Snibe Diagnostic

CE 0123 REF 130201004M: 100 tests
130601004M: 50 tests

MAGLUMI® Total PSA (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of Total Prostate Specific Antigen (Total PSA) in human serum to aid in prostate cancer screening 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 and MAGLUMI X8).

SUMMARY AND EXPLANATION OF THE TEST

Prostate cancer (PC) is one of the leading causes of cancer cases across the globe and unarguably, the second most reason of cancer related deaths among men. In the past two to three decades, there has been a remarkable increase in the incidence of PC throughout the world with the mortality rate increasing in many countries. The increased incidence of PC has led to the widespread usage of serum based screening of asymptomatic men by using the antigen, thought to be specific to prostate specific antigen (PSA)[1]. Prostate-specific antigen (PSA), also known as gamma-seminoprotein or kallikrein-3 (KLK3), is a glycoprotein enzyme encoded in humans by the KLK3 gene and consists of 237 amino acids and one N-linked oligosaccharide chain at Asn45 with a molecular weight of approximately 34,000 Daltons[2-3]. PSA is a member of the kallikrein-related peptidase family and is secreted by the epithelial cells of the prostate gland. PSA is produced for the ejaculate, where it liquefies semen in the seminal coagulum and allows sperm to swim freely[4].

Elevated serum PSA concentrations are found in men with prostate cancer, benign prostatic hyperplasia (BPH) or inflammatory conditions of other adjacent genitourinary tissues, but not in apparently healthy men or in men with cancers other than prostate cancer[5]. PSA has been demonstrated to be an accurate marker for monitoring advancing clinical stage in untreated patients and for monitoring response to therapy by radical prostatectomy, radiation therapy and anti-androgen therapy[6-7]. The main areas in which PSA determinations are employed are the monitoring of progress and efficiency of therapy in patients with prostate carcinoma or receiving hormonal therapy.

PRINCIPLE OF THE TEST

The Total PSA assay is a sandwich chemiluminescence immunoassay.

The sample (or calibrator/control, if applicable), buffer and magnetic microbeads coated with anti-PSA monoclonal antibody are mixed thoroughly and incubated, and then perform a wash cycle. Then add ABEI labeled with another anti-PSA monoclonal antibody, mix thoroughly 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 proportional to the concentration of Total PSA present in samples.

KIT COMPONENTS

Material Provided

Components	Contents	100 tests (REF: 130201004M)	50 tests (REF: 130601004M)
Magnetic Microbeads	Magnetic microbeads coated with anti-PSA monoclonal antibody, containing BSA, NaN_3(<0.1%).	2.5 mL	2.0 mL
Calibrator Low	Containing bovine serum and Total PSA, NaN_3(<0.1%).	2.5 mL	2.0 mL
Calibrator High	Containing bovine serum and Total PSA, 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-PSA 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	Containing bovine serum and Total PSA, NaN_3(<0.1%).	2.0 mL	2.0 mL
All reagents are provided ready-to-use.			

Accessories Required But Not Provided

MAGLUMI Series:

Reaction Module	REF: 630003
Starter 1+2	REF: 130299004M, 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 WHO 1st Reference Reagent 96/670.

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 system. For instructions for use and target value refer to ***Total PSA (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 operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.
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 repeating freeze-thaw cycles. 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.
- 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 and controls) should be tested within 3 hours when placed on board the MAGLUMI System. 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 5 days at 2-8°C, and stored up to 6 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 Total PSA is 20 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 operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer. Each test parameter is identified via a RFID CHIP on the Reagent kit. For further information please refer to the operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.

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 series Fully-auto chemiluminescence immunoassay user software. Please refer to the operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer.

High-Dose Hook
For the Total PSA assay, no high dose hook effect was observed when samples containing Total PSA up to 2,000 ng/mL.

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.
- Determination of the f/t PSA ratio in serum is only useful for diagnostic and screening purposes prior to the initiation of therapy. So far, no valid clinical results are available for its determination in follow-up. Therapeutic intervention may strongly influence the f/t PSA ratio. Manipulations at the prostate (e.g. DRE) may also lead to variations in the f/t PSA ratio[8-11]. F/t PSA rations alone provide no evidence of presence of malignancies; they may be only interpreted in context with the clinical picture and other diagnostic procedures.

