Instruction For Use

【Product Name】

BNP STAT (eCLIA)

【Order Information】

REF NO.	Package Size
0320509701	50T
0320509702	2×50T
0320509703	100T
0320509704	2×100T

【Intended Use】

Immunoassay for the in vitro quantitative determination of B-type natriuretic peptide (BNP) in human plasma. Determination of BNP is used for aid diagnosis of heart failure.

【Summary】

B-type natriuretic peptide (BNP) is an active polypeptide, when the cardiomyocytes are stimulated by the outside world, the alkaline amino acid protease is composed of 108 amino acid residues of brain natriuretic peptide precursor Pro-BNP, resulting in N-terminal brain natriuretic peptide precursor (NT-proBNP) containing 76 amino acid residues and BNP with 32 amino acid residues[1]. The functional domain of BNP is a circular structure of 17 amino acids consisting of two cysteines forming disulfide bonds[1]. Heart failure is an important clinical syndrome caused by factors such as coronary artery disease, hypertension, valvular disease, and myocarditis, mainly manifested by left ventricular systolic or diastolic dysfunction, or simultaneous systolic and diastolic dysfunction. According to the New York Heart Association classification (NYHA grades I to IV), heart failure can be divided into 4 grades according to clinical signs and symptoms, and the severity of the disease increases step by step[2]. Cardiac diuretic sodium peptides have a vasodilatory and diuretic effect[3],The half-life in vivo is about 23 minutes[4]. The cardiac diuretic natriuretic peptide system is excited to the highest level of activity in ventricular dysfunction and plays an important role in maintaining the compensatory period of asymptomatic heart failure and delaying the disease process, and studies have shown that BNP can be used for diagnosis, prognosis and treatment monitoring in patients with heart failure[5]. Clinically, it is mainly used for auxiliary diagnosis of heart failure.

【Test Principle】

Sandwich principle. Total duration of assay: 9 minutes.

45 µL of sample, biotinylated monoclonal BNP antibodies, and monoclonal BNP 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 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; 0.1M PBS, ProClin300	2×1.8 mL	1×1.8 mL	1×3.5 mL	2×3.5 mL
(RB)	biotinylated monoclonal BNP antibodies 1.0 mg/L; 0.1M PBS, ProClin300	2×3.0 mL	1×3.0 mL	1×6.0 mL	2×6.0 mL
(RA)	monoclonal BNP antibodies labeled with ruthenium 1.2 mg/L; 0.1M PBS, ProClin300	2×3.0 mL	1×3.0 mL	1×6.0 mL	2×6.0 mL
Calibrators	BNP antigen, lyophilized	High: 1×1.0 mL Low: 1×1.0 mL			
Control Materials (Optional)	BNP antigen, lyophilized	High: 1×2.0 mL Low: 1×2.0 mL			

Traceability: This method can be traced to manufacturer's selected measurement procedures.

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, eCL9600, eCL9900, eCL9900i:

- 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~8°C	18 months
Store at 2°C~8°C after opening	8 weeks
Stored on the analyzers at 2°C~15°C	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 2°C~8°C	18 months
Store at 2°C~8°C after reconstituted	7 days
Store at -15°C or lower than -15°C after reconstituted	3 months (freeze only once)

【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】

EDTA-K2, EDTA-K3 anticoagulant plasma samples collected using plastic collection tubes 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 can be stored for 4 hours at 18°C- 28 °C, 24 hours at 2°C- 8 °C, 3 months at -15°C or lower than -15°C. Freezing and thawing cycle is permitted only once.

Ensure the samples, calibrators and control materials are at 18°C-28 °C 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 BNP STAT test according to the operational manual.

Put the BNP STAT reagent pack 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%.

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 calibrators to the additional plastic bottles. After bottles is marked and dispensed. If you do not test immediately, you need to store the aliquots immediately at -15°C or lower than -15°C.

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 materials to the additional plastic bottles. After bottles is marked and dispensed. If you do not test immediately, you need to store the aliquots immediately at -15°C or lower than -15°C.

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 4 weeks;

(3) Quality control findings outside the defined limits.

(4) The Buffer of different lots are used.

Quality control

For quality control, use BNP 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 or pmol/L.Conversion factor: 1 pg/mL= 0.2887 pmol/L.

