Instruction For Use

【Product Name】
IL-6 STAT (eCLIA)

【Order Information】

REF NO.	Package Size
0320510103	100T
0320510101	50T
0320510104	2×100T
0320510102	2×50T

【Intended Use】
Immunoassay for the in vitro quantitative determination of interleukin-6 (IL-6) in human serum and plasma.

Interleukin 6 is a cytokine with multiple biological effects. It is a single gene expression, containing 212 amino acid sequences, and the amino terminal is easily lysed to form a polypeptide of 184 amino acids, with a molecular weight of about 22-27Kda[1]. It is mainly produced by monocytes, endothelial cells, and lymphoid cells. It can act on a variety of target cells and has a wide range of biological activities, such as promoting proliferation and differentiation of β cells. PromoteStrial T cell growth and cytotoxic T cell differentiation. Promote hematopoietic stem cell production and growth together with IL-3, G-CSF, GM-CsF, etc.[2]. In 1898, studies reported that immune-responsive complexes with a molecular weight of about 60-70 KDa were found in the body fluids of patients with acute bacterial infections[3]. Interleukin 6 is mainly used to monitor the body's immune status, inflammatory response, etc. Serum levels of IL-6 are usually very small, but are elevated when there is acute or chronic inflammation, such as after surgery, sepsis, rheumatoid arthritis, or trauma. It is therefore widely used in clinical monitoring of acute and chronic inflammation1. In addition, continuous detection of IL-6 concentrations in intensive care patients can assess the severity of systemic inflammatory response syndrome (SIRS) [4-6].

【Test Principle】
Sandwich principle. Total duration of assay: 9 minutes.

30 µL of sample, biotinylated monoclonal IL-6 antibodies, and monoclonal IL-6 antibodies labeled with ruthenium complex react to 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 Component】
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/L; ProClin™300	2×1.8mL	1×1.8mL	1×3.5mL	2×3.5mL
(RB)	biotinylated monoclonal IL-6 antibodies: 1.0 mg/L; 25 mM EPPS, ProClin™300	2×3.0mL	1×3.0mL	1×6.0mL	2×6.0mL
(RA)	monoclonal IL-6 antibodies labeled with ruthenium: 2.0 mg/L; 25 mM EPPS, ProClin™300	2×3.0mL	1×3.0mL	1×6.0mL	2×6.0mL
Calibrators	IL-6 antigen; ProClin™300	High: 1×1.0 mL Low: 1×1.0 mL			
Control Materials (Optional)	IL-6 antigen; ProClin™300	High: 1×1.0 mL Low: 1×1.0 mL			

Traceability: This method can be traced to 1st International Standard for IL-6 from the National Institute for Biological Standards and Control (NIBSC) code 89/548.

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 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, eCL9600, eCL9900, eCL9900i:

- 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, o REF 0320510002, Assay Cup/Assay Tip, 1×6×105

【Storage and Shelf Life】
Store at 2℃-8℃.
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℃~8℃	18 months
Store at 2℃~8℃ after opening	8 weeks
Stored on the analyzers at 2℃~15℃	8 weeks

The calibrators are stable up to the stated expiration date.

Stability of the calibrators and control materials	
Unopened at 2℃~8℃	18 months
Store at 2℃~8℃ after opening	8 weeks

【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 EDTA-K2, EDTA-K3 and heparin lithium anticoagulant plasma are recommended. Blood 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 recommended. Samples would better to be tested in 5 hours after collection, otherwise, should be stable for 1 days at 2-8 ℃ or 3 months at -15℃ or lower than -15℃. Freezing and thawing cycle is permitted only once.
Ensure the samples, calibrators and control materials are at 18℃-28 ℃ prior to measurement.
Due to possible evaporation effects, samples, calibrators and control materials on the analyzers should be analyzed/measured within 2 hours.

【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 IL-6 STAT test according to the operational manual.
Put the IL-6 STAT rackpack into the correct analyzer slot to automatically suspend magnetic beads at least 30 minutes before testing.
Recommended ambient temperature:10~30°C; Relative humidity: ≤ 80%.

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) The Buffers of different lot are used.

Quality control
For quality control, use IL-6 STAT 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 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 pg/mL.

