

# NT-proBNP (amino-terminal prohormone B-type natriuretic peptide)

## Intended use

The measurement of NT-proBNP is intended as an aid in the diagnosis of persons suspected of having congestive heart failure. The test is further indicated for the risk stratification of patients with acute coronary syndrome and congestive heart failure.

## Summary

The amino-terminal fragment of the B-type natriuretic peptide prohormone (NT-proBNP) is a marker for functional cardiac impairment and is increased in heart disease with or without symptoms of heart failure (HF). BNP is a hormonally active natriuretic peptide that is mainly released from the cardiomyocytes in the left ventricular wall. In reaction to stretch and tension of the myocardial wall the prohormone proBNP splits into BNP and the hormonally inactive remnant amino-terminal proBNP (NT-proBNP) by proteolytic cleavage [1,2]. The half-life of NT-proBNP in circulation is around 120 minutes. The normal range for circulating NT-proBNP is below 100 pg/mL [3].

As a rule-out test for HF, NT-proBNP shows good diagnostic properties. In prognosis, NT-proBNP is a consistent independent predictor of mortality and other cardiac composite endpoints for populations with risk of stable coronary artery disease (CAD), diagnosed CAD and diagnosed HF [4].



## Product calibrator traceability

The calibration of the AQT90 FLEX NT-proBNP assay is traceable to in-house reference calibrators, which have been value-assigned to correlate with another commercially available assay.

## Samples

Blood samples are collected by venipuncture. Whole-blood or plasma samples with either EDTA or lithium heparin as anticoagulant can be used.

## Performance characteristics

### *Analytical specificity*

The analytical specificity of the AQT90 FLEX NT-proBNP assay was determined by studying the cross-reactivity with A-type natriuretic peptide, B-type natriuretic peptide and C-type natriuretic peptide at a concentration of 1,000 mg/L and proANP, NT-preproANP fragment (26-55) and NT-preproANP fragment (104-123) at a concentration of 10 mg/L. There was no detectable cross-reaction with A-type natriuretic peptide, B-type natriuretic peptide, C-type natriuretic peptide, proANP, NT-preproANP fragment (26-55) and NT-preproANP fragment (104-123).

### *Analytical sensitivity and measuring range*

The limit of detection has been determined to be 12 ng/L.

The reportable range of the assay is 12–35,000 ng/L.

### *Reference values*

Whole blood (lithium heparin and EDTA) and plasma (lithium heparin and EDTA) were obtained from 497 apparently healthy individuals (248 women and 249 men) and analyzed using the AQT90 FLEX NT-proBNP assay. The 95th percentile was determined to be 133 ng/L.

### *Imprecision*

Within-day and total imprecision was determined by analyzing plasma pools over 20 days, twice a day, two replicates per run.

| Within-run imprecision |       |       |        | Total imprecision |       |       |        |
|------------------------|-------|-------|--------|-------------------|-------|-------|--------|
| 32                     | 101   | 2,366 | 31,817 | 32                | 101   | 2,366 | 31,817 |
| ng/L                   | ng/L  | ng/L  | ng/L   | ng/L              | ng/L  | ng/L  | ng/L   |
| 12.7 %                 | 6.7 % | 2.3 % | 2.8 %  | 16.5 %            | 7.2 % | 3.7 % | 3.3 %  |

The concentration giving the CV of 10 % of the AQT90 FLEX NT-proBNP assay is approximately 73 ng/L.

### *Clinical sensitivity and specificity*

The concentrations of natriuretic peptides, BNP and NT-proBNP, have been shown to be markers for the diagnosis of congestive heart failure (CHF) in several studies. The levels of BNP and NT-proBNP concentrations are shown to increase in subjects with left ventricular dysfunction and correlate with the New York Heart Association (NYHA) classification of heart failure [5, 6, 7, 8, 9, 10, 11].

The recommended decision threshold value is 125 ng/L.

### *Hook effect*

No hook effect was found when NT-proBNP concentrations up to 500,000 ng/L were measured.

### *Carry-over*

Carry-over from a sample with high NT-proBNP value (100,000 ng/L) to an adjacent negative sample was determined to be <100 ppm.

### *Interfering substances*

Hemolytic, lipemic and icteric samples do not interfere with the assay.

The following interfering substances were tested (using plasma samples with 100 ng/L NT-proBNP) at concentrations about five times the upper therapeutic range and found to have no notable effect on the AQT90 FLEX CRP assay (interference <16 %):

Abciximab, acetaminophen, acetylsalicylic acid, allopurinol, ambroxol, ampicillin, ascorbic acid, atenolol, caffeine, captopril, cefoxitin, cinnarizine, cocaine, diclofenac, digoxin, dopamine, drythromycin, ethanol, low molecular weight heparin, sodium heparin, ibuprofen, levodopa, methyldopa, metronidazole, nicotine ( $\pm$ ), nifedipine, nitrofurantoin, nitroglycerin, nystatin, oxytetracycline, phenylbutazone, phenytoin, propranolol, quinidine, rifampicin, tetracycline, theophylline, trimethoprim, verapamil, warfarin.

The following interfering substances were found to have notable effect on the AQT90 FLEX NT-proBNP assay (interference <35 %): Acetylcysteine, cyclosporine, furosemide.

### *Method comparison*

The AQT90 FLEX NT-proBNP assay (y) was compared to the commercially available NT-proBNP assay proBNP for the Roche MODULAR ANALYTICS E170 immunoassay analyzer (x) using lithium-heparin plasma samples in the range of 14–34870 ng/L (with the AQT90 FLEX NT-proBNP assay).

The Passing-Bablok regression and correlation coefficient were found to be:

$$y = 1.008x - 8,196; R^2 = 0.981 (n = 104)$$

## References

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