: 23020037
MAGLUMI X8	REF: 010101008801
Biolumi 8000	REF: 23010001

Please order accessories from Shenzhen New Industries Biomedical Engineering Co., Ltd. (SNIBE) or our authorized representative.

CALIBRATION
Traceability: This method has been standardized against the SNIBE internal reference substance.
Test of assay specific calibrators allows the RLU values to adjust the assigned master curve. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve (10 calibrations) provided via the reagent Radio Frequency Identification (RFID) CHIP.
Recalibration is recommended if any of the following conditions occurs:
- After each exchange of lots (Reagent or Starter 1+2).
- Every week and/or each time a new reagent kit is used.
- After instrument service is required.
- If controls lie outside the expected range.

QUALITY CONTROL
Follow government regulations or accreditation requirements for quality control frequency.
Internal quality control is only applicable with MAGLUMI system. For instructions for use and target value refer to ***2019-nCoV IgM Quality Control Information***. User needs to judge results with their own standards and knowledge.

For details about entering quality control values, refer to the operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.
To monitor system performance, quality control materials (negative control and positive control) are required. Treat all quality control samples with the same level of care as patient samples. A satisfactory level of performance is achieved when analyte values obtained are within the acceptable Control Range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme. If the quality control results do not fall within the Expected Values or within the laboratory's established values, measurement of the quality control should be repeated. If the quality control results still do not fall within the range, do not report results 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 instruction for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

SPECIMEN COLLECTION AND PREPARATION

- Human serum or plasma may be used with the 2019-nCoV IgM (CLIA) assay. Serum including samples collected using standard sampling tubes, tubes containing separating gel or procoagulant inert separation tubes. For plasma samples, the anticoagulants including K_2-EDTA, K_3-EDTA, Na_2 -EDTA, have been tested and may be used with this assay.
- Please pay attention to the risk of infection during sample collection and preparation. According to the "New Coronary Virus Pneumonia Diagnosis and Treatment Guideline" issued in China, it should be performed heat inactivation of the samples by 56℃ for 30 minutes before testing, or according to the requirements by the local government.
- Do not use grossly hemolyzed specimens.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.
- Specimens removed from the separator gel, cells or clot may be stored 3 days at 2-8°C[4].
- If longer storage is required, frozen the specimens at -20°C or colder[4]. Avoid repeated freezing and thawing. Frozen specimens must be mixed thoroughly after thawing by low speed vortexing or by gently inverting.
- For optimal results, specimens should be free of fibrin, red blood cells, or other particulate matter. Such specimens may give inconsistent results and must be transferred to a centrifuge tube and centrifuged at ≥ 10,000RCF (Relative Centrifugal Force) for 10 minutes. 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.
- Before shipping specimens, it is recommended that specimens be removed from the separator, red blood cells or clot. When shipped, specimens should be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Specimens should be shipped frozen.
- The sample volume required for a single determination is 10 µL.

WARNING AND PRECAUTIONS FOR USERS

- IVD For *In Vitro* Diagnostic Use.
- Follow the package insert carefully. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the 29 CFR 1910.1030 Occupational exposure to bloodborne pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- All samples, biological reagents and materials used in the assay should be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.
- This product contains Sodium Azide. Dispose of contents and container must be in accordance with all local, regional and national regulations.
- Refer to safety data sheets, which are available on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not interchange reagent components from different reagents or lots.
- Prior to loading the Reagent Kit on the system for the first time, the Reagent Kit requires mixing to re-suspend magnetic microbeads that have settled during shipment.
- For magnetic microbeads mixing instructions, refer to the Preparation of the Reagent section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and sample.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- 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 Shenzhen New Industries Biomedical Engineering Co., Ltd. (SNIBE) or our authorized representative.
- For detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

STORAGE AND STABILITY

- Store at 2-8°C. Do not freeze.
- Keep upright for storage to facilitate later proper resuspension of magnetic microbeads.
- Keep away from sunlight.
- The stability study is still on-going, the following data is obtained by referring to similar products:

Stability of the reagent	
unopened at 2-8°C	until the stated expiration date
opened at 2-8°C	6 weeks
onboard	4 weeks

- To ensure the best kit performance, it is recommended to place opened kits in the refrigerator after the end of the intraday test work.

