



REF 130219001M: 100 tests
130619001M: 50 tests

MAGLUMI® Chagas (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescent immunoassay for the qualitative determination of IgG antibodies to Trypanosomacruzi (T. cruzi) in human serum and plasma with MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer (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 Chagas infection and for screening of blood donations.

SUMMARY AND EXPLANATION OF THE TEST

Chagas disease, also known as American trypanosomiasis, is a tropical parasitic disease caused by the protist Trypanosomacruzi (T. cruzi)¹. It is spread mostly by insects known as Triatominae or kissing bugs¹. T. cruzi commonly spread to humans and other mammals by the blood-sucking "kissing bugs" of the subfamily Triatominae. These insects are known by a number of local names, including: vinchuca in Argentina, Bolivia, Chile and Paraguay, barbeiro (the barber) in Brazil, pito in Colombia, chinchin in Central America, and chipo in Venezuela²⁻³. The disease may also be spread through blood transfusion, organ transplantation, eating food contaminated with the parasites, and by vertical transmission (from a mother to her fetus)¹. Chagas disease affects 8 to 10 million people living in endemic Latin American countries, with an additional 300,000–400,000 living in nonendemic countries, including Spain and the United States. An estimated 41,200 new cases occur annually in endemic countries, and 14,400 infants are born with congenital Chagas disease annually. In 2010 it resulted in approximately 10,300 deaths up from 9,300 in 1990⁴⁻⁵. The symptoms change over the course of the infection. In the early stage, symptoms are typically either not present or mild, and may include fever, swollen lymph nodes, headaches, or local swelling at the site of the bite¹. After 8–12 weeks, individuals enter the chronic phase of disease and in 60–70% it never produces further symptoms. The other 30 to 40% of people develop further symptoms 10 to 30 years after the initial infection, including enlargement of the ventricles of the heart in 20 to 30%, leading to heart failure⁶⁻⁷. The human disease occurs in two stages: an acute stage, which occurs shortly after an initial infection, and a chronic stage that develops over many years. The acute phase lasts for the first few weeks or months of infection. It usually occurs unnoticed because it is symptom-free or exhibits only mild symptoms that are not unique to Chagas disease. These can include fever, fatigue, body aches, muscle pain, headache, rash, loss of appetite, diarrhea, nausea, and vomiting. The signs on physical examination can include mild enlargement of the liver or spleen, swollen glands, and local swelling (a chagoma) where the parasite entered the body⁸. Of individuals with chronic Chagas disease, 60–80% will never develop symptoms (called indeterminate chronic Chagas disease), while the remaining 20–40% will develop life-threatening heart and/or digestive disorders during their lifetime (called determinate chronic Chagas disease). In 10% of individuals, the disease progresses directly from the acute form to a symptomatic clinical form of chronic Chagas disease^{7,9}. The symptomatic (determinate) chronic stage affects the nervous system, digestive system and heart. About two-thirds of people with chronic symptoms have cardiac damage, including dilated cardiomyopathy, which causes heart rhythm abnormalities and may result in sudden death. About one-third of patients go on to develop digestive system damage, resulting in dilation of the digestive tract (megacolon and megaesophagus), accompanied by severe weight loss. Swallowing difficulties (secondary achalasia) may be the first symptom of digestive disturbances and may lead to malnutrition⁹. Qualitative determination of T. cruzi IgG antibody is intended to be used as an aid in the diagnosis of Chagas infection.

PRINCIPLE OF THE TEST

The Chagas assay is an indirect chemiluminescence immunoassay. The sample (or calibrator/control, if applicable), buffer, magnetic microbeads coated with purified *T. cruzi*-specific recombinant antigens 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 anti-human IgG antibody is added, 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 chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLUs), which is indicative to the concentration of IgG antibodies to *T. cruzi* present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material provided

