Snibe Diagnostic

CE REF 130212007M: 100 tests
130612007M: 50 tests

MAGLUMI® HSV-1/2 IgG (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the qualitative determination of HSV-1/2 IgG in human serum using the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer (including Maglumi 600, Maglumi 800, Maglumi 1000, Maglumi 1000 Plus, Maglumi 2000, Maglumi 2000 Plus, Maglumi 4000, Maglumi 4000 Plus, MAGLUMI X8, MAGLUMI X3 and MAGLUMI X6) and Biolumi series Integrated System (including Biolumi CX8).

SUMMARY AND EXPLANATION OF THE TEST

Herpes simplex virus (HSV) is a member of a family of viruses including Herpes simplex virus 1 and 2 (HSV-1 and HSV-2), also known as human herpesvirus 1 and 2 (HHV-1 and HHV-2), whose genomes consist of a single large double-stranded DNA molecule[1]. The herpes simplex virion consists of four components，an electron-dense core containing viral DNA，an icosadeltahedral capsid，an amorphous, at times eccentric layer of proteins, designated tegument, which surrounds the capsid; and an envelope. Both HSV-1 (which produces most cold sores) and HSV-2 (which produces most genital herpes) are ubiquitous and contagious. They can be spread when an infected person is producing and shedding the virus[2-4].
Primary HSV-1 infections, acquired through direct person-to-person (primarily nongenital) contact, usually occur in the first decade[4]. When the primary HSV-1 infection is clinical, the classic presentation is herpes gingivostomatitis, a serious infection of the gums, mouth, tongue, lip, face and/or pharynx. Due to virus reactivation, recurrent HSV-1 infection in the form of herpes labialis (fever blisters or cold sores) or ocular herpes occurs in up to 40% of the HSV-1 seropositive group[5]. Primary HSV-2 infections, usually acquired through sexual contact, are rarely found before the onset of sexual activity. When the primary HSV-2 infection is clinical, the classic presentation is herpes genitalis, an infection characterized by bilaterally distributed lesions in the genital area accompanied by fever, inguinal lymphadenopathy and dysuria. HSV-2 infections cause approximately 85% of symptomatic primary genital HSV cases, with HSV-1 infections causing the remainder. Since HSV-1 is unlikely to produce recurrent genital infections, 99% of recurrent genital herpes is due to HSV-2 infection[6].
In primary HSV infections, IgM antibodies usually appear between the third and seventh day after onset of symptoms. IgM antibody titer peaks in four to six weeks and usually decline to undetectable levels after two months. IgG antibodies to HSV usually appear one to two weeks after the onset of infection and persist at various levels for life.
The determination of HSV IgG antibodies, can aid in the diagnosis of diseases caused by Herpes simplex virus, is used to assess the serological status of an individual and is indicative for an acute or past infection, together with the detection of HSV IgM. This is particularly important in order to adopt suitable prophylaxis in susceptible individuals.

PRINCIPLE OF THE TEST

The HSV-1/2 IgG assay is an indirect chemiluminescence immunoassay.
The sample (or calibrator/control, if applicable), buffer, magnetic microbeads coated with HSV-1/2 antigen are mixed thoroughly and incubated, forming antibody-antigen complexes. After precipitation in a magnetic field, the supernatant is decanted and then a wash cycle is performed. Then ABEI labeled with mouse anti-human IgG antibody is added, 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 indicative of HSV-1/2 IgG concentration present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material Provided

Components	Contents	100 tests (REF: 130212007M)	50 tests (REF: 130612007M)
Magnetic Microbeads	Magnetic microbeads coated with purified HSV-1/2 antigen, containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	Containing BSA and HSV-1/2 IgG, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator High	Containing BSA and HSV-1/2 IgG, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Buffer	Containing BSA, NaN_3 (<0.1%).	22.5 mL	12.5 mL
ABEI Label	Mouse anti-human IgG monoclonal antibody labeled with, ABEI, containing BSA, NaN_3 (<0.1%).	22.5 mL	12.5 mL
Internal Quality Control	Containing BSA and HSV-1/2 IgG, NaN_3 (<0.1%).	2.0 mL	2.0 mL
All reagents are provided ready-to-use.			

Accessories Required But Not Provided

MAGLUMI and Biolumi Series:

Reaction Module	REF: 630003
Starter 1+2	REF: 130299004M, 130299027M
Wash Concentrate	REF: 130299005M
Light Check	REF: 130299006M
Reaction Cup	REF: 130105000101

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

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 change of lots (Reagent or Starter 1+2).
- Every 4 weeks and/or each time a new reagent kit is used (recommended).
- 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 and Biolumi systems. For instructions for use and target value refer to ***HSV-1/2 IgG (CLIA) Quality Control Information***. User needs to judge results with their own standards and knowledge.
For detailed information about entering quality control values, refer to the corresponding Analyzer Operating Instructions.
To monitor system performance and chart trends, quality control materials are required. Treat all quality control samples the same 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, do not report results. 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 instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical supporters or distributors for assistance.