TEST PROCEDURE

Preparation of the Reagent

- Take the reagent kit out of the box and observe the sealing film and other parts of the reagent kit to see if there is any leakage. In case of leakage, please contact your local agent immediately. And then tear off the kit 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 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

- Click **<Calibration>** or **<Batch Calibration>** button to execute calibration operation; For specific information on ordering calibrations, refer to the Calibration Section of the Operating Instructions.
- Execute recalibration according to the calibration interval required in this manual.

Quality Control

- In order to avoid manually error in entry of QC information, the provided barcode labels of quality control in the kit can be used attached on the test tubes.
- Strictly follow the quality control procedures when using the quality controls.
- If users do not use the provided barcode labels for positive and negative controls contained within the packaging, then quality controls should be

ordered manually.
- For specific information on ordering quality controls, refer to the Quality Control Section of the Operating Instructions.

Sample Testing
- Order the samples in the Sample Area of the software and click the **<Start>** button to execute testing. For specific information on ordering patient specimens, refer to the Sample Ordering Section of the Operating Instructions.

To ensure proper test performance, strictly adhere to the operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.

DILUTION

The high concentration samples can be diluted automatically by analyzers or manually. The recommended dilution is 1:19 with diluent or 2019-nCoV IgM negative human serum.

After manual dilution, multiply the result by the dilution factor. After dilution by the analyzer, the analyzer software automatically takes the dilution into account when calculating the sample concentration.

The automatic sample dilution is available after dilution settings are done in the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer user software. Please refer to the operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.

LIMITATIONS

- This test is suitable only for investigating single samples, not for pooled samples.
- Bacterial contamination or repeated freeze-thaw cycles may affect the test results.
- Assay results should be utilized in conjunction with other clinical and laboratory methods to assist the clinician in making individual patient diagnostic decisions.
- Assay results should not be used as the sole basis for the diagnosis and exclusion of new coronavirus pneumonia, but only as a supplement to existing viral nucleic acid detection reagents.
- It is recommended to be used in conjunction with 2019-nCoV IgG testing to improve clinical sensitivity.
- If the 2019-nCoV IgM results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- HAMA antibodies in test samples may cause interference in immunoassays.

RESULTS

Calculation of Results

The analyzer automatically calculates the 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 AU/mL. For further information please refer to the operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.

Interpretation of Results

Results of reference range study in China using the 2019-nCoV IgM assay was as follows:
- Non-reactive: A result less than 1.00 AU/mL (<1.00 AU/mL) is considered to be non-reactive.
- Reactive: A result greater than or equal to 1.00 AU/mL (≥1.00 AU/mL) is considered to be reactive.
- Results may differ between laboratories due to variations in population. It is recommended that each laboratory establish its own expected ranges.

PERFORMANCE CHARACTERISTICS

Precision

Precision for 2019-nCoV IgM assay was determined as described in the CLSI EP5-A3. 2 controls and 3 samples containing different concentration of analyte were assayed in duplicate at three sites on five days, with 3 runs per day, one lot of reagent for each run and 2 replicates per run. The result is summarized in the following table:

Sample	Mean Value (AU/mL)	N	Repeatability		Between-Lot		Between-Day		Between-Site		Reproducibility	
			SD (AU/mL)	%CV	SD (AU/mL)	%CV	SD (AU/mL)	%CV	SD (AU/mL)	%CV	SD (AU/mL)	%CV
NQC	0.293	90	0.020	NA	0.006	NA	0.007	NA	0.007	NA	0.023	NA
PQC	3.920	90	0.167	4.26	0.046	1.17	0.062	1.58	0.284	7.24	0.339	8.65
S1	0.492	90	0.033	NA	0.016	NA	0.009	NA	0.012	NA	0.040	NA
S2	1.797	90	0.037	2.06	0.018	1.00	0.053	2.95	0.088	4.90	0.111	6.18
S3	3.411	90	0.076	2.23	0.000	0.00	0.049	1.44	0.226	6.63	0.244	7.15

Interference

Two serum samples (one negative sample, one positive sample) were spiked with potential endogenous interference and exogenous interference. The results of the interferences are listed in the following table:

Interference	No interference up to
Bilirubin	40 mg/dL
Triglycerides	1000 mg/dL
Hemoglobin	2000 mg/dL
Rheumatoid Factor	1500 IU/mL
Anti-Mitochondrial	1:64(titer)
HAMA	30 ng/mL
Total IgG	1600 mg/dL
Total IgM	280 mg/dL
Interferon α	1500 U/mL
Ribavirin	90 mg/dL
Oseltamivir	1.0 mg/dL
Levofloxacin	1.776 mg/dL
Azithromycin	1.201 mg/dL
Ceftriaxone sodium	81.03 mg/dL
Meropenem	80.15 mg/dL
Tobramycin	2.4 mg/dL
Diphenhydramine Hydrochloride	4.5 mg/dL
Oxymetazoline	2.5 mg/dL
Sodium chloride	45 mg/dL
Beclomethasone	2.5 mg/dL
Dexamethasone	18 mg/dL
Triamcinolone acetonide	5.5 mg/dL
Budesonide	3.2 mg/dL
Mometasone	2.5 mg/dL
Fluticasone propionate	2.5 mg/dL

Cross-Reactivity

The cross-reactivity study for the with the 2019-nCoV IgM (CLIA) assay was designed to evaluate potential cross reactants. The results are listed in the following table.

Condition	Number of expected negative samples	2019-nCoV IgM (CLIA) assay positive results
Influenza A virus antibodies	17	0
Influenza B virus antibodies	19	0
Parainluenza virus antibodies	23	0
Respiratory syncytial virus antibodies	7	0
Adenovirus antibodies	9	0
EBV NA IgG	10	0
EBV VCA IgG	4	0
EBV VCA IgM	6	0
Mealles virus	2	0
CMV IgG	6	0
CMV IgM	2	0
Varicella zoster virus antibodies	2	0
M.Pneumonia IgG	3	0
M.Pneumonia IgM	4	0
Chlamydia pneumoniae IgG	3	0
Chlamydia pneumoniae IgM	3	0
Monilia albican	1	0
ANA	6	0
2019-nCoV IgG	6	0
Total	133	0

Clinical Sensitivity

The clinical sensitivity was determined by confirmed novel coronavirus infected specimens. The clinical sensitivity for 2019-nCoV IgM assay was calculated to be 78.65%. When used in combination of 2019-nCoV IgM assay and 2019-nCoV IgG assay, the clinical diagnostic sensitivity is 89.89%.

Specimen Category	2019-nCoV IgM (CLIA)			2019-nCoV IgM (CLIA)+2019-nCoV IgG (CLIA)		
	N	Positive	%Sensitivity	N	Positive	%Sensitivity
Clinical confirmed positive samples	89	70	78.65%	89	80	89.89%

Clinical Specificity

The clinical specificity was determined by non- novel coronavirus infected specimens, normal samples and interference samples. The clinical specificity for 2019-nCoV IgM assay was calculated to be 97.50%. When used in combination of 2019-nCoV IgM assay and 2019-nCoV IgG assay, the clinical diagnostic specificity is 96.50%.

Specimen Category	2019-nCoV IgM (CLIA)			2019-nCoV IgM (CLIA)+2019-nCoV IgG (CLIA)		
	N	Negative	%Specificity	N	Negative	%Specificity
negative specimens	200	195	97.50%	200	193	96.50%

REFERENCES

1. Zhou, P., Yang, X., Wang, X. et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature (2020). https://doi.org/10.1038/s41586-020-2012-7.
2. Diagnosis and treatment of pneumonitis caused by novel coronavirus (Trial version 7).
3. Na Zhu, Ph.D., Dingyu Zhang, et al.A Novel Coronavirus from Patients with Pneumonia in China, 2019[J].New England Journal of Medicine, 2020.
4. Prevention and control program of pneumonitis caused by novel coronavirus (version 5).

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SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
8 °C 2 °C	Temperature limit (Store at 2-8°C)		Use-by date
Σ	Contains sufficient for <n> tests		Keep away from sunlight
	This way up	EC REP	Authorized representative in the European Community
IVD	*In vitro* diagnostic medical device	CONTENTS	Kit components
REF	Catalogue number	LOT	Batch code