Snibe Diagnostic

CE REF 130201011M: 100 tests
130601011M: 50 tests

MAGLUMI® CA 19-9 (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of Cancer Antigen 19-9 (CA 19-9) 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

CA 19-9 (carbohydrate antigen 19-9, also called cancer antigen 19-9) is a predominantly carbohydrate antigen which was defined from the culture medium of a colorectal cancer cell line. It is a high molecular weight glycolipid derived from a monoclonal antibody isolated from mice, which is immunised with a human colon cell line[1]. Data are reported on 2283 patients in whom there was unequivocal histological confirmation of malignancy in 945 (41%). The median sensitivity of CA 19-9 for the diagnosis of pancreatic cancer examining pooled data from all series is 79 (70e90%). The median specificity is 82 (68e91%). The median positive predictive value (PPV) 72 (41e95) and the median negative predictive value 81 (65e98)[2-5].

CA 19-9 is the most widely used and best validated marker for pancreatic cancer. It belongs to the large family of mucinous markers: glycoproteins with a transmembrane protein skeleton and the extracellular side consisting of oligosaccharides chains extensively glycosylated, which are a normal component of the glandular secretions of mucous type. In particular, CA 19-9 is synthesized by normal human pancreatic and biliary ductal cells and by gastric, colon, endometrial and salivary epithelia. Normally present in small amounts in serum, in which it exists as mucin, a high molecular mass (200–1000 kDa) glycoprotein complex, CA 19-9 is over expressed in certain inflammatory conditions as pancreatitis and other benign gastrointestinal diseases. Moreover, it exhibits an increase in its plasmatic levels in course of neoplastic disease, during which several processes regulating both the passage of these molecules in the bloodstream and their metabolization appear altered[6-7].

PRINCIPLE OF THE TEST

The CA 19-9 assay is a sandwich chemiluminescence immunoassay.

The sample (or calibrator/control, if applicable), buffer, magnetic microbeads coated with anti-CA 19-9 monoclonal antibody are mixed thoroughly, incubating and performing a wash cycle after a precipitation in a magnetic field. ABEI labeled with anti-CA19-9 monoclonal antibody are then added, reacting to form sandwich 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 CA 19-9 present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material Provided

Components	Contents	100 tests (REF: 130201011M)	50 tests (REF: 130601011M)
Magnetic Microbeads	Magnetic microbeads coated with anti-CA19-9 monoclonal antibody, containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	CA 19-9 antigen, containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator High	CA 19-9 antigen, 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-CA 19-9 monoclonal antibody labeled ABEI, containing BSA, NaN_3 (<0.1%).	12.5 mL	7.5 mL
Diluent	0.9%NaCl.	25.0 mL	15.0 mL
Internal Quality Control	CA 19-9 antigen, 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 ***CA 19-9 (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

- Use standard sampling tubes or tubes containing separating gel. 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 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 secondary tube. Care should be taken to transfer only the clarified specimen without the lipaemic material.
- All samples (patient specimens and controls) should be tested within 3 hours when placed on board the MAGLUMI and Biolumi Systems. Refer to the SNIBE service for more details of onboard sample storage constraints.
- Specimens removed from the separator, red blood cells or clot may be stored up to 30 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 CA 19-9 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 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.

DILUTION

Samples with concentrations above the measuring range can be diluted.

After manual dilution, multiply the result by the dilution factor. After dilution by the analyzers, 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 and Biolumi series Fully-auto chemiluminescence immunoassay analyzer user software. Please refer to the corresponding Analyzer Operating Instructions.

High-Dose Hook

No high-dose hook effect for CA 19-9 concentrations up to 10,000 U/mL.

LIMITATION

- A skillful operation and strict adherence to the instructions are necessary to obtain reliable results. Procedural directions should be followed exactly and careful operation should be used to obtain valid results. Any modification of the procedure is likely to alter the results.
- For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or received immunotherapy may contain human anti-mouse antibodies (HAMA), which may result in falsely elevated or decreased values. Moreover, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples as well. Additional clinical or diagnostic information may be required to determine patient status.

RESULTS

Calculation of Results

The analyzer automatically calculates the CA19-9 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 corresponding Analyzer Operating Instructions.

Interpretation of Results

The expected range for the CA19-9 assay was obtained by testing 352 apparently healthy individuals in China, and gave the following expected value:
<28.0 U/mL (95th percentile);
<37.0 U/mL (97.5th percentile);
<41.0 U/mL (99th percentile).
Results may differ between laboratories due to variations in population and test method. It is recommended that each laboratory establish its own expected ranges.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the CA 19-9 assay was determined as described in the CLSI EP5-A2. 3 human serum pools and 3 controls 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(U/mL) (N=80)	Within-Run		Between-Run		Total	
		SD(U/mL)	%CV	SD(U/mL)	%CV	SD(U/mL)	%CV
Serum Pool 1	41.547	2.353	5.66	1.086	2.61	2.591	6.24
Serum Pool 2	208.135	6.720	3.23	10.997	5.28	12.887	6.19
Serum Pool 3	516.713	7.055	1.37	24.785	4.80	25.770	4.99
Control 1	15.683	1.124	7.17	0.477	3.04	1.221	7.79
Control 2	41.156	2.218	5.39	1.201	2.92	2.522	6.13
Control 3	131.077	4.446	3.39	6.211	4.74	7.638	5.83

Limit of Blank (LoB)

The LoB for the CA 19-9 assay is 1.0 U/mL.

Limit of Detection (LoD)

The LoD for the CA 19-9 assay is 1.5 U/mL.

Measuring Range

1.0-1000 U/mL (defined by the limit of blank and the maximum of the master curve). Values below the limit of blank are reported as <1.0 U/mL. Values above the measuring range are reported as >1000 U/mL.

Linearity

The assay is linear between 1.5 U/mL and 1000 U/mL based on a study performed with guidance from CLSI EP6-A. Nine equally distributed levels of samples were prepared by spiking a serum sample containing CA 19-9 1100 U/mL with a serum sample free of CA 19-9 (0.0 U/mL).The mean sample recovery ranged between 90% to 110%.

Method Comparison

A total of 115 samples in the range of 1.529 to 991.293 U/mL were tested using the CA 19-9 assay (y) and a commercially available immunoassay (x). The data from the resulting linear regressions are summarized as: y =1.097x-4.1585, r^2=0.9866.

Analytical Specificity

The specificity data of the assay was obtained by adding CA125 (400 U/mL), CA15-3 (400 U/mL), CA72-4 (400 U/mL) to serum samples at the indicated concentrations. No interference was found.

Interference

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

Interference	Concentration
Bilirubin	65 mg/dL
Hemoglobin	2200 mg/dL
Triglycerides	1500 mg/dL

RF	1500 IU/ mL
Cisplatin	165 μg/mL
Bleomycin	30 μg/mL
Carboplatin	500 μg/mL
Fluorouracil	400 μg/mL
Cytarabine	30 μg/mL
Methotrexate	909 μg/mL
mitomycin-C	100 μg/mL
Paclitaxel	67 μg/mL
Vinblastine sulfate	500 μg/mL
Doxorubicin hydrochloride	40 μg/mL
Tamoxifen	0.0228 μg/mL
Cyclophosphamide	1000 μg/mL

REFERENCES

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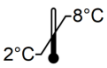
SYMBOLS EXPLANATIONS

	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	EC REP	Authorized representative in the European Community
IVD	*In vitro* diagnostic medical device	CONTENTS	Kit components
REF	Catalogue number	LOT	Batch code