Instruction for Use

【Product Name】

Squamous Cell Carcinoma (eCLIA)

【Order Information】

REF NO.	Package Size
0320501201	50T
0320501202	2×50T
0320501203	100T
0320501204	2×100T

【Intended Use】

Squamous Cell Carcinoma (eCLIA) is an immunoassay reagent for in vitro quantitative determination of Squamous Cell Carcinoma (SCC) in human serum and plasma by Automated ECL Analyzer to aid diagnosis of cervical cancer, non-small cell carcinoma.

【Summary】

Squamous cell carcinoma (SCC) is a malignant tumor of squamous epithelium. Squamous cell carcinoma antigen (SCCA) is a subfragment of TA-4. This protein is a kind of cancer antigen[1], and a glycoprotein with a molecular weight of 42 KDa[2]. Ta-4, obtained from SCC tissues of the cervix, is characterized as the glycoprotein with a molecular weight of 48 KDa and consists of at least 14 subfragments. SCCA exists in normal squamous epithelium and is massively produced in malignant proliferative squamous epithelium and released into the blood[3]. Elevated serum SCCA level has been found in malignant tumors such as cervical cancer, lung cancer, head and neck malignant tumors, esophageal cancer and anal cancer, and also in non-malignant skin diseases and renal failure[4].

Studies on squamous cell carcinoma have shown that in lung cancer and cervical cancer patients, the more advanced the cancer, the higher the level of SCCA. Continuous SCCA monitoring helps assess the recurrence of the disease, residual disease after treatment and therapeutic response[5, 6].

It is used for quantitative determination of SCC in human serum or plasma in vitro. For professionals use only.

【Principles of the testing method】

Sandwich principle. Total duration of assay: 9 minutes.

15 µL of sample, biotinylated SCC monoclonal antibody and the ruthenium (Ru) complex-labeled SCC monoclonal antibody form an antigen-antibody sandwich complex, which is bound to streptavidin coated magnetic particles, and then transferred to the measuring cell where the magnetic particles are captured onto the surface of the electrode, while the unbound substances are washed away. Chemiluminescence is generated after the electrode is electrified, and the generated optical signal is measured by a photomultiplier, processed by an instrument, and the concentration of SCC in the sample is calculated based on the calibration curve.

【Main Components】

The reagent pack consists of MB, RA, RB, calibrators and control materials (optional), and different components and reagents of lot numbers should ne be used interchangeably.

Components	Ingredients	Volume (50T)	Volume (2×50T)	Volume (100T)	Volume (2×100T)
MB	Streptavidin coated magnetic particles, 0.45 mg/mL; 0.1M phosphate-buffered saline (PBS); ProClin300	1×1.8mL	2×1.8mL	1×3.5mL	2×3.5mL
RB	Biotinylated SCC antibody, 1.0 mg/L; 0.1M phosphate-buffered saline (PBS); ProClin300	1×3.0mL	2×3.0mL	1×6.0mL	2×6.0mL
RA	Ru complex-labeled SCC antibody, 1.0 mg/L; 0.1M phosphate-buffered saline (PBS); ProClin300	1×3.5mL	2×3.5mL	1×7.0mL	2×7.0mL
Calibrators	SCC antigen, 0.1M phosphate-buffered saline (PBS); ProClin300	High: 1×1.0 mL Low: 1×1.0 mL			
Control Materials (Optional)	SCC antigen, 0.1M phosphate-buffered saline (PBS); ProClin300	High: 1×1.0 mL Low: 1×1.0 mL			

Traceability:This method can be traceable to Roche Elecsys SCC.

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:

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, 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, or REF 0320510002,

【Storage and Shelf Life】

Store at 2ºC~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.

Stability of the reagents	
Unopened store at 2ºC~8ºC	18 months
Store at 2ºC~8ºC after opening	8 weeks
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 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, preparation and storage】

It is recommended to use human serum samples or plasma samples collected with EDTA-K2, EDTA-K3, heparin lithium blood collection tubes.

Blood samples should be collected in accordance with the standard operation of venipuncture. After the sample is completely coagulated, centrifugation should be performed to remove residual cellular substances. The sample should be free of air bubbles during testing. Lipid layer covering the sample after centrifugation should be removed. It is not recommended to use hemolyzed samples.

Samples can be stored for 5 days at 18~28ºC, 14 days at 2~8°C, and 12 weeks at -15°C or below. Samples can be freeze-thawed only once.

【Testing Procedure】

Testing procedure and precautions

Before testing, the system operation manual of the measuring instrument should be carefully read, so as to obtain relevant information such as system operating procedures, sample management, safety precautions and maintenance, and materials required for testing should be prepared. SCC testing procedures should be called and set up in accordance with the system operating procedures.

Before using the reagent, put it into the analyzer 30 minutes in advance to automatically stir the magnetic bead particles and keep them in suspension.

Recommended environment temperature for testing: 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 Buffer of different lots are used.

Quality Control procedure

For quality control, use SCC 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 can automatically calculate the analyte concentration, with the result in ng/mL.

Specimen dilution

SCC concentration in the sample higher than the upper limit of detection can be diluted manually with sample diluent.

The recommended dilution ratio is 1:20. The results are reported by multiplying the measured values by the dilution ratio.

【Biological Reference Interval】

By analyzing the serum samples of 240 healthy population from hospitals, it was calculated that the upper limit of the reference range of 95% is 2.742 ng/mL.