SPECIMEN COLLECTION AND PREPARATION

- Serum collected using standard sampling tubes or tubes containing separating gel could be applied to the assay. Collect blood aseptically following the universal precautions for venipuncture.
- Ensure that complete clot formation in specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time.
- If the 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.
- Do not use hemolyzed or grossly lipemic specimens as well as specimens containing particulate substance or exhibiting obvious microbial contamination. Inspect all specimens for bubbles, and remove bubbles before analysis for optimal results.
- Avoid repeated freezing and thawing. The serum sample can be frozen and thawed for only two times. Stored samples should be thoroughly mixed prior to use (Vortex mixer). Frozen specimens must be mixed THOROUGHLY after thawing by LOW speed vortexing. Please ask local representative of SNIBE for more derails if you have any doubt.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or a secondary tube. Care should be taken to transfer only the clarified specimen without the lipaemic material.
- All samples (Patient specimens or controls) should be tested within 3 hours when placed on board the MAGLUMI and Biolumi Systems. Refer to the SNIBE service for more details discussion of onboard sample storage constraints.
- Specimens removed from the separator, red blood cells or clot may be stored up to 7 days at 2-8°C, and stored up to 3 months frozen at -20°C or colder.
- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator. 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 of HSV-1/2 IgG 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 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 containers 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 samples.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- For detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

STORAGE AND STABILITY

- Sealed: Stored at 2-8°C until the expiration date.
- Opened at 2-8°C: Minimum stability is 4 weeks.
- On-board: Minimum stability is 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. It is still possible to keep on using the kit beyond the opened or on-board period if the controls are found within the expected ranges.
- Keep upright for storage to facilitate later proper resuspension of magnetic microbeads.
- Keep away from sunlight.

TEST PROCEDURE

Preparation of the Reagent

- 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.
- To ensure proper test performance, strictly adhere to the corresponding Analyzer Operating Instructions. Each test parameter is identified via a RFID CHIP on the Reagent kit. For further information please refer to the corresponding Analyzer Operating Instructions.

LIMITATIONS

- A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
- Bacterial contamination or heat inactivation of the specimens may affect the test results.
- A result within the expected range does not rule out the presence of disease and should be interpreted together with the patient's clinical picture and other diagnostic procedures.
- Diagnosis of a disease should not be based on the result of a single test, but should be determined in conjunction with clinical findings in association with medical judgement.
- Any therapeutical decision should also be taken on a case-by-case basis.
- Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results.

RESULTS

Calculation of Results

The analyzer automatically calculates the HSV-1/2 IgG 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 corresponding Analyzer Operating Instructions.

Interpretation of Results

Results obtained with the HSV-1/2 IgG assay can be interpreted as follows:

- Non-reactive: A result less than 2 AU/mL (<2 AU/mL) is considered to be negative. A nonreactive result generally indicates that the patient has not been infected, but does not always rule out acute HSV infection.
- Reactive: A result greater than or equal to 2 AU/mL is (≥2 AU/mL) considered to be positive. A reactive result is indicative of recent or reactivated infection.

Results from assays of other manufacturers cannot be used interchangeably.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the HSV-1/2 IgG assay was determined as described in the CLSI EP5-A2, 2 controls and 3 human serum pools containing different concentration of analyte were assayed in duplicate at two independent runs per day for 20 testing days. The results are summarized in the following table:

Sample	Mean(AU/mL) (N=80)	Within-Run		Between-Run		Total	
		SD(AU/mL)	%CV	SD(AU/mL)	%CV	SD(AU/mL)	%CV
Negative Serum Pool	0.534	0.041	7.68	0.049	9.18	0.063	11.80
Low Positive Serum Pool	3.394	0.190	5.60	0.128	3.77	0.234	6.89
High Positive Serum Pool l	36.966	0.558	1.51	1.438	3.89	1.542	4.17
Negative Control	0.835	0.054	6.47	0.070	8.38	0.088	10.54
Positive Control	6.233	0.187	3.00	0.317	5.09	0.369	5.92

Limit of Blank (LoB)

The LoB for the HSV-1/2 IgG assay is 0.25 AU/mL.

Analytical Specificity

Clinical HSV-1/2 IgG negative samples, which contain potential cross-reactants including HAV, HBV, HCV, CMV, Rubella, Toxo, HIV, Syphilis, EBV, RF, HSV-1/2 IgM, ANA approved by commercially available CE-marked assay, were used to evaluate the cross-reactivity of HSV-1/2 IgG assay. Of all the potential cross-reactants, none were found to cause false positive in the HSV-1/2 IgG assay. The results were summarized in the following table:

Clinical Category	Number of non-reactive	Number of reactive
Anti-HAV positive	10	0
Anti-HBs positive	20	0
Anti-HCV positive	20	0
Anti-CMV positive	10	0
Anti-Toxo positive	10	0
Anti-Rubella positive	10	0
Anti-HIV positive	10	0
Syphilis positive	10	0
RF positive	10	0
HSV-1/2 IgM positive	15	0
ANA positive	15	0
Anti-EBV positive	15	0
Total	155	0

Endogenous Interference
Substances up to the following concentrations did not interfere with the assay:

- Bilirubin 40 mg/dL
- Hemoglobin 100 mg/dL
- Triglyceride 2000 mg/dL

REFERENCES

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2. Roizman, B. (1979). The structure and isomerization of herpes simplex virus genomes. *Cell*, *16*(3), 481-494.
3. Whitley, R. J., & Roizman, B. (2002). Herpes simplex viruses: is a vaccine tenable?. *The Journal of clinical investigation*, *110*(2), 145.
4. Nahmias, A. J., & Josey, W. E. (1984). Herpes simplex viruses 1 and 2. In *Viral infections of humans* (pp. 351-372). Springer US.
5. Stewart, J (1992). Herpes Simplex Virus. 554-559. In Rose, N, E deMacario, J Fahey, H Friedman, G Penn (eds.). Manual of Clinical Laboratory Immunology. 4th Ed. ASM Press, Washington, D.C.
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SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
2°C 8°C	Temperature limit (Store at 2-8 °C)		Use-by date
Σ	Contains sufficient for		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