Instruction For Use

【Product Name】

SHBG (eCLIA)

【Order Information】

REF NO.	Package Size
0320509001	50 T
0320509002	2×50 T
0320509003	100 T
0320509004	2×100 T

【Intended Use】

Immunoassay for the in vitro quantitative determination of sex hormone binding globulin (SHBG) in human serum and plasma. Determination of SHBG is used for auxiliary diagnosis of various androgen abnormal disease.

【Summary】

Sex hormone-binding globulin (SHBG) is a glycoprotein synthesized by the liver and released into the blood. Its molecular weight is about 80-100kDa [1]. It has a high affinity for 17-hydroxy steroid hormones, such as testosterone and estradiol, and is primarily responsible for the transport of testosterone and estradiol in the blood[2-3]. The molecular structure of SHBG is a dimer composed of two structurally similar amino acids. In the process of sex hormone transport, each molecule of SHBG binds a molecule of sex hormone [4].

SHBG in human plasma is regulated by many factors, such as androgen/estrogen balance, thyroid hormones, insulin, and dietary factors[5]. The concentration of SHBG is positively correlated with the concentration of estrogen in human plasma, but negatively correlated with the concentration of androgen. Therefore, the concentration of SHBG in women is generally higher than that in men. During pregnancy, estrogen production increases significantly, and SHBG levels rise significantly[6]. In addition, SHBG concentrations are also increased in androgen-insensitive patients, patients with hyperthyroidism, and patients with liver cirrhosis, and human SHBG concentrations are also increased by pharmacological stimuli, such as oral contraceptives or antiepileptic medications[7]. The measurement of SHBG is helpful to evaluate patients with androgen metabolism disorders. If the SHBG value of female patients with hirsutism or polycystic ovary syndrome is significantly lower than the normal value, the cause can be confirmed as hormone secretion disorder. In this case, increasing the concentration of estrogen should be used for treatment.

【Test Principle】

Sandwich principle. Total duration of assay: 18 minutes.

5 µL of sample, biotinylated SHBG monoclonal antibody and ruthenium labeled SHBG monoclonal antibody form a sandwich complex. After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with system reagent. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is instrument specifically generated by 2-point calibration and a master curve provided via the RFID.

【Main Components】

The reagent pack consists of MB, RA, RB, calibrators and control materials (optional). Different lots cannot be used at the same time or mixed up together.

Components	Ingredients	Volume (2×50T)	Volume (50T)	Volume (100T)	Volume (2×100T)
MB	Streptavidin-coated microparticles 0.45mg/mL; ProClin300	2×1.8mL	1×1.8mL	1×3.5mL	2×3.5mL
RB	Biotinylated SHBG monoclonal antibody, 1.5mg/L ; 100 mM HEPES; ProClin300	2×3.5mL	1×3.5mL	1×7.0mL	2×7.0mL
RA	Ruthenium labeled SHBG monoclonal antibody, 1.5mg/L, 100 mM HEPES; ProClin300	2×3.5mL	1×3.5mL	1×7.0mL	2×7.0mL
Calibrators	SHBG antigen, lyophilized	High: 1×1.0 mL Low: 1×1.0 mL			
Control Materials (Optional)	SHBG antigen, lyophilized	High: 1×2.0 mL Low: 1×2.0 mL			

Traceability:This method can be traceable to NIBSC 08/266.

See the control material value sheet for the target values and ranges of control materials.

Supporting instruments and materials required but not provided in this pack (provided by Lifotronic)

Additional materials for Automated ECL Immunoassay Analyzer eCL8000, eCL8000i, eCL8000p, eCL8000x:

- REF 679005, Auffer, 480 mL, or REF 679004, Auffer, 6×480 mL
- REF 679007, Buffer, 480 mL, or REF 679006, Buffer, 6×480 mL
- REF 679009, Concentrated Washing Buffer, 1 L, or REF 679008, Concentrated Washing Buffer, 6×1 L
- REF 679011, Assay Cup, 300 T, or REF 679012, Assay Cup, 3000 T

Additional materials for Automated ECL Immunoassay Analyzer eCL8600, eCL8600i, eCL8600p, eCL8800, eCL8800i, eCL8800p:

- REF 0320501804, Auffer, 2×1 L, or REF 0320501805, Auffer, 4×1 L
- REF 0320501904, Buffer, 2×1 L, or REF 0320501905, Buffer, 4×1 L
- REF 0320507502, PreClean, 2×800 mL, or REF 0320507503, PreClean, 4×800 mL
- REF 0320510001, Assay Cup/Assay Tip, 6×6×105, or REF 032120111, Assay Cup/Assay Tip, 12×2×105

Additional materials for Automated ECL Immunoassay Analyzer eCL9000, [illegible]

- REF 0320501801, Auffer, 2×2 L, or REF 0320501806, Auffer, 4×2 L
- REF 0320501901, Buffer, 2×2 L, or REF 0320501906, Buffer, 4×2 L
- REF 0320507501, PreClean, 2×2 L, or REF 0320507504, PreClean, 4×2 L
- REF 0320510001, Assay Cup/Assay Tip, 6×6×105, or REF 0320510002, Assay Cup/Assay Tip, 1×6×105

【Storage and Shelf Life】

Store at 2°C-8°C.

