Snibe Diagnostic

REF 130219002M: 100 tests
130619002M: 50 tests

MAGLUMI® HTLV Ⅰ+Ⅱ (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the qualitative determination of HTLV Ⅰ+Ⅱ in human serum and plasma with MAGLUMI series Fully-auto chemiluminescence immunoassay analyzers (including Maglumi 600, Maglumi 800, Maglumi 1000, 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), and the assay is used for an aid in the diagnosis of HTLV-Ⅰ/HTLV-Ⅱ infection and for screening of blood donations.

SUMMARY AND EXPLANATION OF THE TEST

Human T-cell Lymphotropic Virus (HTLV) family of viruses are a group of human retroviruses that are known to cause a type of cancer called adult T-cell leukemia/lymphoma (ATL), a demyelinating disease called HTLV-Ⅰ associated myelopathy (HAM) or tropical spastic paraparesis (TSP). HTLV-Ⅱ shares approximately 70% genomic homology with HTLV-Ⅰ. HTLV-Ⅰ is high endemic foci in Japan, Melanesia, the Caribbean, and certain parts of South America and Africa. HTLV-Ⅱ is found in Indian groups in North and South America, Africa, and among intravenous drug users in the United States and Europe. HTLV-Ⅰ/Ⅱ have similar routes of transmission with Human Immunodeficiency Virus (HIV) and can have extremely long period of latency prior to manifestation of disease. So screening blood donations for HTLV-Ⅰ/Ⅱ continues to be important in protecting the safety of blood products and controlling the spread of these retroviruses.

PRINCIPLE OF THE TEST

The HTLV Ⅰ+Ⅱ assay is a sandwich immunoassay.

The sample (or calibrator/control, if applicable), buffer and magnetic microbeads coated with HTLV-Ⅰ/Ⅱ specific recombinant antigens are mixed thoroughly and incubated, after precipitation in a magnetic field, decant the supernatant, and perform a wash cycle. Then add ABEI labeled with HTLV-Ⅰ/Ⅱ recombinant antigens, and incubate to form sandwich 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 flash chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLUs), which is proportional to the concentration of HTLV Ⅰ+Ⅱ present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material provided

Components	Contents	100 tests (REF: 130219002M)	50 tests (REF: 130619002M)
Magnetic Microbeads	Coated with HTLV-Ⅰ/Ⅱ specific recombinant antigens, containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	Containing bovine serum and anti-HTLV-Ⅰ, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator High	Containing bovine serum and anti-HTLV-Ⅰ, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Buffer	Containing bovine serum, NaN_3 (<0.1%).	7.5 mL	5.0 mL
ABEI Label	HTLV-Ⅰ/Ⅱ specific recombinant antigens labeled with ABEI, containing bovine serum, NaN_3 (<0.1%).	22.5 mL	12.5 mL
Negative Control	Containing bovine serum, NaN_3 (<0.1%).	2.0 mL	2.0 mL
Positive Control 1	Anti-HTLV-Ⅰ positive, containing bovine serum, NaN_3 (<0.1%).	2.0 mL	2.0 mL
Positive Control 2	Anti-HTLV-Ⅱ positive, containing bovine serum, 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 two 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 ***HTLV Ⅰ+Ⅱ (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, commercially available 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 samples collected using standard sampling tubes or tubes containing separating gel, and plasma samples collected using K2-EDTA tubes, lithium heparin tubes and sodium heparin tubes have been verified and could be applied to the assay. Collect blood aseptically following the universal precautions for venipuncture.
- To ensure consistency in results, specimens must be transferred to centrifuge tubes and centrifuged at ≥10,000 RCF (Relative Centrifugal Force) for 15 minutes.
- Ensure that complete clot formation in 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 specimen is centrifuged before a complete clotting, the presence of fibrin may cause erroneous results. Specimen must be free of fibrin and other particulate substance.
- 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 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 lipemic 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 detailed discussion of onboard sample storage constraints.
- Specimens removed from the separator, red blood cells or clot may be stored up to 24 hours 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 HTLV Ⅰ+Ⅱ is 50 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 should 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 microbeads that have settled during shipment.
- For 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 microbeads takes place automatically when the kit is loaded successfully, ensuring the 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 judgment.
- 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 HTLV Ⅰ+Ⅱ 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 index/mL. For further information please refer to the corresponding Analyzer Operating Instructions.