Specimen dilution

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】

Plasma samples from 1233 non-heart failure individuals (including 615 males and 618 females) were analyzed in the hospital. The population included healthy people and non-hospitalized patients with kidney disease (non-hemodialysis), hypertension, diabetes, and COPD. There were no statistically significant differences between BNP levels in non-hospitalized patients with kidney disease (non-hemodialysis), hypertension, diabetes, and COPD between apparently healthy individuals.

Reference Group - All:

	Age group					
	all	< 45 years old	45-54 years old	55-64 years old	65-74 years old	≥75 years old
Sample size(N)	1233	245	245	255	246	242
95th percentile (pg/mL)	135.2	85.09	87.31	119.1	160.1	254.2

Reference group - male:

	Age group					
	all	< 45 years old	45-54 years old	55-64 years old	65-74 years old	≥75 years old
Sample size(N)	615	125	120	127	122	121
95th percentile (pg/mL)	104.1	73.12	40.23	80.39	150.3	121.1

Reference group - female:

	Age group					
	all	< 45 years old	45-54 years old	55-64 years old	65-74 years old	≥75 years old
Sample size(N)	618	120	125	128	124	121
95th percentile (pg/mL)	150.1	88.62	110.4	155.2	160.3	266.2

According to literature studies, sensitivity and specificity are best when BNP has a threshold of 100 pg/mL for diagnosing heart failure[6].

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 ≤ 20 mg/dL, hemoglobin ≤ 500 mg/dL, triglyceride ≤ 3000 mg/dL, biotin ≤ 20 ng/mL, total protein ≤ 10 g/dL, HAMA ≤100 ng/mL, the interference deviation of the measured results is within ±10.0%.

When the concentration of rheumatoid factor in the sample ≤ 1500 IU/mL, the relative recovery of the test results is between 90% and 110%.

Samples containing 0.6 ng/mL of angiotensin I, 0.6 ng/mL of angiotensin II, 1.0 ng/mL of angiotensin III, 3.1 μg/mL atrial sodium peptide (ANP), 3.5 μg/mL N-terminal brain natriuretic peptide precursor (NT-proBNP), 2.2 μg/mL C-type natriuretic peptide (CNP), 50 ng/mL epinephrine are tested, and the BNP test results are ≤ 10 pg/mL.

When the BNP concentration reaches 100000 pg/mL, the test results are not be affected by the hook effect.

【Measuring Range】

The measuring range of the kit is 1～5000 pg/mL. If the BNP concentration in the sample is lower than the lower limit of detection, the result is reported as < 1 pg/mL; if the BNP concentration in the sample is higher than the upper limit of detection, the result is reported as > 5000 pg/mL (10x diluted sample is reported as > 50000 pg/mL).

【Analytical Performance】

Lower limit of measurement

Limit of Blank = 1 pg/mL

Limit of Detection = 10 pg/mL.

Accuracy

The relative deviation shall not exceed ±10%.

Linearity

The correlation coefficient is not less than 0.9900 in the interval of 10～5000 pg/mL.

Within-run precision (repeatability)

The coefficient of variation (CV) is less than or equal to 7.0%.

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:coefficient of variation (CV) ≤ 10.0%.

Method comparison

kit (x) using clinical samples gave the following correlations:

Number of plasma samples measured: 115

Linear regression:

y=1.0109x+4.7279

r = 0.9971

The sample concentrations were between 11.3 and 4789.7 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.

【Literature References】

1. A.G.SEMENOV, et a1. Processing of Pro-B-Type Natriuretic Pepti: Furin and Corin as Candidate onvertases. Clinical Chemistry, 2010, 56(7): 1 166—1 176.
2. Remme WJ, Swedberg K. Task Force Report: guidelines for the diagnosis and treatment of chronic heart failure. Eur Heart J. 2001;22:1527-60.
3. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. N Engl J Med. 1998;339:321-8.
4. Mair J, Hammerer-Lercher, Puschendorf B. The impact of cardiac natriuretic peptide determination on the diagnosis and management of heart failure. Clin Chem Lab Med. 2001;39:571-88.
5. Sagnella GA. Measurement and significance of circulating natriuretic peptides in cardiovascular disease. Clin Sci. 1998;95:519-29.
6. Maisel AS, Krishaswamy P, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med. 2002;347(3):161-67.

【Symbols Explanation】

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

【Manufacturer】

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【Version and Revision】

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