Specimen dilution

Samples with IL-6 concentrations above the detection range can be diluted with sample dilution. It is recommended to dilute at 1:10 (by instrumental automatic dilution or manual dilution). If diluted by hand, the result should be multiplied by the dilution multiple. If the instrument automatically dilutes, the instrument automatically calculates the result.

【Biological reference interval】

The upper limit of 95% reference interval are calculated to be 6.9 pg/mL by analyzing serum samples from 193 healthy people.

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】

Test results are used only for clinical reference and cannot be used as the basis for diagnosis or rule-out of diseases alone. For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

When the sample containing bilirubin ≤25mg/dL, triglyceride ≤1500mg/dL, biotin ≤30 ng/mL,total protein ≤10 g/dL, hemoglobin ≤1000 mg/dL or HAMA≤100ng/mL, interference deviation of concentration to the test result lies within ±10%. When the RF concentration in the sample is ≤1540 IU/mL, the relative recovery of the test result is between 90%-110%.

When the sample containing interleukin 1α ≤200ng/mL, IL-1β ≤200ng/mL, IL-2 ≤200ng/mL, IL-4 ≤200ng/mL, IL-8 ≤200ng/mL, TNF-α ≤200ng/mL, interferon γ≤200ng/mL, the cross-reaction rate was ≤0.01%. When the sample containing IL-3 ≤50ng/mL, the cross-reaction rate was ≤0.1%.

No high dose hook effect was observed when samples containing up to approximately 200000 pg/mL of IL-6 were assayed.

【Measuring Range】

The measuring range of the kit is 1.0~5000 pg/mL. For samples with IL-6 content below the lower detection limit, the results are reported as < 1.0 pg/mL; If the IL-6 content is above the upper detection limit, the results are reported as > 5000 pg/mL (1:10 diluted samples are reported at >50,000 pg/mL).

【Analytical Performance】

Lower limit of measurement

Limit of Blank = 1.0 pg/mL

Limit of Detection = 1.5 pg/mL.

Accuracy

The relative deviation shall not exceed ±10%.

Linearity

The correlation coefficient is not less than 0.9900 in the interval of 1.5~5000 pg/mL.

Within-run precision (repeatability)

The coefficient of variation (CV) is less than or equal to 6.0%.

Between-lot precision

The coefficient of variation (CV) is less than or equal to 10.0%.

Homogeneity of calibrators and control materials

Within-bottle homogeneity: The coefficient of variation (CV) is less than or equal to 6.0%.

Method comparison

A comparison of the Lifotronic IL-6 STAT assay (y) with the commercial IL-6 Method (x) using clinical samples gave the following correlations:
Number of serum samples measured: 117
Linear regression:
Y=0.9938X-1.9829
r=0.9985
The sample concentrations were between approx 2.474 and 4587 pg/mL.

【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, calibrators and control materials 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.

【Reference】

1. Song M, Kellum JA .Interleukin-6. Crit Care Mcd 2005; 33（Suppl2）:463-465. Kishimoto T, Hirano T. A New Interleukin with Pleiotropic Activities. BioEssaya 1988 Jul:9(1):11-15.
2. Helfgott DC, Tatter SB,Santhanam U, Clarick RH, Bhardwaj N, May LT, Sehgal PB. Multiplc Forms of IFN-β2/IL-6 in Serum and Body Fluids During Acute Bacterial Infection.J Immunol 1989;142:948-953.
3. Pinsky MR, Vincent IL, Alegre M, Dupont E. Serum Cytokine Levels in Human Septic Shock. Relation to Multiple-System Organ Failure and Mortality. Chest 1993;103:565-575.
4. Oda S, Hirasawa H, Shiga H, Nakanishi K, Matsuda K, Nakamura M, Sequential measurement of IL-6 blood levels in patients with systemic inflammatory respones syndrome (SIRS)/sepsis. Cytokine2005;29:169-175.
5. Damas P, Ledoux D, Nys M, Vrindts Y, De Groote D, Frangchimont P, Lamy M. Cytokine Serum Level During Severe Sepsis in Human IL-6 as a Marker of Severity. Ann Surg 1992; 215(4):356-362.

【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		

【Manufacturer】

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【Version and Revision】

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