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Roche CARDIAC proBNP+

cobas®

N-terminal pro B-type natriuretic peptide

REF **05533643** 190 | Σ 10 | SYSTEM **cobas h** 232

English

Intended use

Immunoassay for the in vitro quantitative determination of NT-proBNP in heparinised venous blood for use with the **cobas h** 232 instrument.

The Roche CARDIAC proBNP+ test serves as an aid in the diagnosis of patients with suspected heart failure, in the monitoring of patients with compensated left ventricular dysfunction and in the risk stratification of patients with acute coronary syndromes.

Summary

NT-proBNP is a physiologically inactive fragment which is released when the active hormone BNP is cleaved from its precursor protein proBNP. Synthesis of the precursor protein in the cardiomyocytes is controlled by mechanical factors (dilatation of the ventricular wall) and neurohormonal factors (noradrenalin and angiotensin II). The secretion of NT-proBNP into the blood as a result of cleavage correlates directly with an increase in ventricular volume and ventricular pressure in heart failure. Consequently, when the concentration of NT-proBNP in the blood is low, cardiac dysfunction can be ruled out with high probability. Although the normal range for NT-proBNP is subject to gender and age-specific variability, a clinical cut-off of 125 pg/mL allows sufficient diagnostic accuracy. However, NT-proBNP values should always be interpreted in conjunction with the medical history, clinical findings and other diagnostic information (imaging methods and laboratory results).[1,2,3,4,5]

Test principle

The test contains one monoclonal and one polyclonal antibody against epitopes of the NT-proBNP molecule of which one is gold-labelled and the other biotinylated. The antibodies form a sandwich complex with the NT-proBNP in the blood. Following removal of erythrocytes from the sample, plasma passes through the detection zone in which the gold-labelled NT-proBNP sandwich complexes accumulate and the positive signal is displayed as a reddish line (the signal line). Excess gold-labelled antibodies accumulate along the control line, signalling that the test was valid. The intensity of the signal line increases in proportion to the NT-proBNP concentration.

The optical system of the instrument detects the two lines and measures the intensity of the signal line. The integrated software converts the signal intensity to a quantitative result and shows it in the display.

Reagents

One test contains:

Biotinylated polyclonal anti-NT-proBNP antibodies > 0.4 µg

Gold-labelled monoclonal anti-NT-proBNP antibodies > 0.1 µg

Buffer and non-reactive components > 2.0 mg

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

Storage and stability

Until the printed expiration date at 2-8 °C.

Up to 1 week at room temperature (15-25 °C).

The test can be used immediately after removal from the refrigerator.

The test must be used within 15 minutes once the pouch has been opened.

Sample stability: 8 hours at room temperature. Do not refrigerate or freeze sample.

Specimen collection and preparation

Use **heparinised** venous **whole blood** only.

Do not use other anticoagulants, capillary blood, serum or plasma, blood collection tubes containing EDTA, citrate, sodium fluoride or other additives.

The following heparin blood collection tubes have been tested: Sarstedt Monovette, Becton Dickinson Vacutainer, Becton Dickinson Vacutainer PST II, Greiner Vacuette, Terumo Venosafe. In the case of Sarstedt Monovettes, only tubes without separating gel are suitable.

No data is available for blood collection tubes supplied by other manufacturers. An influence on the test result in individual cases cannot be ruled out.

Sample volume: 150 µL

Materials provided

- REF 05533643190, Roche CARDIAC proBNP+ test
- 1 code chip

Materials required (but not provided)

- REF 11622889190, Roche CARDIAC Pipettes, 20 disposable syringes (150 µL)
- REF 04890493190, Roche CARDIAC Control proBNP (2 x 1 mL)
- REF 04880668190, Roche CARDIAC IQC
- REF 04901126190, **cobas h** 232 instrument (software version ≥ 01.04.01)
- REF 04901142190, **cobas h** 232 instrument with scanner (software version ≥ 01.04.01)

General laboratory equipment

Calibration

Each test strip lot of the Roche CARDIAC proBNP+ test is calibrated against the Elecsys proBNP test.

The instrument automatically reads in the lot-specific calibration data from the code chip, eliminating the need for calibration by the user.

Calibration has been performed so that the results obtained are comparable to those obtained using the Elecsys proBNP reference method with heparin plasma as the sample material.

Lot code

Every kit contains a lot-specific code chip. The instrument display prompts the user to insert the chip. To ensure that the code chip and test strip lot match, compare the lot number in the display with the number on the code chip. The code chip provides the instrument with all required lot-specific information. An error message is displayed if the wrong code chip is inserted for a test strip lot.

Quality control

For quality control, use Roche CARDIAC Control proBNP.

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.

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

Display of results

At the end of the reaction time, the **cobas h** 232 instrument shows the result in the display. The reaction time for the Roche CARDIAC proBNP+ test to display a quantitative result is 12 minutes. In addition, approximately 2 minutes are required for sample detection. Depending on the measured concentration, the result may be displayed in different ways.