Components	Contents	100 tests (REF: 130219001M)	50 tests (REF: 130619001M)
Magnetic Microbeads	Magnetic microbeads coated with <i>T. cruzi</i> -specific recombinant antigens, containing BSA, NaN ₃ (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	Low concentration of antibodies to <i>T. cruzi</i> , containing BSA, NaN ₃ (<0.1%).	2.5 mL	2.0 mL
Calibrator High	High concentration of antibodies to <i>T. cruzi</i> , containing BSA, NaN ₃ (<0.1%).	2.5 mL	2.0 mL
Buffer	Containing BSA, NaN ₃ (<0.1%).	12.5 mL	7.5 mL
ABEI Label	Anti-human IgG antibody labeled with ABEI, containing BSA, NaN ₃ (<0.1%).	22.5 mL	12.5 mL
Negative Control	Containing BSA, NaN ₃ (<0.1%).	2.0 mL	2.0 mL
Positive Control	Low concentration of antibodies to <i>T. cruzi</i> , containing BSA, 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 2 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 **Chagas (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, sodium heparin tubes and sodium citrate tubes have been verified and 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 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. Specimens 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 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 details 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 Chagas 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 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 Chagas 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 Chagas 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 (≥1.0 index/mL) is considered to be positive.

Assay results should be interpreted in conjunction with the patient's clinical presentation, history, and other laboratory results. All initially reactive should be redetermined in duplicate with the Chagas. If the concentration values <1.0 index/mL are found in both cases, the samples are considered negative. And repeatedly reactive samples must be confirmed according to recommended confirmatory algorithms.

Results may differ due to variations in population. It is recommended that each laboratory establish its own expected ranges.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the Chagas assay was determined as described in the CLSI EP5-A2. 2controls and 2 samples 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) (N=80)	Within-Run		Between-Run		Total	
		SD (index/mL)	%CV	SD (index/mL)	%CV	SD (index/mL)	%CV
Low Positive Serum Pool	1.994	0.128	6.42	0.070	3.51	0.170	8.53
High Positive Serum Pool	8.046	0.307	3.82	0.230	2.86	0.437	5.43
Negative Control	0.302	NA	NA	NA	NA	NA	NA
Positive Control	3.006	0.125	4.16	0.067	2.23	0.164	5.46

Note: NA=Not Applicable.

Analytical Specificity

The specificity of the Chagas assay was evaluated for potential cross-reactivity with other viral infections and disease state specimens. The results are shown in the table below:

Condition	Number of non-reactive	Number of reactive
Anti-Toxo positive	12	0
Anti-Rubella positive	11	0
Anti-CMV positive	10	0
Anti-HSV-1/2 positive	10	0
Anti-HTLV-1/2 positive	7	0
Anti-EBV positive	8	0
Anti-HAV positive	12	0
Anti-HBV positive	10	0
Anti-HCV positive	11	0
Anti-HIV-1/2 positive	16	0
Syphilis positive	12	0
Total	119	0

Clinical Sensitivity

These values were determined in a study where specimens from individuals clinically diagnosed with Chagas infection and classified disease status were tested. The sensitivity of the Chagas assay was 100.0%.

Category	Total (N)	Reactive (N)	%Sensitivity
Preselected <i>T. cruzi</i> Serologic Positive	95	95	100.0

Clinical Specificity

In a group of randomly selected blood donors, hospitalized patients and potentially cross-reacting blood-specimens, the specificity of the Chagas assay was found to be 99.70%.

Group	Total(N)	Reactive (N)	Non-reactive (N)	Confirmed positive (N)	%Specificity
Unselected donors	420	2	418	1	99.76
Hospitalized patients	100	2	98	1	98.99
Potentially cross-reacting blood-specimens	150	0	150	0	100.00
Total	670	4	666	2	99.70

Endogenous Interference

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

- Bilirubin 50 mg/dL
- Triglyceride 2000 mg/dL
- Hemoglobin 500 mg/dL
- RF 1500 IU/mL
- HAMA 40 ng/mL

REFERENCES

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SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
	Temperature limit (Store at 2-8 °C)		Use-by date
	Contains sufficient for		Keep away from sunlight
	This way up		Kit components
	<i>In vitro</i> diagnostic medical device		Batch code
	Catalogue number		