Interpretation of Results

Results obtained with the HTLV Ⅰ+Ⅱ assay can be interpreted as follows:

- Non-reactive: A result less than 1.0 index/mL (<1.0 index/mL) is considered to be negative.
- Reactive: A result greater than or equal to 1.0 index/mL is (≥1.0 index/mL) considered to be positive.

Since there is no HTLV Ⅰ+Ⅱ international standard material yet, different IVD manufacturer have different traceability chain. Therefore results from assays of other manufacturers cannot be used interchangeably.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the HTLV Ⅰ+Ⅱ assay was determined as described in the CLSI EP5-A2. 3 controls and 4 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(index/mL)	Within-Run		Between-Run		Total	
	(N=80)	SD(index/mL)	%CV	SD(index/mL)	%CV	SD(index/mL)	%CV
anti-HTLV-Ⅰ (Low Positive)	2.053	0.054	2.63	0.059	2.87	0.080	3.90
anti-HTLV-Ⅱ (Low Positive)	2.047	0.068	3.32	0.071	3.47	0.098	4.79
anti-HTLV-Ⅰ (High Positive)	15.076	0.210	1.39	0.191	1.27	0.297	1.97
anti-HTLV-Ⅱ (High Positive)	15.190	0.550	3.62	0.071	0.47	0.604	3.98
Positive Control 1	2.043	0.050	2.45	0.080	3.92	0.094	4.60
Positive Control 2	3.043	0.086	2.83	0.087	2.86	0.123	4.04
Negative Control	0.205	N/A	N/A	N/A	N/A	N/A	N/A

Note: NA=Not Applicable

Analytical Specificity

The HTLV Ⅰ+Ⅱ assay was evaluated for potential cross-reactivity with other viral infections and disease state specimens. The results were listed in the following table:

Clinical Category	Number of non-reactive	Number of reactive
Anti-Toxo positive	12	0
Anti-Rubella positive	11	0
Anti-CMV positive	13	0
Anti-HSV-1/2 positive	10	0
Syphilis positive	7	0
Anti-EBV positive	8	0
Anti-HAV positive	12	0
Anti-HBV positive	9	0
Anti-HCV positive	12	0
Anti-HIV-1/2 positive	16	0
Total	110	0

Clinical Sensitivity

These values were determined in a study where specimens from individuals clinically diagnosed with HTLV infection and classified disease status were tested. The sensitivity of the HTLV Ⅰ+Ⅱ assay for both the anti-HTLV-Ⅰ and anti-HTLV-Ⅱ populations was 100.0%.

Antibody Type	Total (N)	Reactive (N)	%Sensitivity
anti-HTLV-Ⅰ	150	150	100.00
anti-HTLV-Ⅱ	50	50	100.00
Total	200	200	100.00

Clinical Specificity

In a group of randomly selected blood donors, hospitalized patients and potentially cross-reacting blood-specimens, the specificity of the HTLV Ⅰ+Ⅱ assay was found to be 99.51%.

Group	Total (N)	Reactive (N)	Non-reactive (N)	Confirmed positive (N)	%Specificity
Unselected donors	350	3	347	1	99.43
Hospitalized patients	105	2	103	1	99.04
Potentially cross-reacting blood-specimens	165	0	165	0	100.00
Total	620	5	615	2	99.51

Endogenous Interference

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

- Bilirubin 50 mg/dL
- Triglyceride 500 mg/dL
- Hemoglobin 2000 mg/dL
- RF 1500 IU/mL
- HAMA 30 ng/mL

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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	CONTENTS	Kit components
IVD	*In vitro* diagnostic medical device	LOT	Batch code
REF	Catalogue number		