NT-proBNP concentration	Result displayed
less than 60 pg/mL	proBNP < 60 pg/mL
between 60 pg/mL and 9000 pg/mL	for example "proBNP 2000 pg/mL"
greater than 9000 pg/mL	proBNP > 9000 pg/mL

When the measured concentration is significantly higher than 9000 pg/mL, the instrument displays "proBNP > 9000 pg/mL" after 5 minutes.

Limitations - interference

The assay is unaffected by icterus (bilirubin ≤ 30 mg/dL), hemolysis (Hb ≤ 178 mg/dL), lipemia (triglycerides ≤ 300 mg/dL), haematocrit values in the range of 30-50 %, and biotin ≤ 10 ng/mL.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 300 IU/mL.

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High concentrations of lipoic acid (e. g. in pharmaceuticals or as food additive) can lead to lower measurement values.

There is no high-dose hook effect at analyte concentrations up to 30000 pg/mL.

Very high concentrations of NT-proBNP (approx. > 25000 pg/mL) may cause the control line to fail to appear and the instrument may display an error message. In this case, determination must be carried out using another method, like the Elecsys proBNP test.

Patient samples may contain heterophilic antibodies which could react in immunoassays to give falsely elevated or decreased results. Reasons for the presence of heterophilic antibodies might be for example elevated levels of rheumatoid factors or the treatment of patients with monoclonal mouse antibodies for therapeutic or diagnostic purposes.

The Roche CARDIAC proBNP+ test contains ingredients that minimise interference from heterophilic antibodies. However, complete elimination of interference from all samples cannot be guaranteed.

Interferences caused by pharmaceuticals at therapeutic concentrations are not known.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Measuring range

60–9000 pg/mL.

Expected values

The circulating NT-proBNP concentration was determined using the Elecsys proBNP test in samples from 1981 blood donors aged between 18 and 65 as well as 283 elderly patients aged between 50 and 90. Both populations were without known cardiac risks, symptoms or medical history.

The descriptive statistics for NT-proBNP concentrations (pg/mL) in the reference group are shown in the following table:

All						
Age (years)	18-44	45-54	55-64	65-74	≥ 75	Total
N	1323	408	398	102	33	2264
Mean	35.6	49.3	72.6	107	211	50.3
SD	30.2	63.3	84.4	85.9	152	62.4
Median	20.4	30.7	47.3	85.1	174	27.9
95th percentile	97.3	121	198	285	526	149
97.5th percentile	115	172	263	349	738	196

Males						
Age (years)	18-44	45-54	55-64	65-74	≥ 75	Total
N	815	278	259	61	13	1426
Mean	27.7	39.0	57.2	105	163	39.8
SD	25.5	63.6	74.5	87.9	116	55.3
Median	20.0	21.6	37.7	83.9	151	20.0
95th percentile	62.9	83.9	161	241	486	113
97.5th percentile	85.8	121	210	376	486	169

Females						
Age (years)	18-44	45-54	55-64	65-74	≥ 75	Total
N	508	130	139	41	20	838
Mean	48.2	71.5	101	109	243	68.2
SD	32.8	56.7	94.0	83.8	167	69.3
Median	37.1	55.4	79.6	85.2	191	47.8
95th percentile	116	169	247	285	738	177
97.5th percentile	130	249	287	301	738	254

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the instruments are given below. Results obtained in individual laboratories may differ.

Precision

Repeatability was measured with 3 lots of the Roche CARDIAC proBNP+ test and heparinised human blood. The mean of the variation coefficients was below 15 % in the range of 60-1200 pg/mL, and below 20 % in the range of 1200-9000 pg/mL. Intermediate precision was measured with the Roche CARDIAC Control proBNP quality control in 6 different hospitals. When using concentration 1, the mean of the standard deviation was < 34 pg/mL. The mean of the variation coefficients for level 2 was below 20 %.

Method comparison

Comparison of 3 lots of the Roche CARDIAC proBNP+ test with the Elecsys proBNP test in a clinical patient population showed slopes between 0.80 and 1.20 in the majority of the method comparisons. The majority of the correlations in these method comparisons was ≥ 0.9.

References

1 Bayés-Genís A et al. N-terminal probrain natriuretic peptide (NT-proBNP) in the emergency diagnosis and in-hospital monitoring of patients with dyspnoea and ventricular dysfunction. Eur J Heart Fail 2004;6:301-308.

2 McDonagh TA et al. NT-proBNP and the diagnosis of heart failure: a pooled analysis of three European epidemiological studies. Eur J Heart Fail 2004;6:269-273.

3 Richards AM et al. Plasma N-terminal pro-brain natriuretic peptide and adrenomedullin: new neurohormonal predictors of left ventricular function and prognosis after myocardial infarction. Circulation 1998;97:1921-1929.

4 Svendstrup Nielsen L, et al. N-terminal pro-brain natriuretic peptide for discriminating between cardiac and non-cardiac dyspnoea. Eur J Heart Failure 2004;6:63-70.

5 Troughton RW, et al. Treatment of heart failure guided by plasma aminoterminal brain natriuretic peptide (N-BNP) concentrations. Lancet 2000;355:1126-1130.

For further information, please refer to the appropriate operator's manual for the instrument concerned, and the Method Sheets of all necessary components.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard.

SYSTEM	Analyzers/Instruments on which reagents can be used

CE

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
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Roche