Do not freeze.

Store the reagent kit upright in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Damaged, expired or contaminated reagents should be discarded.

Stability of the reagents	
Unopened at 2°C~8ºC	18 months
Store at 2°C~8ºC after opening	8 weeks
Stored on the analyzers at 2ºC~15ºC	8 weeks

The calibrators and control materials are stable up to the stated expiration date..

Stability of the calibrators and control materials	
Unopened store at 2ºC~8ºC	18 months
Store at 2ºC~8ºC after reconstituted	7 days
Store at -25ºC~-15ºC after reconstituted	3 months (freeze-thawed only once)

Store calibrators and control materials upright in order to prevent the calibrators and control materials from adhering to the cap of the vial.

【Applicable Instrument】

Automated ECL Immunoassay Analyzers: eCL8000, eCL8000i, eCL8000p, eCL8000x, eCL8600, eCL8600i, eCL8600p, eCL8800, eCL8800i, eCL8800p, eCL9000, eCL9600, eCL9900, eCL9900i.

【Specimen collection, handling and storage】

Human serum and anticoagulant plasma with heparin lithium, heparin sodium are recommended. Samples should be collected by standard operation of venous puncture; after complete coagulation, the tangible component should be removed by centrifugation. The sample should avoid bubbling during testing. Lipid layer floating on the upper of the sample should be removed. Samples with severe hemolysis are not in suggestion. Samples should be stable for 1 day at 18~28℃, 7 days at 2~8 ℃, 6 months at -15℃ or lower than -15℃. Freezing and thawing cycle is permitted only once.

【Assay Procedure】

Testing procedures and precautions

Previous to operation, one should read the operational manual carefully to obtain system operation procedure, sample processing, security precaution, maintenance and other related information.

Set up SHBG test according to the operational manual.

Put the SHBG reagent pack into the correct analyzer slot to automatically suspend magnetic beads at least 30 min before testing..

Recommended ambient temperature:10~30°C; Relative humidity: ≤ 80%.

Handing of lyophilized calibrators and control materials

Carefully dissolve the contents of calibrator by adding exactly 1.0 mL of distilled or deionized water and allow to stand closed at room temperature for at least 15 minutes to reconstitute. Mix carefully, avoiding foam formation. Transfer aliquots of the reconstituted calibrator to additional plastic bottles and mark them. All the bottles must be stored at -15°C or lower than -15°C immediately if you do not test immediately after dispensed and marked.

Carefully dissolve the contents of control materials by adding exactly 2.0 mL of distilled or deionized water and allow to stand closed at room temperature for at least 15 minutes to reconstitute. Mix carefully, avoiding foam formation. Transfer aliquots of the reconstituted control material to additional plastic bottles and mark them. All the bottles must be stored at -15°C or lower than -15°C immediately if you do not test immediately after dispensed and marked.

Calibration

Calibration should be performed using lot-matching reagent and calibrators.

Before calibration, the reagent and main curve information should be imported into the analyzer via radio frequency identification reagent card (refer to instrument user manual). The analyzer adjusts the main curve to produce working curve according to the calibrator results, and identifies validity of the working curve automatically.

Recalibration is recommended when:

(1) The reagents of different lot are used;

(2) The same lot of reagents were used on the analyzer beyond 28 days;

(3) Quality control findings outside the defined limits;

(4) Change buffer with different batch numbers.

Quality control

Use SHBG Control Materials for quality control.

For quality control, use SHBG control materials.

In addition, other suitable control material can be used.

Control materials for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples is concerned.

Follow the applicable government regulations and local guidelines for quality control.

Please make sure that the correct values are used.

Calculation
The system software automatically calculates the analyte concentration using particular algorithm, and the result unit is nmol/L, μg/ml or mg/L.
Conversion factors: nmol/L × 0.095 = μg/mL = mg/L.

Sample dilution
Samples with SHBG concentrations above the detection range can be diluted with sample diluents. It is recommended to dilute by 1:10 (automatic dilution by instrument or manual dilution). If manual dilution is used, the result should be multiplied by dilution. If the dilution is automatic, the instrument will calculate the result.

【Biological reference interval】
Based on the analysis of serum samples from healthy people in hospitals in Guangdong, China, the reference intervals of 5% and 95% were calculated as follows.

People	Sample number	Reference interval（nmol/L）
Male（20～49 years old）	124	18.27～54.13
Male（≥50 years old）	130	20.65～76.74
Female（20～49 years old）	125	32.44～128.5
Female（≥50 years old）	122	27.17～128.4

Due to differences in the region, race, gender and age, laboratories are recommended to set up their own reference ranges. Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

【Result Interpretation】
For explaining the result, the patient's overall clinical manifestation should be referred to, including symptoms, medical history and other relevant data and information.