Due to the differences in geography, race, gender and age, it is recommended that each laboratory determine the applicability of reference range through tests, and establish the reference range of this laboratory if necessary.

【Interpretation of results】

When interpreting the test results, it is necessary to refer to the patient's overall

corresponding data and information.

【Limitations】

Test results are used only for clinical reference and cannot be used alone as the basis for diagnosis or exclusion of cases.

The detection range of the kit is 0.03~70 ng/mL. If the SCC concentration in the sample is lower than the lower limit of detection, the result is reported as less than this value (for example, <0.03 ng/mL); if the SCC concentration in the sample is higher than the upper limit of detection, the result is reported as greater than this value (for example, >70 ng/mL), or the sample is manually diluted with sample diluent at the dilution ratio of 1:20, and the result is reported with the measured value multiplied by the dilution ratio.

When jaundice (bilirubin) is ≤20 mg/dL, hemolysis (hemoglobin) is ≤500 mg/dL, lipemia (triglyceride) is ≤1000 mg/dL, biotin is ≤35 ng/mL, total protein is ≤70 mg/mL, and HAMA is ≤90 ng/mL in the sample, the interference deviation of the measured results is within ±10%. When the concentration of rheumatoid factor in the sample is less than or equal to 1200 IU/mL, the relative recovery of the test results is between 90% and 110%.

Twenty-four kinds of drugs are added to the serum samples containing SCC to make interference samples, and the concentrations of drugs added are as follows: ascorbic acid (300 mg/L), cyclosporine (5 mg/L), methyldopa (20 mg/L), metronidazole (200 mg/L), butazodine (400 mg/L), acetylsalicylic acid (1000 mg/L), paracetamol (200 mg/L), ibuprofen (500 mg/L), theophylline (100 mg/L), 5-fluorouracil (900 mg/L), carboplatin (600 mg/L), cisplatin (180 mg/L), cyclophosphamide (500 mg/L), dexamethasone (20 mg/L), adriamycin (120 mg/L), erlotinib (150 mg/L), etoposide (300 mg/L), gefitinib (250 mg/L), gemcitabine (1500 mg/L), ifosfamide (7200 mg/L), methotrexate (150 mg/L), metoclopramide (7.5 mg/L), paclitaxel (265 mg/L), gentamicin sulfate (3 mg/L) and vinorelbine tartrate (53.1 mg/L), The SCC contents in the interference sample and the control sample (without drug addition) are measured respectively, and the relative deviation of the measured results is within ±10%.

When the SCC concentration reaches 2000 ng/mL, there is no high-dose hook effect; when the SCC concentration reaches 10000 ng/mL, the test results are not be affected by the hook effect.

【Analytical Performance】

Lower limit of measurement

Limit of Blank = 0.03 ng/mL.

Limit of Detection = 0.1 ng/mL.

Accuracy

Testing standard traceability of accuracy control products, the relative deviation of it's test results is within ±10%.

Linearity

Within the range of 0.1 ng/mL~70 ng/mL, the correlation coefficient (r) of the kit should not be less than 0.9900.

Within-run imprecision (repeatability)

The coefficient of variation (CV) ≤ 6%.

Between-lot imprecision

The coefficient of variation (CV) ≤ 10%.

Accuracy of calibrators

The supporting calibrators of the kit are tested, the relative deviation of their test results is within ±10%.

Measured values of quality control

The measured results of supporting assigned quality control of the kit should be within the quality control range.

Homogeneity of calibrator and quality control

Intra-vial homogeneity: Coefficient of variation (CV) ≤ 6%;
Inter-vial homogeneity: Coefficient of variation (CV) ≤ 10%.

Method comparison

A comparison of the Lifotronic SCC assay (y) with the Roche Elecsys SCC method (x) using clinical samples gave the following correlations:
Number of serum samples measured: 122
Linear regression:
Y=0.9802X+0.3315
r = 0.983
The sample concentrations were between 0.57 and 67.51 ng/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.

【References】

1. Kato H, Torigoe T. Radioimmunoassay for Tumor Antigen of Human Cervical Squamous Cell Carcinoma. Cancer 1977;40:1621-1628.
2. Kato H, Morioka H, Aramaki S, et al. Radioimmunoassay for Tumor-Antigen of Human Cervical Squamous Cell Carcinoma. Cell Mol Biol 1979;25:51-56.
3. Xu D, Wang D, Wang S, et al. Correlation between squamous cell carcinoma antigen level and the clinicopathological features of early-stage cervical squamous cell carcinoma and the predictive value of squamous cell carcinoma antigen combined with computed tomography scan for lymph node metastasis. Int J Gynecol Cancer 2017;27(9):1935-1942.
4. Salvatici M, Achilarre MT, Sandri MT, et al. Squamous cell carcinoma antigen (SCC-Ag) during follow-up of cervical cancer patients: role in the early diagnosis of recurrence. Gynecol Oncol 2016;142(1):115-119.
5. Henry RJW, Dodd JK, Tyler JPP, et al. SCC Tumor Marker and Its Relationship to Clinical Stage in Squamous Cervical Cancer. Aust NZl Obstet Gynaecol 1987;27:338-340.
6. Kenter G, Bonfrer JMG, Heintz APM. Pretreatment tumorantigen Ta-4 in serum of patients with squamous cell carcinoma of the uterine cervix. Br J Cancer 1987;56:157-158.

【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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