RESULTS

Calculation of Results
The analyzer automatically calculates the Total PSA 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 ng/mL. For further information please refer to the operating instructions of MAGLUMI series Fully-auto chemiluminescence immunoassay (CLIA) analyzer.

Interpretation of Results
The expected ranges for the Total PSA assay were obtained by testing 535 apparently healthy individuals (269 males and 266 females), and gave the following reference values listed below:
Males: <4 ng/mL (95th percentile)
Females: <0.5 ng/mL (95th 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 Total PSA 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 (ng/mL) (N=80)	Within-Run		Between-Run		Total	
		SD (ng/mL)	%CV	SD (ng/mL)	%CV	SD (ng/mL)	%CV
Serum Pool 1	0.492	0.032	6.50	0.028	5.69	0.043	8.74
Serum Pool 2	4.529	0.254	5.61	0.174	3.84	0.308	6.80
Serum Pool 3	119.855	2.396	2.00	2.043	1.70	3.149	2.63
Control 1	2.967	0.173	5.83	0.143	4.82	0.224	7.55
Control 2	14.544	0.518	3.56	0.612	4.21	0.802	5.51

Limit of Blank (LoB)
The LoB of the Total PSA assay is 0.01 ng/mL.

Limit of Detection (LoD)
The LoD of the Total PSA assay is 0.02 ng/mL.

Limit of quantitation (LoQ)
It is defined as the concentration of Total PSA that can be measured with an inter assay CV of 20%. The LoQ for the Total PSA assay is 0.03 ng/mL.

Measuring Range
0.01-400 ng/mL (defined by the limit of blank and the maximum of the master curve). Values below the limit of blank are reported as<0.01 ng/mL. Values above the measuring range are reported as >400 ng/mL.

Linearity
The assay is linear between 0.02 ng/mL and 400 ng/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 Total PSA 440 ng/mL with a serum sample containing Total PSA 0.02 ng/mL. The mean sample recovery ranged between 90% to 110%.

Recovery
The Total PSA assay has a mean recovery of 100%±10%. Two different levels of Total PSA were spiked into three samples resulted in the following data:

Sample	Amount Added (ng/mL)	Observed (ng/mL)	%Recovery
S1	-	0.451	/
	10.00	10.124	96.73
	200.00	211.318	105.43
S2	-	3.623	/
	10.00	13.743	101.20
	200.00	198.223	97.30
S3	-	107.887	/
	10.00	117.724	98.37
	200.00	306.154	99.13

Method Comparison
A total of 110 samples in the range of 0.017 and 367.666 ng/mL were tested by the Total PSA assay (y) and a commercially available immunoassay (x). The data from the resulting linear regressions are summarized as: y=0.979x-0.4598, r^2=0.9525.

Analytical specificity
The specificity of the assay was obtained by adding CA199 (100 U/mL) and CEA (100 ng/mL) to three serum samples containing 0.5 ng/mL, 4 ng/mL and 120 ng/mL of Total PSA, respectively. No interference was found.

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

- Bilirubin 65 mg/dL
- Hemoglobin 2200 mg/dL
- Triglyceride 1500 mg/dL
- RF 1500 IU/mL
- HAMA 30 ng/mL

Drug Interference
Drugs up to the following concentrations did not interfere with the assay:

Drugs	Concentration
Aspirin	500 µg/mL
Cisplatin	165 µg/mL
Cyclophosphamide	700 µg/mL
Doxorubicin	1.16 µg/mL
Methotrexat	30 µg/mL
Biotin	50 ng/mL
Acetaminophen	200 µg/mL
Cyclosporine C	2.97 ng/mL
Mitomycin C	60 µg/mL
Vinblastine	12 µg/mL
Ibuprofen	400 µg/mL
5-Fluorouracil	400 µg/mL
Digoxin	5 ng/mL

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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