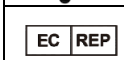
【Limitations】
The test results are only for clinical reference and cannot be used alone as the basis for diagnosis or exclusion of cases.
The measuring range of the kit is 0.02~200 nmol/L. For samples with SHBG content below the lower detection limit, the results are reported as < 0.02 nmol/L; If the SHBG content is above the upper detection limit, the results are reported as > 200 nmol/L (10× diluted sample is reported as > 2000 nmol/L).
When the concentration of jaundice (bilirubin) ≤66 mg/dL, hemolysis (hemoglobin) ≤1100 mg/dL, triglyceride ≤2700 mg/dL, biotin ≤30 ng/mL, HAMA≤100 ng/mL, the relative deviation of the results was within ±10%. When the concentration of rheumatoid factor in the samples was less than 1200 IU/mL, the relative recoveries were between 90% and 110%.
When detected with 20 mg/mL transferrin, 50 mg/mL fibrinogen, 0.2 mg/mL thyroid-binding globulin (TBG), 1 mg/mL thyroglobulin (TG), 0.0125 μg/mL thyroid stimulating hormone (TSH), 10 μg/mL alpha-fetoprotein (AFP), 0.05 μg/mL testosterone, 0.005 μg/mL estradiol (E2), 3000 μg/mL plasminogen, the determination result was not higher than 0.3 nmol/L.
There is no hook effect when the concentration of SHBG reaches 1000 nmol/L, and the detection result is not affected by hook effect When the concentration reaches 49500 nmol/L.

【Analytical Performance】
Lower limits of measurement
Limit of Blank = 0.02 nmol/L
Limit of Detection = 0.3 nmol/L.
Accuracy
The relative deviation shall not exceed ±10%.
Linearity
The correlation coefficient is not less than 0.9900 in the interval of 0.3 ~ 200 nmol/L.
Within-run precision (repeatability)
The coefficient of variation (CV) is less than or equal to 8.0%.
Between-lot precision
The coefficient of variation (CV) is less than or equal to 10.0%.
Homogeneity of calibrators and control materials
Between-bottle homogeneity: The coefficient of variation (CV) is less than or equal to 10.0%.
Accuracy of calibrators
The supporting calibrators of the kit are tested, the relative deviation of test results is within ±10%.
Measured values of control materials
The measured results of supporting assigned quality control of the kit should be within the quality control range.
Method comparison
A comparison of the Lifotronic SHBG assay (y) with the Roche Elecsys SHBG (x) using clinical samples gave the following correlations:
Number of serum samples measured: 110
Linear regression:
y=1.0126x-1.7407
r = 0.998
The sample concentrations were between 4.76 and 189.8 nmol/L.

【Precaution and Warning】
The kit is only used for in vitro diagnostics.
Exercise the normal precautions required for handling all laboratory reagents.
All reagents and samples including specimen, reagents and calibrators should avoid foaming before and during test.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.
This product contains animal-sourced materials and may have potential biological risk. All samples and test wastes should be treated as the source of infection, and all wastes must be disposed according to local regulations.
Any serious incident that would be occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.
The preservative ProClin™300 which contain Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-Methyl-2H-isothiazol-3-one (3:1): May cause an allergic skin reaction. thus, proper personal protection should be adopt while handling the reagent: avoid breathing dust/fume/gas/mist/vapours/spray, wear protective gloves and contaminated work clothing should not be allowed out of the workplace. If skin irritation or rash occurs: get medical advice/attention, take off contaminated clothing and wash it before reuse, and dispose of contents/container to an approved waste disposal plant.

【Literature References】
1. Petra PH. The plasma sex steroid binding protein (SBP or SHBG). A critical review of recent developments on the structure, molecular biology and function. J Steroid Biochem Molec Biol. 1991;40:735-753.
2. Selby C. Sex hormone binding globulin: origin, function and clinical significance. Ann Clin Biochem. 1990;27: 532–541.
3. Munell F, Suarez-Quian C, Selva D, Tirado O, Reventos J. Androgen binding protein and reproduction: where do we stand? J of Andrology. 2002;23: 598–609.
4. Hammond GL, Bochinfuso WP. Sex hormone-binding globulin/androgen-binding protein: steroid-binding and dimerization domains. J Steroid Biochem Molec Biol. 1995;53:543-552. .
5. Bonnet F, Velayoudom Cephiset FL, Gautier A, et al. Role of sex steroids, intrahepatic far and liver enzymes in the association between SHBG and metabolic features. Clin Endocriol. 2013;79:517-522.
6. Hedderson MM, Xu F, Darbinian JA, et al. Prepregnancy SHBG Concentrations and Risk for Subsequently Developing Gestational Diabetes Mellitus. Diabetes Care. 2014;37(5):1296-1303.
7. Simó R, Sáez-López C, Barbosa-Desongles A, et al. Novel insights in SHBG regulation and clinical implications. Trends in Endocrinol Metab. 2015;26(7):376-383.

【Symbols Explanation】

Symbol	Title of Symbol	Symbol	Title of Symbol
	Manufacturer		Consult instructions for use
	Use-by date		In vitro diagnostic medical device
	Batch code		Sufficient for <n> tests
	Serial number		Biological risks
	Temperature limit		This way up
	Authorized representative in the European Community		Indicates this device is in compliance with Europe Directive.
	Catalogue number	P/N	Material code
	Warning		Date of manufacture
	Unique device identifier		

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